A

CRITICAL INVESTIGATION

OF

METHODS OF PREPARING MONOHYDRIC PHENOLS

AND

DERIVATIVES THEREFROM.

by

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A thesis submitted
in fulfilment of the
requirements for the
degree of Doctor of
Philosophy of Glasgow
University.

March, 1934.

The author wishes to express his gratitude to the Late Professor Thomas Gray, Royal Technical College, for his advice and careful supervision of the initial portion of this work and to Professor F. J. Wilson, Royal Technical College, whose helpful suggestions and kindly criticisms have proved invaluable during the latter stages of this investigation.

The author also wishes to record his indebtedness to the Trustees of the Ferguson Bequest Fund for the award, and extension, of a Ferguson Fellowship in Applied Chemistry.

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Summary.

The work described in the following pages was initially intended as a sequel to Professor Gray's investigation of Scottish Shale Oil phenols and as a corollary to the work of my predecessor in the Ferguson Fellowship who investigated the antiseptic properties of mixtures of phenols from different sources.

When this work was commenced there was very little known about mono-hydric phenols other than the cresols and xylenols and the number of known derivatives of these phenols which might have been useful as a means of separation was small. Therefore, after having conducted some preliminary work on the phenols derived from Scottish Shale oil and having attempted to isolate individual members, it became evident that, without more definite information about the higher homologues of phenol, any attempted separation would be a complicated process, the success of which would be doubtful.

Accordingly the preparation of phenol homologues was undertaken. Phenols have been prepared by two general methods; from hydroxy-aldehydes and ketones and from amines. The main portion of the work has therefore been devoted to the preparation of the intermediates. Individual xylidines have been separated from a mixture, and o- and p-amino-ethyl benzene/

benzene have been prepared directly from ethyl benzene. Ring methylation of xylidines has been used to prepare mesidine and pseudo-cumidine. The hydroxy-ketones have been prepared by the Fries reaction. Certain abnormalities in this method have become apparent in the course of the present work but no fundamental investigation of the reaction mechanism has been attempted as the present intention was to prepare the hydroxy-ketones. Both Gattermann and Reimer-Tiemann synthesis of hydroxy-aldehydes have been conducted and it has been shown that the Gattermann reaction, which, until recently, has been considered to give exclusively p-hydroxy-aldehydes gives also o-substituted products. Thus from m-cresol all three theoretically possible hydroxy-aldehydes have been isolated. An inaccuracy in the published description of the anil of one of these hydroxy-aldehydes has also been indicated.

Both the hydroxy-aldehydes and ketones have been subjected to Clemmensen reduction and by this means the corresponding phenols have been obtained. The Clemmensen reduction has been shown to be ineffective in the case of m-hydroxy-acetophenone and, while it is felt that this is due to some extent to the orientation of the molecule and in particular to the o-p-directing properties of the hydroxyl group, these points have not been followed up as it was considered/

considered that such an investigation was outwith the scope of the present work. Thus m-substituted phenols which could have been prepared in a round about way from the corresponding p-substituted phenols are not included in the phenols here investigated.

Derivatives of the prepared phenols have been made and while a number of these derivatives were already known some of them, such as the p-nitro-benzoates, 3:5-dinitro-benzoates and phenoxy-acetate of the ethyl and ethyl-methyl phenols, have been described since this work was commenced. In other cases the derivatives are new. The value of the present work on these derivatives is considered to be the determination and comparison of the solubilities. The solubilities given, while only rough approximations, are sufficiently accurate to indicate any possibilities of easy means of separation by fractional crystallisation. The p-nitro-benzoates and 3:5-dinitro-benzoates have been shown to be useless as a means of separating mono-hydric phenols from a mixture. The phenoxy-acetates allow of a rough separation of o- and p-substituted phenols being made. By the use of phenoxy-acetates a reasonably complete separation of the cresols can be made but these derivatives are not so satisfactory for the separation of the higher homologues.

Part 1

Separation of Phenols from Scottish Shale Oil.

Very little work has been done on the phenols derived from shale oil chiefly because the quantity of phenols normally present in shale oils is small. The first systematic investigation of shale oil phenols was carried out by T. Gray (J.S.C.I., 1902, 21, 845) He extracted the phenols from the "green naphtha" fraction of Scottish shale Oil by means of caustic soda solution and decomposed the resulting phenate with mineral acid. The phenols were then fractionally distilled and the individual fractions were sulphonated and nitrated. The presence of phenol, o-and m-cresol was indicated by this means, and by bromination of the higher fractions 1:2-dimethyl-4-hydroxy- and 1:3-dimethyl-5-hydroxy-benzene were proved present. Nitration and bromination were found to be unsuitable as a means of identifying phenols above the xylenol fraction. More recently Kogermann (J.S.C.I., 1927, 46, 138T.) working on Estonian shale oil examined the phenols obtained from the fraction boiling between 230 and 270°C. The oil was fractionated and the percentage of phenols in each fraction was determined. The phenols were fractionated at 60mm. and the cresol content of the lower fractions was determined by the methods/

methods of Lederer and Raschig. Xylenols were identified as xylenoxy acetic acids and 1:4-dimethyl-5-hydroxy- and 1:2-dimethyl-4-hydroxy-benzene were identified. Indications of a trimethyl and a propyl phenol were also obtained. The presence of phenol ethers of the guaiacol type was indicated by the Zeisel test.

Phenols from Low Temperature Tar and other Sources.

Phenols, chiefly those from Low Temperature Tar have attracted considerable attention within recent years and a great number of papers have appeared on this subject. No attempt has been made to give a complete survey of all the work done in this field as this has already been summarised, in the case of Low Temperature Tar, by E. Parrish (History of Low Temperature Tar, Fuel, 1926, 5,436-465) The earliest work of note is that of Béhal and Choay, (Compt. rend. 118,1339-43;119, 166-69;)who,in a thorough investigation of phenols from beech wood and oak tar, identified individual phenols by conversion to the corresponding benzoates. They thus were able to show the presence of phenol, the three cresols, an ethylphenol, 1:3-dimethyl-4-hydroxy- and 1:3-dimethyl-5-hydroxy-benzene, guaiacol, creosol and ethyl guaiacol. Von Boyen, (Zeits, angew, chim.1892,675: Ber.15,1893), separated individual phenols by sulphonation followed by fractional crystall-

-isation of the sodium salts of the sulphonic acids. He also used nitro derivatives as a means of identification (J.C.S.I., 875,1902). Recent work is, however, of much more interest. Gluud and Breuer (Ges.Abhandl. zur Kenntnis der Kohle, 1917,2, 236-56) working on the Phenols from Low Temperature Tar used phenoxy-acetates as a means of identification. They showed that in the tar there is a trace of catechol, no methylated polyhydroxy phenols or phenol itself, while all three cresols, most of the xylenols and some trimethyl phenols were present. Catechol was found in the liquor occuring with the tar. Marcusson and Picard (Mitt. Material-prünfungsant, 39, 329-34, 1921 A.C.A. 1922, 4329., attempted the separation of lignite and generator tar phenols by means of preferential solvation. They digested the tars with petroleum ether and filtered off about 2% insoluble matter. The remainder was treated with sodium hydroxide solution and the uncombined material was extracted with ether. The residue in sodium hydroxide solution was separated into hydroxy-acids, fatty acids and phenols. A similar method was used by Gluud and Breuer (Ges. Abhandl.zur Kenntnis der Kohle 1918, ii,236) Weindel (Brennstoff/chemie, 3, 245-9, 1922) separated phenols from Low Temperature Tar and carefully fractionated. The carbon and hydrogen content of each fraction was determined and compared with those of known phenols of similar boiling range. In this way the presence of unsaturated and polyhydric phenols was suspected and suggested as a reason for the low hydrogen content of some of the fractions. Fromm and Echard (Ber., 56, 1, 948, 1923.) identified phenols by the formation and crystallisation of phenylurethanes. R. Avenarius (Zeits. für. angew. chem., 36, 165-8, 1923.) separated, from lignite tar, phenol the three cresols, 1:4-dimethyl-5-hydroxy-, 1:3-dimethyl-4-hydroxy- and 1:2-dimethyl-4-hydroxy-benzene as carbamic and allophanic esters. Maihle (J. usines gaz, 49, 268, 1925.) from the same type of tar isolated the same phenols as phenylurethanes. Weindel (Brennstoff chem., 6, 217-21, 234-8, 1925.) separated the phenols from Low Temperature Tar into what he has called "e" and "ne" phenols. The "e" phenols are soluble in phenate liquor from which they can be extracted with ether or benzene. The "ne" phenols, on the other hand, are not extractable from alkaline solution by ether or benzene. Edwards (J.S.C.I., 43, 143 T. 1924.) has worked on similar lines to Weindel and has separated Low Temperature Tar phenols into true homologues of phenol and what he has termed "rhetinols". These "rhetinols" were/

were obtained by steam distilling the tar, dissolving the steam residue in benzene and separating the benzene insoluble material ('Ulmins') and then extracting the benzene solution with sodium hydroxide solution. The phenols obtained were mixed with those obtained from the steam distillate. The total phenols were then dissolved in petroleum ether. Petroleum ether insoluble material separated and was dissolved in ether. This treatment resulted in the precipitation of 'ulmins' and the ether solution contained 'rhetinols'. These 'rhetinols' always contain 'ulmins' from which they cannot be completely separated. 'Rhetinols' are soluble in sodium hydroxide solution and on distillation they decompose into water, true homologues of phenol, aromatic hydrocarbons and pitchy residues. 'Ulmins' are bodies which are soluble in many tar products especially phenols and phenate liquors. They are insoluble in caustic alkali and ether but are soluble in pyridine. Edwards' work also showed the presence of traces of pyro-catechol and α - and β -naphthol in Low Temperature Tar phenols.

Brittain, Rowe and Sinnatt (Fuel in Science & Practice, 4, 263-9, 299-307, 1925) also isolated bodies from Low Temperature Tar similar to Edwards' 'rhetinols' /

'rhetinols' and 'ulmins'. They separated the true homologues of phenol into the low boiling phenols; phenol, the cresols and xylenols, and high boiling less acidic bodies by treatment with hot milk of lime. Phenol was estimated by the freezing point method and m-cresol by Raschig's nitration method (Zeits. angew. chem., 31, 795, 1900). From the higher boiling fraction catechol was isolated by lead acetate and obtained in the free state by decomposition of the lead compound by hydrogen sulphide. By fusion of the higher boiling fractions with phthalic anhydride and anhydrous zinc chloride indications were obtained which pointed to the presence of resorcinol. Similar methods were used by Parrish and Rowe (J.S.C.I., 1926, 45, 99 T.) who determined the phenol content of the lower fractions by the method of Fischer and Breuer (Ges. abh. Kennt. Kohle, 3, 82, 1918) which utilises the greater acidity of phenol as a means of separation. The less acidic phenols are fractionally precipitated from phenate solution by addition of mineral acid in small quantities at a time. Pyro-catechol was also shown to be present by these workers. J.J.Morgan and Soule (Chem. and Met. Eng., 26, 20, 923, 977-81, 1922) showed the presence of naphthol derivatives in Low Temperature Tar though naphthol/

naphthol itself was absent. Steinkopf and Höpner (J. pr. chem, 113, 137-58, 1926) studied the phenols obtained from producer tar from Bohemian brown coal. After fractionation the phenol in the low boiling fractions was estimated by the freezing point method and identified positively as the benzoate. The presence of o-,m-, and p-cresol was shown by the formation and separation of the corresponding phenoxyacetates. m-Cresoxy-acetate could not be obtained in a state of complete purity. 1:3-dimethyl-5-hydroxy-benzene was identified as the tribromide and phenoxyacetate, and was isolated, in an almost pure state, by the separation of its sodium salt from a concentrated alkaline solution. Formation of the phenylurethane also proved the presence of this xylenol and after the removal of this phenol, as indicated above, 1:2-dimethyl-3-hydroxy-benzene was separated as phenylurethane. The higher fractions, after distillation under reduced pressure, were converted to phenoxyacetates and p-ethyl phenol was separated as the barium salt of its phenoxyacetate and 1:2-dimethyl-3-hydroxy-benzene as the silver salt.

Story and Snow (Ind. and Eng. Chem., 20, 4, 359, 1928) examined the phenols from straight-run- and cracked petroleum distillates. The phenols were extracted/

extracted in the usual way and fractionated. The average formula weights were determined for each fraction by the method of Morgan and Meighan (Ind. and Eng. Chem., 18, 354, 1927) who collected the hydrogen evolved from a known weight of phenol fraction by the action of metallic sodium. Phenol and m-and p-cresol were detected and the latter two isolated as phenylurethanes. Phenylurethanes were prepared from the xylenol fractions but these derivatives were not obtained in a crystalline form.

Brown & Branting (Ind. and Eng. Chem., 20, 392, 1928) examined phenols from low temperature carbonisation of Utah coal by a method essentially the same as that of Brittain, Rowe, and Sinnatt, (Loc. cit.). As phenoxyacetates, o-,m-,and p-cresol, 1:2-dimethyl-4-, and 1:3-dimethyl-5-hydroxy-benzene were isolated and phenol itself was identified as the tribromo derivative.

G.T. Morgan (J.S.C.I., 47, 131 T, 1928) in conducting a chemical study of Low Temperature Tar used methods which avoided any chance of thermal decomposition. The phenols were extracted by sodium hydroxide solution from an ether solution of the tar which had previously been heated to 120°C. to remove light oil. This phenate dissolved amorphous non-phenolic bodies

and/

and it was found that if the ether solution was extracted with sodium hydroxide solution, saturated with brine, then the non-phenolic substances were not dissolved in the phenate. The phenols obtained from this phenate were further separated into 'resinols' and crystallisable phenols by treatment with petroleum ether which precipitates the 'resinols'. Details were not given of the identification of individual phenols.

Brüchner (Zeits. für angew. chem., 37, 1043; 41, 1062, 1928) has conducted extensive experiments on the separation of phenols by the formation of sulphonic acids and subsequent decomposition. He found that sulphonic acids from different phenols decomposed at different temperatures and gives the decomposition temperature range for the sulphonic acids of phenol, the cresols, xylenols and ethyl phenols. This method has been applied to the separation of phenols from high temperature tar and the individual phenols have been identified as phenoxyacetates. The presence has thus been shown of phenol, the three cresols, 1:2-dimethyl-4- 1:3-dimethyl-4- and 1:3-dimethyl-5-hydroxy benzene in high temperature tar.

von Hessert (Zeits. angew. chem., 43, 771-774, 1930) first oxidised all unstable bodies by passing air through/

through the warm phenate solution obtained from the extraction of brown coal tar with sodium hydroxide solution. The phenols obtained from this phenate were stable and could be distilled up to 260°C at atmospheric pressure without decomposition. Individual fractions were converted to potassium aryl sulphates by treatment, in concentrated alkaline solution, with potassium pyrosulphate (Baumann, Ann., 148, 1878). These esters were oxidised by alkaline potassium permanganate and the recovered hydroxy-acids were separated and identified. In this way the presence of o-,m- and p-cresol, all the xylenols, and m-and p-ethyl phenol was shown. No trimethyl phenols were identified but naphthols were present in the higher boiling fractions.

Holzmann and von Pilat (Brennstoff chem., <u>11</u>, 409-13, 1930) separated phenols from Polish petroleum. The crude material was treated with superheated steam and the phenols were separated from the distillate. Phenol and the cresols were found in solution in the aqueous portion of the steam distillate and were identified as phenoxyacetates. The main bulk of the phenols was fractionally distilled and the individual fractions were converted to phenoxyacetates. In this manner the three cresols and 1:2-dimethyl-4-, 1:4-dimethyl-5-, and 1:3-dimethyl/

-dimethyl-4-hydroxy-benzene were proved present. Brüchner's sulphonation method was tried and was found to be unsatisfactory with a mixture of phenols. 1:3-Diemthyl-5-hydroxy-benzene was separated as its sodium salt and 1:3-dimethyl-4-hydroxy-benzene was isolated by utilising the insolubility of the potassium salt of its sulphonic acid in potassium chloride solution. The presence of trimethyl phenols was indicated and β -naphthol was isolated. No phenols containing long side chains or methoxy groups were present.

Krüber and Schmitt (Ber., 64, B, 2270-77, 1931) used, in their studies on coal tar phenols, methods very similar to those employed by Brüchner (loc. cit.). The presence of m-and p-ethyl phenol has been shown while 1:3-dimethyl-5-, 1:2-dimethyl-4-hydroxy-benzene, Iso-pseudo-cumenol and 3-methyl-5-methyl phenol have also been found present in fractions boiling below 240°C. 2:3:5:6-Tetra-methyl phenol was found to accompany indole in fractions boiling above 240°C.

Experimental Work.

Shale Oil Phenols.

The phenols used in this investigation were supplied by the Scottish Oils Ltd. and still contained about 40% hydrocarbon oils. The initial work, which was an endeavour to determine the best method of removing the hydrocarbons, was carried out on a small sample of these phenols. The mixed phenol-hydrocarbon oil was found to be completely soluble in alcohol and ether, partly soluble in petroleum ether, while glacial acetic acid precipitated a little wax. In order to remove carboxylic acids the oil was washed with 8% sodium carbonate solution and the phenols were extracted by washing three times with an equal volume of 10% sodium hydroxide solution. In this washing it was found that emulsion formation was troublesome but if the oil and the sodium hydroxide solution was first heated to between 50 and 60oC. a clear separation was made possible. The phenate thus obtained was washed with benzene and the last traces of benzene were removed by steam distillation. From this phenate solution the phenols were liberated by addition of a slight excess of dilute sulphuric acid. Distillation under atmospheric pressure gave the following boiling range. The total weight of phenols distilled was 83.6 grams. These phenols were/

were heated to 120°C and freed from water. The phenols which distilled with the water were separated and added to the main bulk. The weight, 83.6 grams, given above refers to dry phenols.

Temperature °C.	Percentage by Weight.
190-215	12.7
215-225	14.9
225-235	13.4
235-245	16.5
245-255	5.4
255-265	4.0
265-320	15.7
Residue	17.3
Loss	2.1

In the initial stages of distillation hydrogen sulphide was given off and the first fractions had a distinct smell of sulphur.dioxide. The fractions were at first colourless but on standing they turned through yellow to red. Slight decomposition took place during the distillation and the residue in the flask had the appearance of a very soft pitch.

Another portion of the phenols obtained in exactly the same way was treated with different solvents in/

in an attempt to separate by preferential solvation. Phenols were dissolved in five times their own volume of ordinary ether and allowed to stand for some time. A small amount of a dark brown solid, representing less than 1% of the total phenols, separated. This solid was partially soluble in dilute sodium hydroxide solution, the insoluble portion being found to be soluble in phenol and pyridine. This alkali in-soluble solid seems to be similar to the 'Ulmins' of Marcusson and Edwards.

The ether solution of the phenols was distilled on a water bath to remove the ether. The last fraction from the ether distillation contained a small amount of a red oil which contained sulphur and was apparently volatile in the ether as it distilled by heating on a boiling water bath. The exact nature of this substance was not determined. The ether-free phenols were then dissolved in a large excess of petroleum ether and allowed to stand for two days. A black solid separated on the sides of the vessel but further dilution by petroleum ether did not cause any further precipitation. The black solid was partially soluble in dilute sodium hydroxide and the alkali insoluble portion was insoluble in ordinary ether. This black solid therefore appears to be a mixture of 'rhetinols' or 'resinols' and 'Ulmins'. The amount of 'rhetinols' obtained from the shale oil phenols investigated was very small.

An attempt was made to separate the phenols by hot milk of lime. This method removes the more acidic phenols as water soluble calcium salts. With the phenols under consideration this method proved unsatisfactory since the amount of phenols removed as calcium salts was very small and the residue was a highly viscous mass due to contamination with suspended calcium hydroxide.

The method of Burke and Caplan (Ind. and Eng. Chem., 1927, 19, 34) for the removal of polyhydric phenols was tried. This method consists in treating the phenols with a solution of borax when any polyhydric phenols react with the boric acid to form comparatively highly ionised complexes which, being acidic in character, form sodium salts with the alkali from the borax. No polyhydric phenols were obtained in this manner.

Fractional precipitation of the phenols from a phenate solution by the addition of acid was tried. 50 cc. of the phenols were dissolved in 100 cc. of 10% sodium hydroxide solution. Successive quantities of 10% sulphuric acid were added and the phenate was extracted with ether after the addition of each quantity of acid. The first additions of acid precipitated only a very small quantity while the latter portions liberated practically all the phenols. Thus it is evident that fractional precipitation by acid is not of much value in this/case.

Separation on a Larger Scale.

The phenol-hydrocarbon mixture was cooled in an ice-chest and the separated solids, waxes, were filtered off. 4,200cc. of this filtered oil were treated by the scheme outlined on page 20. This page can be extended and the scheme may be read in conjunction with the description.

The phenate liquor, (A), was extracted twice with benzene and the hydrocarbons obtained were added to the main bulk of neutral oil. On steam distillation a milky distillate (B), was obtained which on standing separated a red oil. This distillate reduced a solution of silver nitrate in the cold and with ferric chloride solution gave a green colouration. When treated with a solution of lead acetate it gave a white precipitate. The steam distillate was washed with benzene and the benzene extract was treated first with 10% sodium hydroxide solution and then with 20% sulphuric acid. In this way a small amount of both acidic and basic substances were obtained. The sodium hydroxide extract was decomposed with acetic acid, and lead acetate was added to the acidic layer after separation of the liberated phenols. A bulky white precipitate of a lead organic compound was obtained. Some/

Some of this substance was treated with hot dilute hydrochloric acid and a few globules of oil separated but appeared to dissolve on further heating. Hydrogen sulphide was passed through this solution and the precipitated lead sulphide filtered off. Traces of hydrogen sulphide were removed by reducing the pressure and, with addition of ferric chloride to this solution, a green colouration was obtained. The foregoing facts point to the presence of dihydric phenols with the hydroxyl groups in the ortho position to one another. The phenols which were separated by the addition of acetic acid did not give a precipitate with lead acetate but gave a red colouration with ferric chloride.

The phenate, (C), after steam distillation was filtered and found to contain a small amount of brown solid. This solid was only very slightly soluble in sodium hydroxide solution and in ether. The ether soluble portion was found to be soluble in sodium hydroxide solution and on acidification of the alkaline solution was precipitated as a light brown coloured solid. This filtered solid thus appears to be a mixture of 'Ulmins' and 'rhetinols'. The phenate solution before steam distillation contained substances other than hydrocarbons extractable with benzene. These substances appear to be partly/

partly non-phenolic bodies in solution in the phenate and partly due to hydrolysis of the sodium salts of the less acidic phenols. Extraction of such substances by benzene at this stage was considered to be unsatisfactory as this extraction would not be complete unless the washing with benzene was carried out for a long time. Therefore the benzene extracts were washed with sodium hydroxide and the phenate thus obtained was added to the main bulk.

To remove the carboxylic acids from the separated phenols it was found necessary to dissolve in benzene as direct washing of the phenols with sodium carbonate solution resulted in the formation of very troublesome emulsions.

From this treatment the following results were obtained :-

Oil treated	4,200cc.
Hydrocarbons	2,025cc.
Phenols	1,830cc.
Carboxylic acids	15cc.
Loss	330cc.

The crude phenols thus obtained had specific gravity 25/25 1.06

These phenols were distilled under pressure of 10mm. and the following fractions collected :-

Fraction 1	90° - 140°C.	522.0gms.	55.4%
Fraction 2	140° - 170°C.	138.8gms.	14.8%
Fraction 3	170° - 200°C.	132.5gms.	14.0%
Residue	above 200°C.	138.5gms.	14.8%
Total phenols distilled		942.0gms.	
Loss			1.0%

Fraction 1 Light yellow liquid which darkened in colour on standing. Sp.Gr. 25/25 1.023. From consideration of the previous distillation at atmospheric pressure this fraction probably boils at ordinary pressure between 190° and 230°C.

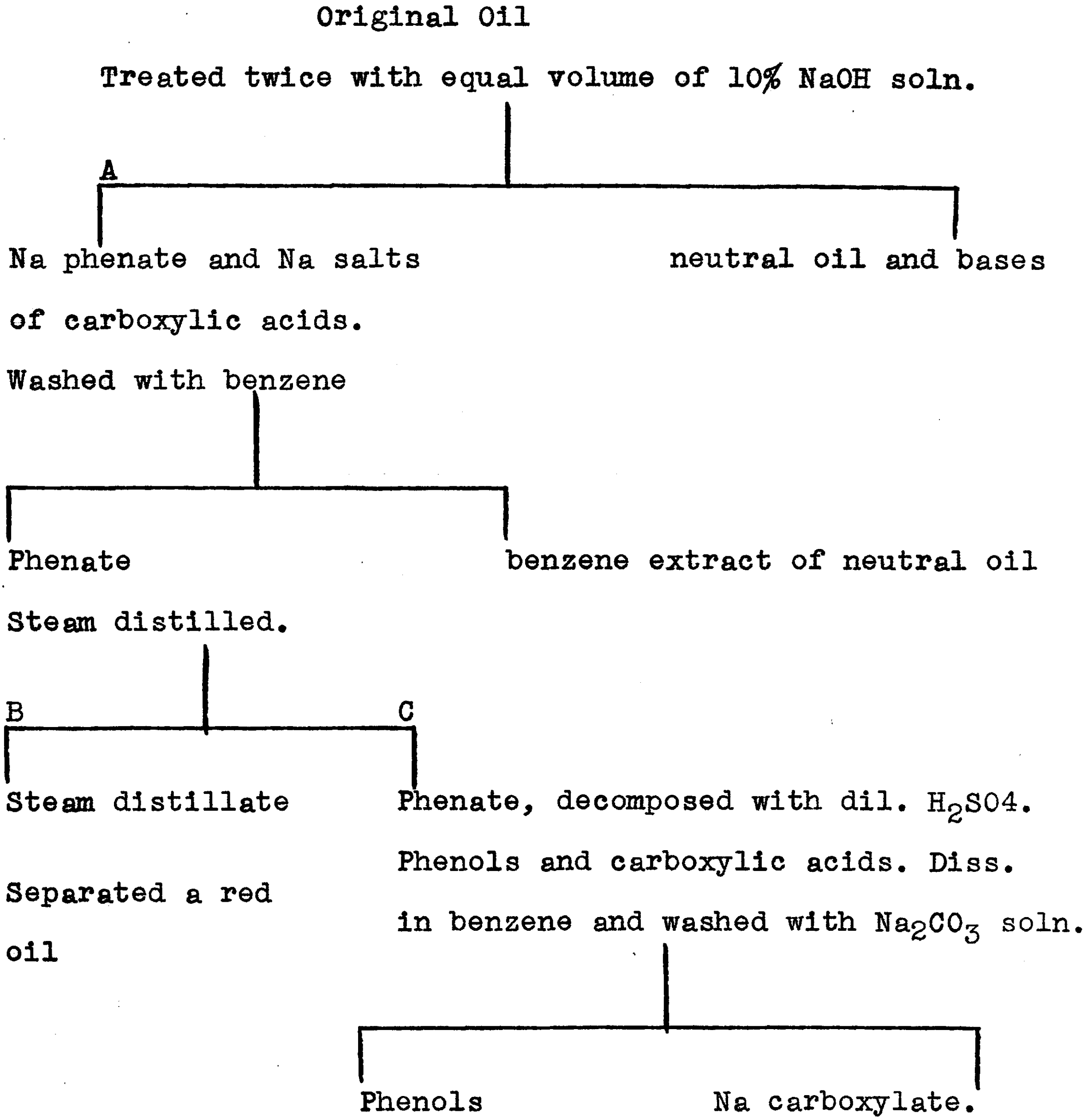
Fraction 2 This fraction was darker in colour than 1 and was more viscous. Sp. Gr. 25/25 1.042.

Fraction 3 Was red in colour and very viscous. Sp.Gr.25/25 1.078.

Residue This was a black brittle pitch like solid. It was partly soluble in sodium hydroxide solution and completely soluble in benzene, alcohol, and ether but was practically insoluble in petroleum ether.

Fraction 1 was refractionated using a plain fractionating column with twelve constrictions in it. The rate of distillation was regulated at approximately 1 drop per second.

EXTRACTION CHART FOR PHENOLS


Original Oil
Treated twice with equal volume of 10% NaOH soln.
A
Na phenate and Na salts of carboxylic acids.
Washed with benzene
neutral oil and bases
Phenate
Steam distilled.
benzene extract of neutral oil
B
C
Steam distillate
Separated a red oil
Phenate, decomposed with dil. H_2SO4.
Phenols and carboxylic acids. Diss. in benzene and washed with Na_2CO_3 soln.
Phenols
Na carboxylate.

Fractionation 1

522gms. phenols B.P. 90-140°C. (10mm.).

No.	Temp.	Wt. gms.	% on total phenols (942 gms.)	Sp.Gr. 25/25
1	-205	34.6	3.7	1.046
2	205-210	56.2	6.0	1.025
3	210-215	111.5	11.9	1.020
4	215-220	61.9	6.6	1.016
5	220-225	64.4	6.8	1.012
6	225-230	47.8	5.0	1.010
7	230-235	22.0	2.3	1.010
8	235-240	20.6	2.2	1.012
	above 240	74.8	7.9	1.037

Column 3 gives the weight of each fraction obtained and column 4 gives the percentage on the total amount of phenols used (942gms.). The specific gravities were determined by means of a pyknometer.

The first fractions were colourless when distilled but on standing they became pink, the first two turning distinctly red. The higher fractions were slightly yellow in colour/

colour and the residue was reddish brown. Hydrogen sulphide was evolved in the early stages of the distillation and at 240°C. decomposition took place and the distillation was stopped. It will be noted that there is a fall in specific gravity up to fraction 235-240°C. This is probably due, according to Edwards, (loc.cit), to the presence of alkylated phenols with increasing length of side chain.

Fractionation 11

Fractions 1 to 4 (up to 220°C.) from fractionation 1 were distilled in the same way as in the previous fractionation.

No.	Temp.°C.	Wt.Gms.	% on total phenols (942gms.)
1	-200	15.1	1.6
2	200-205	51-4	5.5
3	205-210	68.5	7.3
4	210-215	38.2	4.0
5	215-220	40.6	4.3
	above-220	30.5	3.2

These fractions were of the same nature as the first fractions in the previous distillation.

Fractionation 111

Fractions 5 to 8 (220-240°C.) of the first fractionation were mixed with the residue above 220 from fractionation 11.

No.	Temp. °C.	Wt. Gms.	% on total phenols 942 gms.
1	-220	39.6	4.2
2	220-235	107.0	11.3
	above 235	27.9	3.0

Fractionation 1V

The phenols distilled in this fractionation were the high boiling fractions, 140-170°C. 170-200°C. (10mm.) from distillation 1 together with the residues, above 235°C. from fractionations 1 and 111. This distillation was conducted at a pressure of 8mm. and no fractionating column was used.

Temp. °C.	Wt. Gms.	% on total phenols 942 gms.
up to 140	45.0	3.8
above 140	283.9	30.0

Fractionation V

Phenols used were those obtained in fractionation 11 boiling up to 220°C.

No	Temp. °C.	Wt. Gms.	% on total phenols 942 gms.
1	-200	51.0	5.4
2	200-205	57.7	6.0
	Residue	99.4	10.1

Both fractions were water white on distillation but on standing showed tendency to turn pink.

Fractionation VI

Residue from fractionation V, above 205°C. was added to fraction 1 up to 220°C. from fractionation 111. Distillation/

Distillation was carried out at atmospheric pressure using the same column as in previous cases.

No.	Temp.°C.	Wt.Gms.	% on total phenols 942 gms.
1	-200	7.4	0.8
2	200-205	52.3	5.6
3	205-210	31.1	3.3
4	210-215	27.6	2.9
	Residue	18.1	1.9

The lower fractions turned pink on standing.

Fractionation VII

Fraction 2 (220-235°C.) from fractionation 111, residue from VI, above 215°C. and fraction 1, up to 140°C. 8mm., from IV were mixed and distilled as previously.

No.	Temp.°C.	Wt.gms.	% on total phenols 942 gms.
1	-205	7.2	0.8
2	205-210	7.2	0.8
3	210-215	32.0	3.4
4	215-220	26.0	2.8
5	220-225	25.3	2.7
	above 225	58.8	6.2

The lower fractions were again pink and hydrogen sulphide was given off.

Fractionation VIII

In this a Dufton column, 12 inches long, was used. Phenols comprising fractions 1 and 2 from VI, up to 205°C, 1 and 2 from V, up to 205°C. and fraction 1 from VII, up to 205°C, were distilled.

No.	Temp.°C.	Wt.Gms.	% on total phenols 942 gms.
1	-185	0.8	-
2	185-190	2.0	0.2
3	190-195	40.9	4.3
4	195-197	36.3	3.9
5	197-201	19.8	2.1
	Residue	71.7	7.6

The first fraction was chiefly water with some unknown substance with an exceedingly disagreeable smell.

Fractionation IX

Phenols, comprising fraction 3 from VI (205-210°C.) 3,4, and 5 from VII (210-225°C.) and the residue from VII, above 201°C. were refractionated.

Table given overleaf.

Fractionation IX

No.	Temp. °C.	Wt. Gms.	% on total phenols (942 gms)
1	201-205	4.0	0.4
2	205-210	50.1	5.3
3	210-212	48.9	5.2
4	212-217	33.8	3.6
5	217-220	16.3	1.7
	Residue	28.6	3.0

Fractionation X

Phenols distilling up to 201°C. from VIII redistilled.

No	Temp. °C.	Wt. Gms.	% on total phenols (942 gms)
1	185-190	3.4	0.3
2	190-195	39.5	4.2
3	195-197	20.3	2.1
4	197-200	15.7	1.7
	Residue	19.1	2.0

Fractionation XI

Phenols: residue from X, above 200°C. and fractions up to 220°C. from IX.

No.	Temp. °C.	Wt. Gms.	% on total phenols (942 gms.)
1	200-205	17.5	1.9
2	205-207	40.0	4.2
3	207-210	34.8	3.7
4	210-212	38.9	4.1
	Residue	45.5	4.8

Fractionation XII

Phenols; residue from XI, IX, and VII and fraction 4 (210-215°C.) from VI.

No.	Temp. °C.	Wt. gms.	% on total phenols (942 gms.)
1	212-217	26.9	2.9
2	217-220	31.7	3.4
3	220-225	35.7	3.8
4	225-230	17.4	1.8
5	230-235	20.0	2.1
	Residue	24.7	2.6

Complete Fractionation

No.	Temp.°C.	Wt.Gms.	% on total phenols 942 gms.	Amt.in gms. per degree.
1	185-190	3.4	0.3	0.07
2	190-195	39.5	4.2	0.8
3	195-197	20.3	2.1	10.2
4	197-200	15.7	1.7	5.2
5	200-205	17.5	1.9	3.5
6	205-207	40.0	4.2	20.0
7	207-210	34.8	3.7	11.6
8	210-212	38.9	4.1	19-5
9	212-217	26.9	2.9	5.4
10	217-220	31.7	3.4	10.5
11	220-225	35.7	3.8	7.1
12	225-230	17.4	1.8	3.5
13	230-235	20.0	2.1	4.0
	above 235	24.7	2.6	---

Total phenols from fractionation	366.5 gms.
Weight of high boiling residue from IV	283.9 gms.
Residue from distillation I	138.5 gms.
Loss (942-788.9 gms.)	153.1 gms.
Percentage loss	16.3

Separation of Individual Phenols.

Attempts were made to isolate individual phenols by the formation and separation of derivatives which could by hydrolysed with the regeneration of the phenol. The derivatives used were phenoxyacetates and p-nitro-benzoates.

Fraction 1 B.P. 185-190°C.

This fraction consisted of only 3.4 gms. so it was set aside until more definite information was available regarding the higher fractions.

Fraction 2 B.P. 190-195°C.

Part of this fraction was dissolved in a slight excess of 25% sodium hydroxide solution and the requisite amount of mono-chloracetic acid was added. The whole was heated under reflux condenser for three hours and on cooling the liquid was acidified with dilute sulphuric acid. A white solid, which turned pink on standing, was thus obtained. This was crystallised from hot water and the more insoluble portions were recrystallised from benzene. o-Cresoxy-acetic acid, m.p. 152°C. (mixed m.p. 153.5°C; pure m.p. 154°C.) was isolated and by a long series of recrystallisations from water and benzene a solid fraction, m.p. 95-99°C, was obtained. The smallmess of this fraction prevented further purification. Mixed m.p. with phenoxyacetic acid (m.p.98°C.) 92°C. and with m-cresoxy-acetic acid (m.p.103°C.) 93-95°C. From this evidence/

evidence the substance was concluded to be a mixture of phenoxyacetic acid and m-cresoxy-acetic acid.

Fraction 3 B.P. 195-197°C.

Some of this fraction was converted into phenoxyacetic acids in the manner already indicated. These derivatives were separated into two main portions by allowing the solution of the sodium salts to stand for some time. The sodium salts which separated, (B), were filtered off and the liquor acidified with dilute sulphuric acid to give solids (A). (A) was crystallised from benzene and gave ortho-cresoxy-acetic acid, m.p. and mixed m.p. 152-153°C. Pure o-cresoxy acetic acid melts at 153°C. From (B) the free acids were liberated and on recrystallisation from water and benzene gave more o-cresoxy acetic acid. After prolonged crystallisation from water a derivative, m.p.100-102°C, was obtained. Mixed m.p. 98-101°C. with pure m-cresoxy acetic acid (m.p. 103°C.) showed that it was not quite pure but seemed to be evidence of the presence of m-cresol.

Fraction 4 B.P.197-200°C.

Phenoxyacetates were again formed and on allowing the solution of the sodium salts to stand no solids separated. Crystallisation of the free acids from hot water and benzene gave a fraction m.p. 150°C (o-cresoxy-acetic acid). Other fractions/

fractions melting about 100°C. were obtained but though these undoubtedly contained m-cresoxy-acetic acid a pure sample of this substance could not be isolated. A fraction, m.p. 97-103°C, was recrystallised from petroleum ether (b.p. 60-80°C.) and melted at 98-103°C; mixed m.p. with pure m-cresoxy-acetic acid, (m.p. 103°C.), 103°C. Further crystallisation from petroleum ether of solids melting below 100°C. gave a small amount of substance, m.p. 70-75°C, which may be phenoxyacetate of m-ethyl phenol, m.p. 76°C. A pure sample of this latter substance was not available in order to test by mixed melting point.

Fraction 5 B.P.200-205°C.

Phenoxyacetates were formed in the usual manner and separated by crystallisation from water and benzene. o-Cresoxy-acetic acid, (m.p.150-151°C.) was isolated and a small amount of a derivative melting at about 160°C. was also obtained. This may possibly have been 1:2:4-xylenoxy acetic acid, m.p. 162.5°C. m-Cresoxy acetic acid was again isolated but still could not be obtained in a pure state. Small amounts of derivatives melting about 70°C. were also obtained.

Work on the phenoxyacetates was stopped at this stage and p-nitro-benzoates were used in an endeavour to find a more suitable method for the isolation of m-cresol.

p-Nitro-Benzoates.

Fraction 2. B.P.190-195°C.

Part of this fraction was dissolved in three times its weight of dry pyridine and a slight excess of p-nitro-benzoyl chloride dissolved in pyridine was added. After standing overnight solid separated, was filtered and washed with dilute sulphuric acid to remove pyridine and an oil, which soon solidified, was obtained. This was fractionally crystallised from alcohol but no pure derivatives corresponding to phenol or any of the cresols were obtained. A crystalline compound, m.p. 43-44°C, separated but did not correspond in melting point to any known p-nitro-benzoate. Analysis gave nitrogen 5.40%. Calculated for p-nitro-benzoate of cresol nitrogen 5.45%, and for ethyl phenol 5.20%. This derivative was hydrolysed by boiling with 50% hydrochloric acid and the hydrolysis product boiled at 204°C. (press. 743mm.). On benzoylation and crystallisation from alcohol a derivative melting at 39 °C. was isolated. o-Ethyl phenol benzoate melts at 39°C. but the p-nitro-benzoate of this phenol melts at 56-57°C. The benzoate obtained from the hydrolysis product gave indications of the presence of another substance but the quantity was too small for further investigation.

Fraction 3. B.P. 195-197°C.

p-Nitro-benzoates of this fraction were formed in the same way and were recrystallised from alcohol. The results were similar to those from the previous fraction.

Owing to the unsatisfactory nature of the results so far obtained it became evident that some method of effecting a preliminary separation before formation of crystallisable derivatives was desirable.

Sulphonic Acids.

Brüchner (Zeits. f. angew. chem., 41, 1062, 1928) has devised a method which depends on a difference in the temperature of decomposition by steam of sulphonic acids of different phenols. Below is given a table of decomposition temperatures as determined by Brüchner.

Compound	Decomp.Temp.°C.
1-hydroxy-benzene-4-sulphonic acid	123-126
1-methyl-2-hydroxy-benzene-5-sulphonic acid	133-136
1-methyl-3-hydroxy-benzene-6-sulphonic acid	116-119
1-methyl-4-hydroxy-benzene-3-sulphonic acid	133-136
1:2-dimethyl-3-hydroxy-benzene-6- do. do.	115-118
1:2-dimethyl-4-hydroxy-benzene-5- do. do.	107-111
1:3-dimethyl-2-hydroxy-benzene-5- do. do.	124-128
1:3-dimethyl-4-hydroxy-benzene-5- do. do.	121-125
1:3-dimethyl-5-hydroxy-benzene-4- do. do.	105
1:4-dimethyl-2-hydroxy-benzene-5- do. do.	115-118
1-ethyl-2-hydroxy-benzene-5-sulphonic acid	105
1-ethyl-3-hydroxy-benzene-6-sulphonic acid	125-130
1-ethyl-4-hydroxy-benzene-3-sulphonic acid	105

Before such a scheme could be applied larger quantities of individual fractions were required and more phenols were therefore extracted.

It has already been shown that the amount of carboxylic acids present in the phenols under investigation was small so no attempt was made to separate them in this case.

10,000 cc. crude phenolic oil, Sp.Gr. 25/25 0.97, were washed, in quantities of 500 cc, with an equal volume of 10% sodium hydroxide solution at a temperature between 50 and 60°C. The once washed oil was again treated in the same way and the phenate solutions were combined. The phenols were liberated from the phenate solution by acidification with 20% sulphuric acid. In this way 5,000 gms. of phenols were obtained. These were then distilled, in quantities of 700 to 800 gms, under a pressure of 3 mm.of mercury. The following fractions were collected.

Fraction 1	75-130°C.	2,272 gms.	45.4%
Residue	above 130°C.	2,475 gms.	49.5%
Water		184 gms.	
Distillation loss		49 gms.	

The water which came over was separated from small amounts of phenols which accompanied it and these were returned/

returned to the distillation flask. The lower fraction was red in colour and was fairly mobile while the residue was dark brown and viscous.

Fraction 1,B.P. 75-130°C. (10mm.), was redistilled at atmospheric pressure in an atmosphere of nitrogen. A four pear Young distillation column was used and the distillation rate was regulated at approximately 1 drop per second.

No.	Temp.°C.	Wt.Gms.	% on Fr.	% on total
0	-180	18.5	0.8	0.4
1	180-190	47.3	2.1	1.0
2	190-195	237.5	10.7	4.9
3	195-200	162.8	7.4	3.4
4	200-203	137-0	6.2	2.9
5	203-207	188.1	8.5	4.0
6	207-210	178.8	8.1	3.8
7	210-215	176.8	8.0	3.7
8	215-218	195.5	8.8	4.1
9	218-220	74.0	3.4	1.6
10	220-224	189.2	8.6	4.0
	Residue	574.0	26.0	12.1

Total phenols distilled	2,210 gms.
Total phenols collected	2,190 gms.
Distillation Loss	20 gms.

Fraction No. 0 contained water and a clear phenolic layer which turned red on standing. Other fractions were of the same general character as those previously obtained, the lower ones turning red on standing the higher ones yellow.

Before attempting to identify the phenols in the fractions thus obtained Brüchner's sulphonation method was used to separate a known mixture of cresols.

10 gms.each of o- and m-cresol were mixed with 30 gms. of concentrated sulphuric acid and heated for 1 hour at 103°C. The mixture was cooled and diluted to 500cc. with 10% sulphuric acid. A small amount of resinous material was formed and filtered off. This liquid boiled at 106°C. and a slow current of steam was passed through it. When the temperature rose to 114°C. a milky steam distillate appeared and was collected till temperature reached 120°C. A second steam distillate was collected from 120-133°C. A third distillate was taken between 133 and 140°C. All distillates were extracted with ether, ether extract dried with anhydrous sodium sulphate and ether distilled.

Fraction 1.	114-120°C.	7.45 gms.
Fraction 2.	120-133°C.	1.50 gms.
Fraction 3.	133-140°C.	6.10 gms.

Fraction 1 should consist entirely of m-cresol. This was/

was estimated by Rashig's nitration method. The entire fraction was heated with 11.5 gms. of concentrated sulphuric acid for 1 hour in a steam oven. On cooling the mixture was transferred to a litre flask and 60cc. conc.nitric acid added. The flask was shaken for thirty seconds and the contents were poured into 30cc.of water, the flask being washed out with another 30cc. 8.00 gms. of pale yellow trinitro-m-cresol, m.p. 103-106°C., were obtained. 1 gm. m-cresol gives 1.74 gm. trinitro derivative. 8.00 gm. corresponds to approximately 4.6 gm. m-cresol.

Fraction 3. Part of this fraction was brominated in glacial acetic acid and, on recrystallisation, the resulting bromo compound was shown to be 4:6-dibromo-o-cresol. This fraction consists almost completely of o-cresol while the intermediate fraction 2 appears to be a mixture of o- and m-cresol.

Another mixture consisting of 5 gms. each of phenol and o-cresol and 11 gms. m-cresol was treated in the same way. The steam distillate coming over between 115 and 120°C. consisted of 10.3 gms. of phenol and m-cresol. 6.0 gms. distilled between 130 and 145°C. This was almost pure o-cresol; crude dibromide, m.p. 49-54°C,,recrystallised once from alcohol melted at 56.5-57°C. (4:6 Dibromo-o-cresol m.p. 57°C.

The intermediate fraction 120-130°C., 3.0 gms. was not investigated.

This sulphonation method was applied to fractions 1, 2, 3 and 4 obtained from the last distillation of phenols but so much resinification occured during sulphonation and steam distillation and the amounts of steam distillates were so small that the method was abandoned as unsatisfactory.

After the failure of the sulphonation method attempts were again made to identify phenols in the individual fractions by the formation of derivatives.

Fraction 0.

1 gram of this fraction was dissolved in glacial acetic acid and bromine in glacial acetic acid added. After standing overnight the liquid was largely diluted with water and an oil and whitish precipitate separated. The white solid was filtered off and on crystallisation from alcohol melted at 92°C. This corresponds to tribromophenol, m.p. 94°C.

Another part of this fraction was converted into phenoxy-acetates by heating gently under reflux condenser with the requisite amount of powdered sodium hydroxide and mono-chloracetic acid. A vigorous reaction which was complete in about 2 minutes took place. From the phenoxy-acetates thus formed no definite derivatives were isolated on crystallisation from water and benzene.

Benzoylation by the Schotten-Baumann method of another portion of the fraction resulted in the formation of a liquid derivative.

Fraction 1 B.P. 180-190°C.

Phenoxyacetates were formed as in the case of the previous fraction and crystallised first from water and then from benzene. o-Cresoxy acetic acid (pure M.P.153°C), m.p. 150°C. was isolated and a small quantity of impure m-cresoxy acetic acid, m.p. 97-99°C, mixed m.p. with m-cresoxy acetic acid (m.p. 103°C), 92-94°C, was also obtained. This substance when mixed with pure phenoxy-acetic acid, (m.p. 98°C.), melted below 80°C.

Another portion was brominated in glacial acetic acid and a solid bromo-derivative which on crystallisation from dilute alcohol melted at 53-57°C. This was identified as 4:6-dibromo-o-cresol, m.p. 57°C.

Raschig's nitration method for the estimation of m-cresol was applied but the nitration product was liquid.

Fraction 2. B.P. 190-195°C.

A part of this fraction was nitrated in the usual manner by sulphonation with an equal volume of concentrated sulphuric acid in a steam oven; dilution with half volume of water was followed by addition of concentrated nitric acid.

a sticky mass was obtained and was dissolved in alcohol. The separated solid from the alcohol crystallisation was dissolved in petroleum ether (b.p. 60-80°C.) and gave crystals melting at 84-86°C. 4:6-Dinitro-o-cresol melts at 86°C.

Phenoxyacetates were formed and after a prolonged fractional crystallisation from water, benzene and petroleum ether (b.p. 60-80°C.) indications were obtained of o-cresol (impure o-cresoxy acetate, m.p. 148-150°C. m.p. with o-cresoxy acetate (m.p. 153°C.) 152°C.), m-cresol (impure m-cresoxy acetate, m.p. 93-99°C. mixed m.p. with m-cresoxy acetate, (m.p. 103°C.) 95-100°C.) and a derivative, m.p. 74-76°C. which might possibly be m-ethyl phenoxyacetate (pure, m.p.76°C.).

Attempts to estimate m-cresol by Raschig's method gave only sticky non-crystalline material.

Fraction 3. B.P. 195-200°C.

Phenoxyacetates were formed but no individual derivatives were separated. Raschig's method again resulted in the formation of sticky material.

Solid phenoxyacetates have been formed from the higher fractions but so far no attempt has been made to separate them.

A little work was done on the higher boiling phenols.

Fraction above 130°C. (3mm.)

A portion of this fraction was dissolved in a slight excess of 5% sodium hydroxide solution and extracted continuously with ether in a Haggemann apparatus. The ether removed 63% of this fraction from solution in 5% sodium hydroxide. This ether extract was a highly viscous oil and probably consists of the less acidic phenols and bodies held in solution by the phenate. The sodium salts still left in solution after the ether extraction were treated with saturated brine solution. A brown solid was precipitated. Treatment of the phenate with brine solution previous to ether extraction gave a black viscous liquid which could not be filtered or otherwise satisfactorily separated from the bulk of the phenate.

Part 2.

Examination of Methods of Preparing Monohydric Phenols.

A review of the literature showed that there were only two general methods of preparing phenols which could be expected to give reasonable yields.

These methods are :-

(1) Preparation from the corresponding amines by diazotisation.

(2) Preparation from the corresponding hydroxy-aldehydes and ketones by the reduction of the carbonyl to the methyl and methylene groups respectively.

Since the production of phenols from amines and hydroxy-aldehydes and ketones is a relatively simple process most of the work done in this section has been concerned with the preparation of what may be called the final starting materials, the amines and the hydroxy-aldehydes and ketones. It is therefore proposed to deal with these substances under two headings :-

(a) Preparation and Separation of Amines.

(b) Preparation of Hydroxy-Aldehydes and Ketones.

Section (a).

This section will be further sub-divided into

(1) Separation of Xylidines.

(2) Preparation of Amines by Ring Methylation.

(3) Preparation of Amino-Ethyl Benzenes.

(1)

As phenol and the three cresols can be obtained commercially in a pure state there seemed no point in considering the preparation of these phenols from aniline and the toluidines. Attention was therefore first directed to the separation of the xylidines. Samples of technical ortho, meta, and para, xylidine were subjected to standard methods of separation. These methods have been used to show that technical xylidine contains all the isomeric xylidines with the exception of 3:5-dimethyl-1-amino-benzene.

Technical meta-Xylidine.

Technical meta-xylidine was treated with glacial acetic acid and the acetate of 1:3-dimethyl-4-amino-benzene was separated without any difficulty. (Birnhoff, Ber., 1887, 20, 871; D.R.P. 39947.). The xylidine thus obtained was positively identified by conversion to the formyl derivative. A small amount of the formyl derivative of 1:4-dimethyl-2-amino-benzene was obtained but there was no evidence of the presence of 1:3-dimethyl-2-amino-benzene.

Technical para-Xylidine.

Technical para-xylidine was treated according to the method of Hodgkinson and Limpach (J.C.S., 1900, 65). Failure to separate any solid acetate showed the absence of any considerable amount of 1:3-dimethyl-4-amino-benzene and subsequent/

subsequent conversion of the bases to hydrochlorides resulted in the separation of the greater part of the para-xylidine. This base was identified as its formyl derivative and by converting the residual bases from the hydrochloric acid treatment to formyl derivatives and fractionally crystallising from alcohol a further separation was effected. In this way the presence of 1:3-dimethyl-2-amino and 1:3-dimethyl-4-amino-benzene was shown.

Technical Ortho-Xylidine.

(1) Modified Method of Hodgkinson and Limpach (Loc.cit.)

The separation of technical ortho xylidine proved much more troublesome and various methods of separation were tried. The first of these was a modification of the method of Hodgkinson and Limpach (loc.cit.). These authors make provision for the separation of 1:3-dimethyl 2-amino, 1:2-dimethyl-4-amino- and 1:2-dimethyl-3-amino-benzene after the removal of 1:3-dimethyl-4-amino- and 1:4-dimethyl-2-amino-benzene in the usual way. The bases are then converted to hydrochlorides and from the mixture the hydrochloride of 1:3-dimethyl-2-amino-benzene can be sublimed. The two ortho xylidines which remain can be separated by taking advantage of a difference in the rate of crystallisation of the formyl derivatives. This method/

method was rejected as it seemed that considerable decomposition might take place during the separation by sublimation. Accordingly, a modified method was adopted. (Busch, Ber., 1899, 32, 1008; Noyes, A.C.J., 1898, 20, 791; Morgan and Hickinbottom, J. S. C. I., 1926, 45, 221 T; Brüchner, Zeits. für. Ang. chim., 1928, 41, 34, 955,). The acetate (1:3:4), hydrochloride (1:4:2), were separated as previously and the residual bases were converted to sulphates. A solid sulphate was obtained and since according to Noelting and Pick (Ber., 1888, 21, 3151) the sulphate of 1:3-dimethyl-2-amino-benzene is more soluble in water than the sulphates of 1:2-dimethyl-3-amino- or 1:2-dimethyl-4-amino-benzene, a separation should have been possible. A partial separation was obtained but was by no means complete since it was only after a long fractional crystallisation of the formyl derivatives obtained from the soluble sulphate that a small amount of pure derivative of 1:3-dimethyl-2-amino-benzene was isolated. The bases from the insoluble sulphate should have consisted mainly of the two ortho xylidines but on conversion to formyl derivatives and subsequent crystallisation from alcohol the only derivative which was obtained in a solid form was the formyl derivative of p-xylidine.

(2) Method of Morgan and Hickinbottom. (J. S. C. I., 1926,

(2) Method of Morgan and Hickinbottom. J.S.C.I., 1926, 45, 221 T.).

In this method the preliminary separation is carried out in the usual manner with concentrated hydrochloric acid and glacial acetic acid. The acetic acid treatment was applied first and the bases liberated from the acetate liquor were converted into sulphates. The crude sulphate which separated was converted through the free base into the hydrochloride. This separated p-xylidine. The bases from the sulphate liquor were converted to picrates by heating with picric acid in alcohol solution. The picrate of 1:2-dimethyl-4-amino-benzene was separated. The residual bases were converted to sulphates and fractionally crystallised and 1:3-dimethyl-2-amino-benzene which gives an easily soluble sulphate was obtained.

Morgan's method has been followed closely in this present work and 1:3-dimethyl-4-amino-, 1:4-dimethyl-2-amino-, and 1:2-dimethyl-4-amino-benzene have been separated as acetate, hydrochloride and picrate respectively. A slight modification in the published method was introduced after removal of the solid picrate, as the bases, after crystallisation of the sulphates, were converted to formyl and benzoyl derivatives. The picrate obtained melted at 220°C. as described in the literature but decomposition/

decomposition at the melting point took place. This picrate was decomposed and the base liberated by warming with aqueous ammonia. The bases were extracted with benzene and after drying the benzene was distilled. Before the base started to distil a small amount of a yellow liquid boiling below 200°C. was obtained and the evolution of hydrogen sulphide was detected. The presence of this impurity in the picrate probably accounts for the slight decomposition at the melting point but the small amount of this substance obtained prevented its being investigated further. The bases left after the removal of the xylidines indicated above were converted to sulphates and crystallised from water. Formyl derivatives were prepared from the insoluble and soluble sulphates. The derivatives from the insoluble sulphate could not be obtained in a solid form and were converted to benzoyl derivatives. The only derivative separated by this means was the benzoyl derivative of 1:3-dimethyl-2-amino-benzene. The formyl derivative from the soluble sulphate was solid but melted at 145-155°C. (the formyl derivative of 1:3-dimethyl-2-amino-benzene melts at 164-165°C. Hodgkinson and Limpach, (loc.cit.),). This formyl derivative on crystallisation from alcohol melted at 162-163°C.

(3) Preliminary Separation of Secondary and Tertiary Bases.

The presence of a sulphur containing material noted above and the possibility of secondary bases interfering with the isolation of pure formyl derivatives in the latter stages of the separation prompted an attempt to remove these substances initially. Secondary and tertiary bases were removed by the zinc chloride method of Morgan (E.P. 102, 834, 1916.) This depends on the formation of sparingly soluble additive compounds of the primary aromatic bases and zinc chloride of the general formula B_2ZnCl_2. These complexes are formed by the addition of a 50% aqueous solution of zinc chloride to the mixed bases and the uncombined secondary and tertiary bases are extracted from the solid product with petroleum ether. The primary bases so obtained were treated in the same manner as in the previous section. 1:3-dimethyl-4-amino-, and 1:4-dimethyl-2-amino-benzene were separated as acetate and hydrochloride respectively and the residual bases were further separated into soluble and insoluble sulphates. The bases from the soluble sulphates were converted to formyl derivatives but even after two months in an ice chest these derivatives remained liquid. The formyl derivative was hydrolysed and the bases reconverted to sulphate and by concentrating and cooling the sulphate liquor/

liquor more solid sulphate separated. The bases from the liquor were acetylated and the melting point of the acetyl derivative showed that they were not pure. An attempt was made to separate, from these bases, 1:3-dimethyl-2-amino-benzene as zincichloride (E. P. 328, 418.)-. A small amount of zincichloride was separated and from this almost pure 1:3-dimethyl-2-amino-benzene was recovered. The method was not satisfactory as difficulty was experienced in getting the correct conditions for crystallisation of the zincichloride. From the more insoluble sulphate 1:2-dimethyl-4-amino-benzene was separated as picrate. The residue from the picrate formation gave bases which were distilled under reduced pressure. During the latter part of the distillation hydrogen sulphide was evolved and decomposition with liberation of water finally took place. The lower boiling fractions were converted to formyl derivatives which were obtained in a solid form and from which, on crystallisation from alcohol, the formyl derivative of 1:3-dimethyl-2-amino-benzene, m.p. 163°C, was isolated.

Preparation and Separation of Xylidine.

Since sulphur containing substances had not been eliminated from technical xylidine by treatment with zinc/

zinc chloride it was decided to prepare xylidines. Another reason for the adoption of this course was the fact that in all samples of tech.-o-xylidine treated the loss was so considerable that it could not be accounted for except by concluding that the mixtures treated contained substances other than xylidines. Xylene, free from sulphur bodies, was nitrated by a mixed acid (sulphuric and nitric acids.) at a temperature below 20°C. The nitro-xylene was reduced by iron filings and hydrochloric acid and a mixture of xylidines was obtained. The method of separation used in this case was a combination of the best methods available for the separation of individual xylidines. 1:3-dimethyl-4-amino-benzene was first separated as acetate and the bases were divided into soluble and insoluble sulphates. The bases from the insoluble sulphate were converted to hydrochloride and 1:4-dimethyl-2-amino-benzene was removed. The filtrate from which the hydrochloride separated was decomposed with sodium hydroxide solution and the bases reconverted to sulphates. The total sulphate liquor was mixed and cooled and the sulphate which separated (K) by this treatment was decomposed and the liberated bases were heated, in alcohol with picric acid. The picrate of 1:2-dimethyl-4-amino-benzene separated. It was found that the best method of decomposing/

decomposing the picrate and picrate liquors was to treat with sodium hydroxide and steam distil. The previous method was by means of aqueous ammonia and the bases were extracted from the ammonia solution by ether. This extraction sometimes proved troublesome as ammonium picrate separated out. The bases from the soluble sulphate were treated with cuprous chloride in concentrated hydrochloric acid. (Jones and Kenner J.C.S., 1932, 715). The cuprous chloride complex of 1:3-dimethyl-2-amino-benzene was decomposed with sodium hydroxide and steam distilled. From the steam distillate 1:3-dimethyl-2-amino-benzene was obtained in an almost pure state.

The residual bases from the picrate separation were converted to formyl derivatives. These derivatives partly solidified and, on crystallisation from alcohol, gave small amounts of the formyl derivatives of 1:3-dimethyl-2-amino- and 1:3-dimethyl-4-amino-benzene. Further recrystallisation from alcohol and water gave a small amount of a derivative which, from its melting point and mixed melting points with the formyl derivatives of 1:3-dimethyl-4-and 1:4-dimethyl-2-amino-benzene, appears to be the formyl derivative of 1:2-dimethyl-3-amino-benzene.

This study on the separation of technical xylidine has shown that the separation of 1:3-dimethyl-4-, and/

and 1:4-dimethyl-2-amino-benzene as acetate and hydrochloride is satisfactory though it is not a complete separation in either case as both these xylidines have been obtained as formyl derivatives in the final stages of the separation. The separation of 1:3-dimethyl-2-amino-benzene by means of the solubility of its sulphate is not so convenient when a small quantity of bases is being treated, as is the cuprous chloride method. Separation of 1:2-dimethyl-4-amino-benzene as picrate is much to be preferred to the formyl derivative method as in every case difficulty has been experienced in obtaining the formyl derivatives in a solid state. A satisfactory method for the separation of 1:2-dimethyl-3-amino-benzene has not yet been discovered though the separation of this xylidine as formyl derivative might be easier on a much larger scale than has been used here, as this xylidine is present in technical xylidine in only a small amount.

Section (a)

Experimental. (1).

Separation of Technical Meta Xylidine.

The sample used was obtained from the British Drug House and had a boiling range 214-215°C.

93 Gms. of the freshly distilled xylidine were mixed with 46 gms.of glacial acetic acid and heated on a water bath. On cooling and being allowed to stand crystals separated and were filtered and pressed. The melting point of the crude acetate thus obtained was 67-69°C. From this solid acetate the bases were liberated by treatment with dilute sodium hydroxide solution and, after separation, were dried over solid potassium hydroxide. These bases, on treatment with formic acid (Sp. Gr. 1.2) on a boiling water bath, gave a formyl derivative melting at 111-113°C., (Pure Formyl 1:3-dimethyl-4-amino-benzene melts at 113.5°C. Hodgkinson and Limpach J.C.S., 1900, 65.) On crystallisation of the crude formyl derivative from aqueous alcohol a pure product, melting at 113.5°C. was obtained. From the acetic acid solution the remaining bases were liberated by neutralisation with sodium hydroxide solution and the bases thus obtained were converted to formyl derivatives and crystallised from aqueous alcohol. In this way a further/

further quantity of the formyl derivative of 1:3-dimethyl-4-amino-benzene, m.p. 112-113°C., was isolated and from the latter crystallisations a small quantity of the formyl derivative of 1:4-dimethyl-2-amino-benzene, m.p. 115-117°C., was obtained. (Pure formyl 1:4-dimethyl-2-amino-benzene melts at 117°C. Hodgkinson and Limpach (loc.cit.),).

Xylidine	Derivative	Weight	Free Base	Percentage
1:3:4	formyl m.p. 113.5°C.	86.0 gms	70 gms.	75
1:4:2	formyl m.p.115-117°C.	2.0 gms.	1.6 gms	1.7

Separation of Technical Para Xylidine.

The sample used was obtained from British Drug House and had a boiling range between 210-213°C.

92 Gms. were heated with 45 gms. of glacial acetic acid on a boiling water bath. The resultant product was cooled in an ice chest for five days but no solid separated. The bases were liberated by neutralisation with dilute sodium hydroxide solution, separated, and converted into hydrochlorides by treatment with a slight excess of concentrated hydrochloric acid. The solid hydrochloride which separated was filtered off and recrystallised from dilute hydrochloric acid. The bases from this hydrochloride gave a formyl derivative, which, after one crystallisation from dilute alcohol, melted at 116-117°C. (Formyl 1:4-dimethyl-2-amino-benzene melts at 117°C.).

The liquor from the hydrochloride was made alkaline with sodium hydroxide and the separated bases were converted to formyl derivatives by heating with formic acid (Sp.Gr. 1.2). On crystallisation from aqueous alcohol the formyl derivatives of 1:3-dimethyl-2-amino-benzene, m.p. 163°C; 1:3-dimethyl-4-amino-benzene, m.p. 112-113°C; and 1:4-dimethyl-2-amino-benzene were isolated. The formyl derivative of 1:3-dimethyl-2-amino-benzene is the/

the least soluble in alcohol. The m.p. of this derivative is given as 164-165°C. by Hodgkinson and Limpach (loc.cit.).

The following table shows the yields obtained using 92 gms. technical p-xylidine:-

Xylidine	Derivative	Weight	Free Base	Percentage
1:4:2	hydrochloride	60.0 gms.	50.0 gms.	66.7
1:4:2	formyl m.p.116-117°C.	15.0 gms.	11.5 gms.	
1:3:4	formyl m.p.112-113°C.	7.4 gms.	6.5 gms.	7.0
1:3:2	formyl m.p. 163°C.	12.0 gms.	9.2 gms.	10.3
Loss				16.0

Separation of Technical Ortho-Xylidine.

(1) Modified Method of Hodgkinson and Limpach.

The schematic outline of this method is given on the extending page 62.

The xylidine used was obtained from the British Drug House and distilled between 205 and 220°C., the bulk passing over between 212 and 215°C.

440 gms. xylidine were heated on a boiling water bath with 170 gms. glacial acetic acid. On cooling, solid acetate, A, separated and was filtered off and pressed. A small portion of the acetate was decomposed with sodium hydroxide solution and liberated bases were converted to formyl derivatives. After one crystallisation from aqueous alcohol a product melting at 112-113°C. was obtained ...... 1:3-dimethyl-4-amino-benzene. (formyl derivative, m.p.113.5°C.

The acetic acid liquor, B, was decomposed with dilute sodium hydroxide solution and approximately 300 gms. of bases were separated. A small portion was dissolved in concentrated hydrochloric acid and cooled in an ice-chest. No solid separated. The main portion of the bases was then dissolved in the calculated amount of 30% sulphuric acid and cooled. Solid sulphate, D, separated and was filtered off. This sulphate was decomposed with sodium hydroxide and the liberated bases (100 gms.) were converted to formyl derivatives These derivatives were crystallised from aqueous alcohol and gave a product melting/

melting at 116-117°C.....1:4-dimethyl-2-amino-benzene (formyl derivative, m.p. 117°C.). The residual derivatives from this crystallisation were liquid.

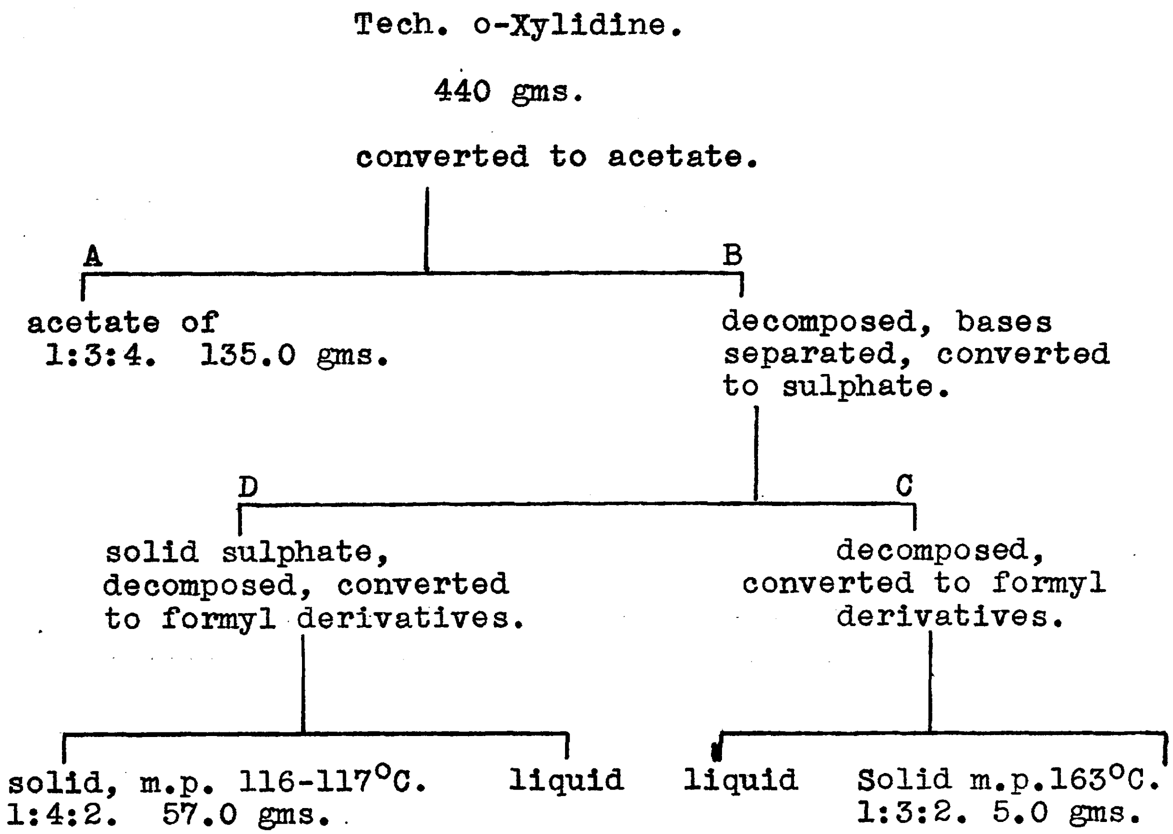
The liquor, C, from the separated solid sulphate was also decomposed with sodium hydroxide and the formyl derivatives of the liberated bases were formed. On crystallisation from alcohol a small amount of a derivative, m.p. 163°C, was isolated but the bulk of the derivative remained liquid. The formyl derivative of 1:3-dimethyl-2-amino-benzene melts at 164-165°C.

The scheme given on the extending page 62 outlines the method of separation.

The yields obtained were as follows :-

Xylidine	Derivative	Weight	Free Base	Percentage
1:3:4	acetate	135.0 gms.	90.0gms.	20.5
1:4:2	formyl m.p. 116-117°C.	57.0 gms.	50.0 gms.	11.4
1:3:2	formyl m.p. 163°C.	5.0 gms.	4.5 gms.	1.0

(1) Modified Method of Hodgkinson and Limpach.



Tech. o-Xylidine.

440 gms.

converted to acetate.

A

acetate of
1:3:4. 135.0 gms.

B

decomposed, bases
separated, converted
to sulphate.

D

solid sulphate,
decomposed, converted
to formyl derivatives.

solid, m.p. 116-117°C.
1:4:2. 57.0 gms.

liquid

C

decomposed,
converted to formyl
derivatives.

liquid

Solid m.p.163°C.
1:3:2. 5.0 gms.

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(2) Method of Morgan and Hickinbottom.

The schematic outline of this method is given on the extending page 68.

Technical o-xylidine (210 gms.) was mixed with glacial acetic acid (80 gms.) and allowed to stand for 24 hours. The solid acetate, A, was filtered off and a further crop of crystals was obtained from the liquor. The bases obtained from the acetate, A, gave a formyl derivative melting at 108-110°C., showing this fraction of the bases to be almost pure 1:3-dimethyl-4-amino-benzene. (formyl derivative of 1:3-dimethyl-4-amino-benzene melts at 113.5°C.).

The bases were liberated from the acetate liquor, B, by dilute sodium hydroxide solution, separated and mixed with 385 cc. of dilute sulphuric acid. (1cc. conc. sulphuric acid and 10 cc. water). Solid sulphate, C, separated and was filtered off. The bases were liberated from the separated sulphate, C, and from the filtrate from the sulphate, D.

Bases, C.

These bases (about 70cc.) were mixed with 60 cc. of conc. hydrochloric acid and allowed to stand for 24 hours. Solid hydrochloride, E, separated and, on recrystallisation/

recrystallisation from dilute hydrochloric acid, melted at 223-225°C. (hydrochloride of p-xylidine melts at 228°C.).

The original filtrate, F, from the hydrochloride, was mixed with the liquor from the recrystallisation of the hydrochloride and the bases were liberated ..... 35 gms., b.p. 210-215°C.

Bases D.

A small portion of this fraction was treated with concentrated hydrochloric acid and cooled in an ice-chest for over a week. No hydrochloride separated and the formyl derivative prepared from these bases remained liquid.

Mixed Bases.

The residual bases from F were mixed with the bases D. The mixed bases (111 gms.) were mixed with 70 gms. of picric acid and 150 cc. alcohol. Solution was effected by heating on a water bath and, on cooling, the picrate, G, separated out. After washing with alcohol the picrate was crystallised five times from this solvent and melted at 220°C. with slight decomposition. The picrate of 1:2-dimethyl-4-amino-benzene melts at 220°C. (G.T. Morgan and Hickinbottom, loc. cit.). The bases were obtained by decomposition of the picrate with aqueous ammonia and extraction/

extraction with benzene. The extract was dried with solid potassium hydroxide and the benzene was distilled off. On distillation of the residue a small amount of a yellow oil, boiling below 200°C., was obtained and hydrogen sulphide was evolved. The residue above 200°C. partly solidified and one crystallisation of the solid obtained gave flat plates, light brown in colour, m.p.49°C. The solvent used was petroleum ether (60-80°C.).Jacobsen (Ber., 17, 160.) gives m.p. of 1:2-dimethyl-4-amino-benzene as 49°C. The residue from the crystallisation of this base was liquid and did not give a solid formyl derivative.

The bases, H, obtained from the decomposition of the original picrate liquor were converted through the free base to sulphates by treatment with 15% sulphuric acid. The solid sulphate, I, was filtered off and washed with dilute sulphuric acid and the sulphate liquor, K, was set aside for further treatment.

Solid Sulphate, I.

The separated sulphate, I, was crystallised once from water and the aqueous liquor, L, was retained. The recrystallised sulphate, J, was decomposed and the bases were converted to formyl derivatives. These derivatives were liquid and did not solidify after standing in/

in an ice-chest for three weeks. They were finally decomposed by heating with hydrochloric acid and benzoylated by the Schotten-Baumann method. The benzoyl derivatives were crystallised from alcohol and gave a product melting at 162-163°C. Benzoyl derivative of 1:3-dimethyl-2-amino-benzene, m.p. 168-168.5°C., Bamberger, Rising (Ann., 316, 303). Apart from this no further separation could be obtained by continued crystallisation of the benzoyl derivatives from alcohol and benzene.

The aqueous liquor, L, was neutralised with sodium hydroxide solution and the liberated bases were converted to formyl derivatives. One crystallisation from aqueous alcohol gave a product melting at 145-155°C. Further crystallisations from the same solvent gave a small amount of pure formyl 1:3-dimethyl-2-amino-benzene m.p. 163°C.

Soluble Sulphate, K.

The bases obtained from the sulphate liquor,K, were converted to formyl derivatives which, after long standing and repeated crystallisation from aqueous alcohol, yielded formyl 1:3-dimethyl-2-amino-benzene m.p. 163°C.

Yields of individual bases obtained are given overleaf.

Yields obtained using 210 gms. of tech. o-xylidine.

Xylidine	Derivative	Weight	Free Base	Percentage
1:3:4	acetate	60.0 gms.	40.0 gms.	19.0
1:4:2	hydrochloride	30.0 gms.	23.0 gms.	10.9
1:3:2	formyl m.p. 163°C.	3.0 gms.	2.5 gms.	1.2
1:2:4	picrate m.p. 220°C.	21.0 gms.	7.5 gms.	3.6

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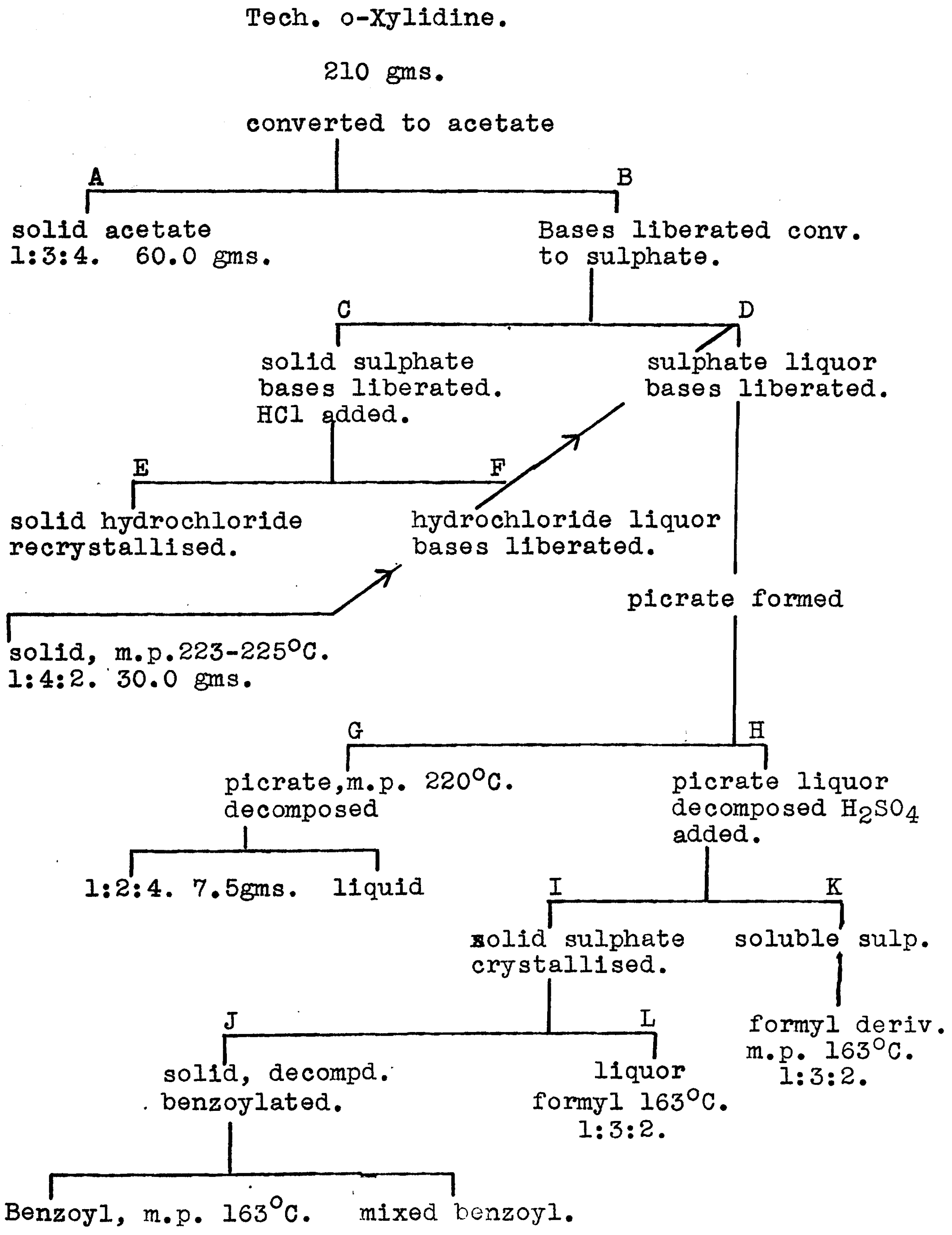
(2) Method of Morgan and Hickinbottom.



Tech. o-Xylidine.

210 gms.

converted to acetate

A
solid acetate
1:3:4. 60.0 gms.

B
Bases liberated conv.
to sulphate.

C
solid sulphate
bases liberated.
HCl added.

E
solid hydrochloride
recrystallised.

solid, m.p.223-225°C.
1:4:2. 30.0 gms.

F
hydrochloride liquor
bases liberated.

D
sulphate liquor
bases liberated.

picrate formed

G
picrate, m.p. 220°C.
decomposed

1:2:4. 7.5gms.

liquid

H
picrate liquor
decomposed H_2SO_4
added.

I
solid sulphate
crystallised.

J
solid, decompd.
benzoylated.

Benzoyl, m.p. 163°C.

mixed benzoyl.

L
liquor
formyl 163°C.
1:3:2.

K
soluble sulp.

formyl deriv.
m.p. 163°C.
1:3:2.

(3) Separation of Technical o-Xylidine after removal of Secondary and Tertiary Bases.

500 gms. of technical o-xylidine were treated with a slight excess of a 50% aqueous solution of zinc chloride. The precipitated zincichloride of the primary bases was filtered, pressed and washed with petroleum ether (60-80°C.) until the extract was almost colourless. The zincichloride was decomposed with concentrated ammonia, the liberated bases were washed free from ammonia, separated and dried with solid potassium hydroxide. On distillation the bulk distilled between 212-220°C. Weight 330 gms. As obtained these bases were almost colourless but soon turned red on standing. (Separation scheme on extending page 74.)

The bases were mixed with 126 gms. of glacial acetic acid and from this liquor solid acetate, A, separated on standing. The liquor, B, was decomposed and the bases were mixed with 430 cc. of dilute sulphuric acid. (1 cc.conc. H_2SO_4 in 10 cc. of water). This sulphate liquor was heated on a water bath and allowed to cool. The solid sulphate, C, was filtered and pressed and the liquor, D, was set aside.

The solid sulphate, C, was decomposed and the separated/

separated bases were mixed with an equal volume of concentrated hydrochloric acid and allowed to stand for 48 hours. The hydrochloride, E, which separated was filtered off and crystallised from dilute hydrochloric acid. (20 cc. conc. HCl in 100 cc. water). The hydrochloride liquor F, was treated with sodium hydroxide solution and the bases, about 100 gms., were separated and mixed with 300 cc. dilute sulphuric acid (15 cc.of conc. H_2SO_4 and 100 cc. water) and added to the original sulphate liquor, D. These combined liquors were heated on a water bath and allowed to cool. As much solid sulphate as possible was separated by cooling in an ice-chest. The liquor, G, from the separated sulphate, H, was neutralised and the bases were extracted with ether and dried over solid potassium hydroxide. The ether was removed and the bases distilled between 208 and 221°C., chiefly at 214-215°C. Weight 90 gms. These bases were mixed with 45 gms. of formic acid and heated on a water bath. The formyl derivative thus obtained was kept in an ice-chest for two months but did not solidify. The bases were regenerated by heating with concentrated hydrochloric acid and reconverted to sulphate. By cooling and concentrating more solid sulphate/

sulphate was separated. The bases which still remained in solution as sulphate were liberated. Weight 50 grams. These should have been almost pure 1:3-dimethyl-2-aminobenzene (acetyl derivative, m.p. 177°C.). The acetyl derivative obtained melted at 120°C. 30 grams zinc chloride were dissolved in 60 cc. water and added to the bases obtained from the soluble sulphate. The zincichloride obtained was dissolved in concentrated hydrochloric acid and from this solution white needles separated. These were decomposed by concentrated ammonia and a small amount of a base which gave a formyl derivative, m.p. 163°C. was obtained. .... 1:3:2.

Solid Sulphate H.

83 grams of the separated sulphate were decomposed with sodium hydroxide solution and the bases were extracted with ether and dried over solid potassium hydroxide. Weight 52 grams. These bases were mixed with 30 grams of picric acid in 60 cc. alcohol, heated on a water bath, and gave, on cooling a picrate, I, which on crystallisation from alcohol melted with decomposition at 215-220°C. The picrate was decomposed by heating with dilute ammonia and the bases were extracted with benzene. The benzene was distilled off and 1:2:4 xylidine, m.p. 49°C., was obtained from the residue by crystallisation from petroleum ether.

The liquor, J, from the original picrate and liquors from picrate crystallisation were mixed and freed from alcohol. The bases were obtained by treatment with aqueous ammonia and extraction with benzene. The benzene extract was dried over solid potassium hydroxide and the benzene distilled. The bases thus obtained were distilled under 7 mm. pressure and the following fractions were collected.

Fraction 1	80-85°C.	20 gms.
Fraction 2	85-92°C.	12 gms.
Fraction 3	92-115°C.	2 gms.

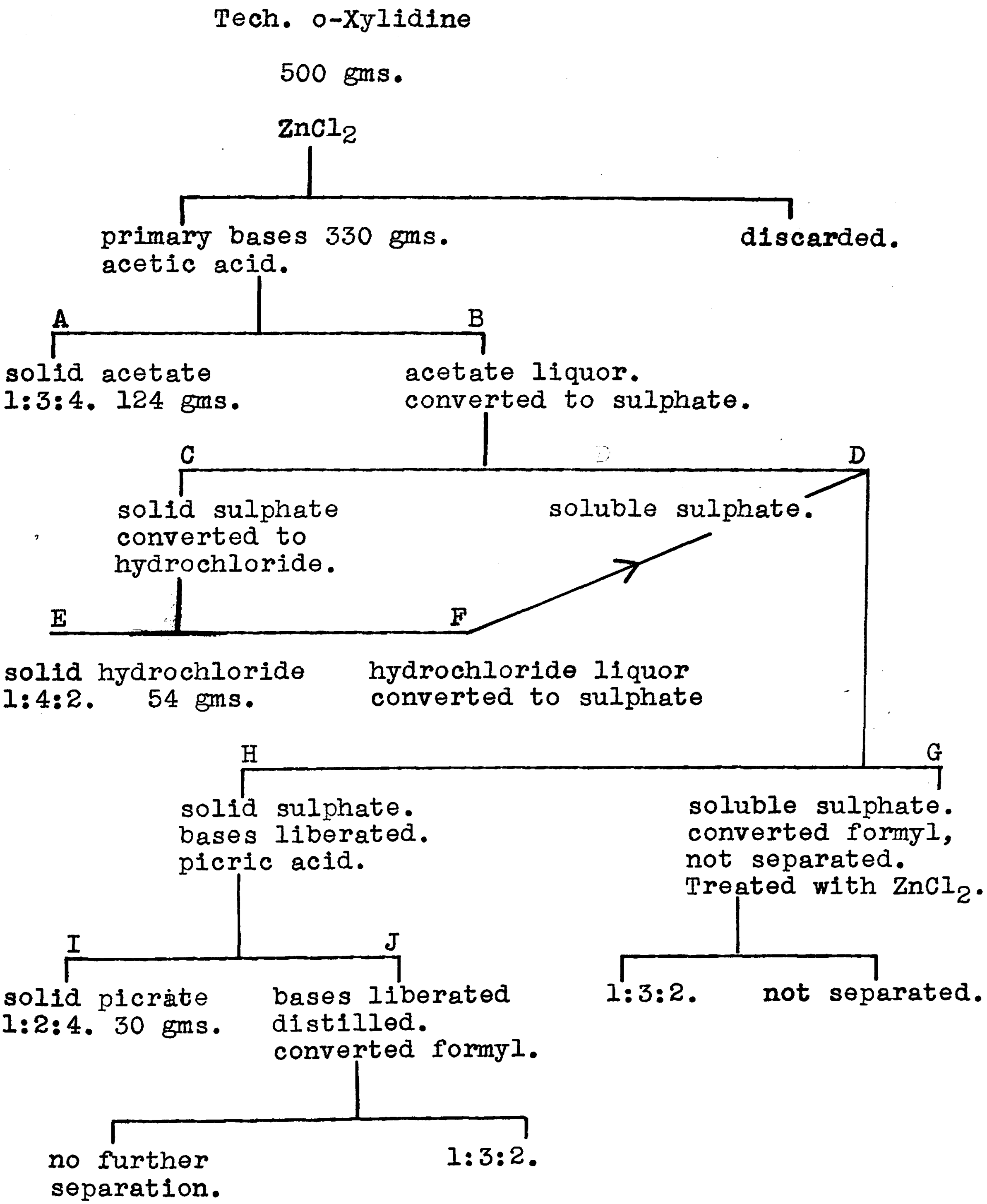
At 85°C. there were signs of decomposition with evolution of water and above 105°C. the temperature rose rapidly. Hydrogen sulphide was evolved during the distillation. Fractions 1 and 2 were mixed and heated on a water bath with formic acid. A solid formyl derivative was obtained on pouring the reaction mass into water. On crystallisation from alcohol small white needles, m.p. 163°C., were obtained ..... 1:3:2.

Fraction 3 was also treated with formic acid but the derivative obtained remained liquid and was not investigated further.

Xylidine	Derivative	Weight	Free Base	Percentage
1:3:4	acetate	124 gms.	83.0 gms.	25.0
1:4:2	hydrochloride	54 gms.	42.0 gms.	12.7
1:2:4	Picrate m.p.215-220°C.	30 gms.	10.0 gms.	3.0
1:3:2	formyl m.p. 163°C.	4 gms.	3.2 gms.	1.0

The percentage yields given in the final column of the above table were calculated on 330 gms. primary bases which were obtained from 500 gms. Technical e-xylidine.

(3) Separation of Technical o-Xylidine after removal of Secondary and Tertiary Bases.


Tech. o-Xylidine
500 gms.
$ZnCl_2$
primary bases 330 gms.
acetic acid.
discarded.
A
B
solid acetate
1:3:4. 124 gms.
acetate liquor.
converted to sulphate.
C
D
solid sulphate
converted to
hydrochloride.
soluble sulphate.
E
F
solid hydrochloride
1:4:2. 54 gms.
hydrochloride liquor
converted to sulphate
H
G
solid sulphate.
bases liberated.
picric acid.
soluble sulphate.
converted formyl,
not separated.
Treated with $ZnCl_2$.
I
J
solid picrate
1:2:4. 30 gms.
bases liberated
distilled.
converted formyl.
1:3:2.
not separated.
no further
separation.
1:3:2.

Separation of Prepared Xylidine.

Nitration of Xylene.

50 gms. of xylene, b.p. 136-141°C, were nitrated with mixed acid consisting of 43 gms.nitric acid (Sp.Gr. 1.42) and 65 gms.sulphuric acid (Sp.Gr.1.84). The acid was run into the xylene over a period of 1½ hours, the xylene during this time being stirred vigorously by a mechanical stirrer so that the temperature did not rise above 20°C. When all the acid had been added the temperature of the reaction mixture was raised to 50°C. On cooling the acid layer was separated and the residual nitro-xylene washed with dilute sodium carbonate solution. The nitro-compound was steam distilled and the main bulk separated from the distillate. The remaining nitro-xylene was extracted from the steam distillate with ether and the extract was added to the main bulk which was dried over anhydrous calcium chloride. After removal of ether the nitro-xylene was distilled. 5 gms. of a clear mobile liquid distilled below 200°C. and then the temperature rose rapidly. A fraction, which boiled between 235 and 241°C., was collected. This was a pale yellow liquid which turned red on standing. Weight 45 gms. Percentage yield 60.

Six such nitrations were conducted with similar yields.

Reduction of Nitro-Xylene.

100 gms. nitro-xylene were added in small amounts to a reduction mixture consisting of 100 gms. iron filings suspended in 60 cc. of water to which had been added 15 cc. conc. hydrochloric acid. The temperature was maintained at 90-95°C. When the smell of nitro-xylene had ceased to be noticeable the xylidine was steam distilled. The distillate was extracted with ether and the extract was dried over solid potassium hydroxide. On removal of the ether the xylidine distilled between 210 and 220°C., though the bulk passed over between 214 and 216°C. Yield 65 gms. Percentage yield 81.

Separation of Xylidines. (Scheme on extending page 82.)

200 gms. of crude xylidine were mixed with 76 gms. glacial acetic acid and, after standing for some time, the separated acetate, A, was filtered off........ 1:3-dimethyl-4-amino-benzene.

The acetate liquor, B, was decomposed with sodium hydroxide solution and the bases were separated. Approximately 100 gms. were thus recovered and were mixed with 190 cc. of dilute sulphuric acid (1 cc. conc. sulphuric acid and 10 cc. water). The less soluble sulphate, C, which separated out was filtered off, and the bases were liberated from it by sodium hydroxide solution/

solution. The sulphate liquor, D, was set aside.

(C). The bases were mixed with an approximately equal volume of conc. hydrochloric acid and, on cooling, a solid hydrochloride, E, separated ..... 1:4-dimethyl-2-amino-benzene. The liquor, F, from the hydrochloride was neutralised with sodium hydroxide solution and the separated bases were dissolved in a slight excess of dilute sulphuric acid and added to the main bulk of sulphate liquor, which on cooling in ice separated more sulphate.

(G). The bases were liberated from the sulphate filtrate, H, and a small quantity was acetylated. The crude acetyl derivative softened at 135°C. and melted completely at 145°C.

The total amount of bases obtained at this stage was about 25 gms. and these were mixed with 26 cc. of concentrated hydrochloric acid. To this solution was added 11 gms. of cuprous chloride in 60 cc. concentrated hydrochloric acid. The mixture was allowed to stand overnight and a complex salt, I, separated out, contaminated with cuprous chloride. This complex was decomposed with sodium hydroxide solution and steam distilled. Common salt was added to the steam distillate and the xylidine was extracted with benzene. This extract was/

was dried over solid potassium hydroxide and a small quantity was treated with acetic anhydride. Small white needles, m.p. 170-175°C., were obtained and recrystallised from benzene, m.p. 176°C. The acetyl derivative of 1:3-dimethyl-2-amino-benzene melts at 177°C. (Hodgkinson and Limpach, J.C.S., 77, 67).
On evaporation of the benzene from the above extract 10 gms. xylidine, b.p. 214-215°C., were obtained ..... 1:3-dimethyl-2-amino-benzene.
The hydrochloric acid liquor, J, from which the cuprous chloride complex separated was decomposed with sodium hydroxide solution and steam distilled. The bases were mixed with the main quantity obtained from the solid sulphate, G,

Solid Sulphate, G.

25 gms. of bases obtained from solid sulphate, G, were dissolved in 25 cc. of alcohol and 12 gms. picric acid were added. The mixture was heated on a water bath until all the picric acid had passed into solution. On cooling the picrate separated, was filtered off, and crystallised twice from alcohol, m.p. 218-220°C. (slight decomposition)....... 1:2-dimethyl-4-amino-benzene.

The free base was obtained from the picrate by treating/

treating with dilute sodium hydroxide solution and steam distilling.

The residual liquors and those obtained from the picrate crystallisations were mixed and the bases liberated by sodium hydroxide solution and then separated by steam distillation. The steam distillate was extracted with ether and the ether extract was dried over solid potassium hydroxide. After distillation of the ether 12 gms. bases remained. These were mixed with 6 cc. of formic acid (Sp.Gr. 1.2) and 1 drop of concentrated sulphuric acid was added. After heating on the water bath the reaction mixture was cooled in an ice-chest and, after standing for a few days, partly solidified. The solid was filtered off and crystallised from alcohol. This treatment separated the formyl derivatives into two main fractions .....(1) the less soluble portion melting at about 155°C., and (2) solids melting at about 100°C.

Fraction (1).

Further crystallisation from alcohol gave white needles, m.p. 163°C....... 1:3-dimethyl-2-aminobenzene.

Fraction (2).

Crystallisation from dilute alcohol gave a solid/

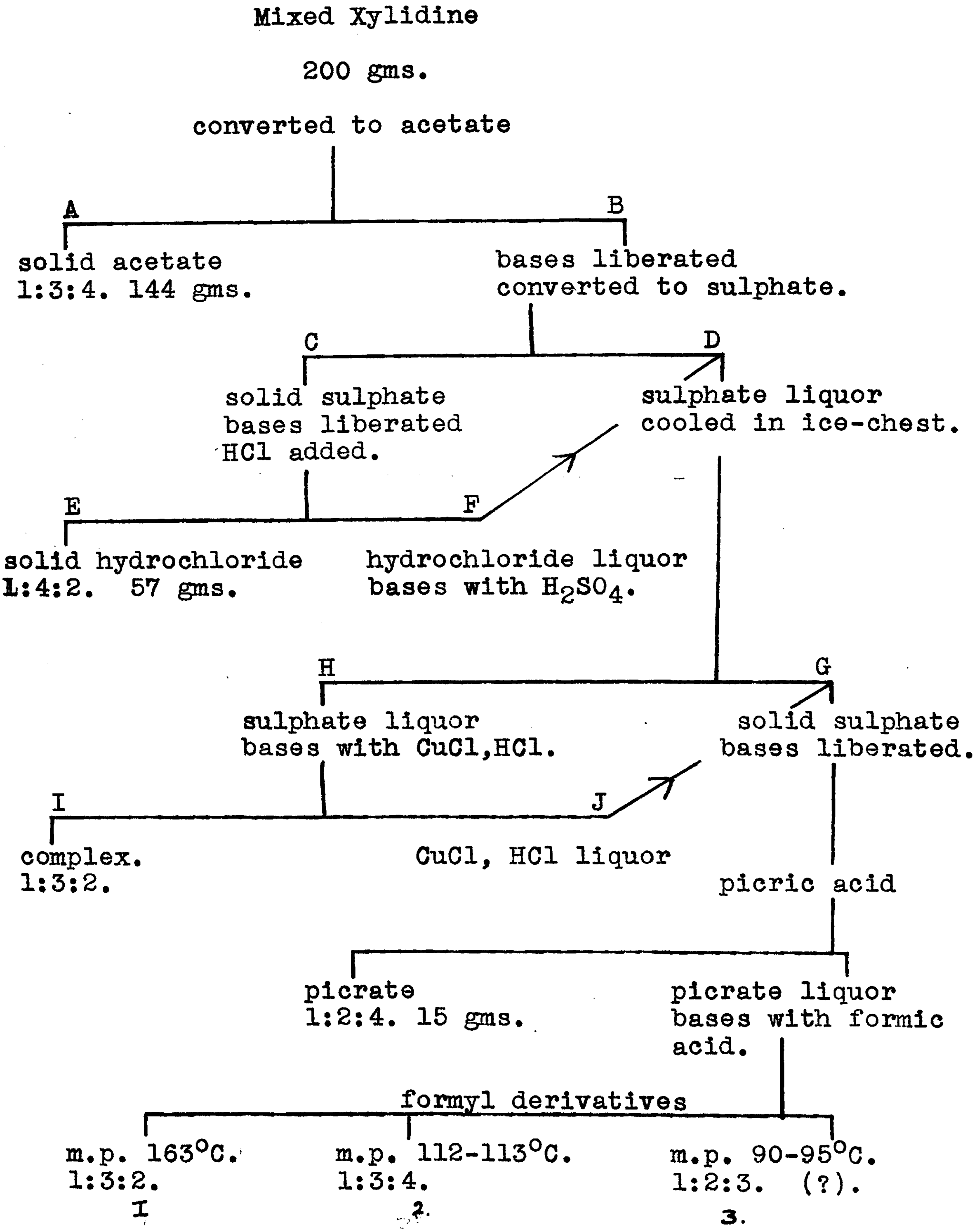
solid, m.p. 112-113°C., mixed m.p. with the formyl derivative of 1:3-dimethyl-4-amino-benzene (113.5°C.), 113°C. On evaporation of the solvent a semi-solid residue was obtained. This was pressed free from liquid on a porous plate and melted at about 80°C. On crystallisation from water a solid, m.p. 90-95°C., was isolated. Mixed m.p. with the formyl derivative of 1:3-dimethyl-4-amino-benzene, (113.5°C.), was 85-89°C. and with the formyl derivative of 1:4-dimethyl-2-amino-benzene, (117.5°C.), was 85-90°C. The solid isolated may therefore be an impure sample of the formyl derivative of 1:2-dimethyl-3-amino-benzene. Hodgkinson and Limpach (loc. cit.) give m.p. of the formyl derivative of this xylidine as 100-102°C.

A table showing yields obtained is given overleaf.

Yields obtained using 200 gms. crude xylidine.

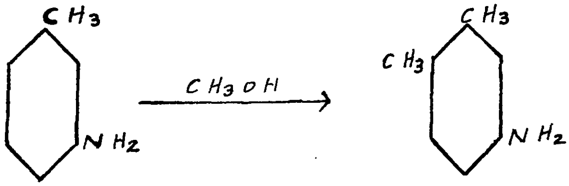
Xylidine	Derivative	Weight	Free Base	Percentage
1:3:4	acetate	144 gms.	96 gms.	48.0
1:4:2	hydrochloride	57 gms.	44 gms.	22.0
1:3:2	cuprous chloride	-	10 gms.	5.0
1:2:4	picrate m.p. 218-220°C.	15 gms.	5 gms.	2.5
1:3:2	formyl m.p. 163°C.	small amount.	-	
1:3:4	formyl m.p. 112-113°C.	small amount.	-	
1:2:3	formyl m.p. 90-95°C.	small amount.	-	
Loss				22.5

Separation of Mixed Xylidines.


Mixed Xylidine
200 gms.
converted to acetate
A
solid acetate
1:3:4. 144 gms.
B
bases liberated
converted to sulphate.
C
solid sulphate
bases liberated
HCl added.
D
sulphate liquor
cooled in ice-chest.
E
solid hydrochloride
1:4:2. 57 gms.
F
hydrochloride liquor
bases with H_2SO_4.
H
sulphate liquor
bases with CuCl,HCl.
G
solid sulphate
bases liberated.
I
complex.
1:3:2.
J
CuCl, HCl liquor
picric acid
picrate
1:2:4. 15 gms.
picrate liquor
bases with formic
acid.
formyl derivatives
m.p. 163°C.
1:3:2.
1
m.p. 112-113°C.
1:3:4.
2.
m.p. 90-95°C.
1:2:3. (?).
3.

(2) Preparation of Amines by Ring Methylation.

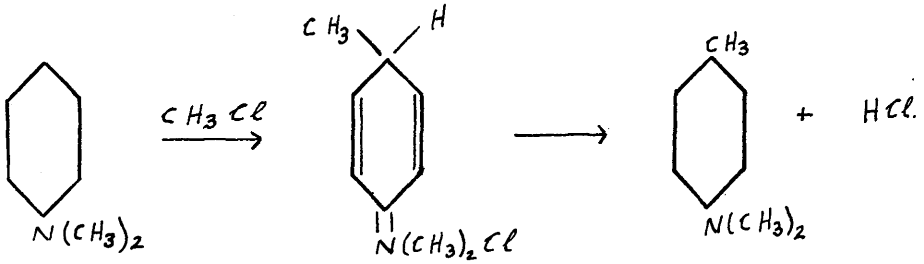
Since the separation of the two ortho-xylidines, 1:2-dimethyl-3-, and 1:2-dimethyl-4-amino-benzene, had proved so troublesome other methods for the preparation of these substances were considered. The Hofmann-Martius reaction seemed to offer a possibility of effecting this object since Limpach (Ber., 1888, 21, i, 643) has shown that 1:3-dimethyl-4-amino-benzene is produced by heating p-toluidine hydrochloride with methyl alcohol in sealed tubes. As the reaction is of general application it seemed possible to produce 1:2-dimethyl-4-amino-benzene from m-toluidine since it is known that substitution takes place first in the position para to the amino group. If the para position is occupied substitution then takes place in the ortho position if free, and it has recently been shown that substitution may also take place in the meta position. (Hey, J.C.S., 1931, 1581). Thus from m-toluidine 1:2-dimethyl-4-amino-benzene should be formed.



A survey of the actual results obtained will be given after/

after the reaction mechanism has been discussed.

The reaction is considered to take place through the initial formation of secondary and then tertiary bases by the interaction of the alcohol and the amine hydrochloride. This reaction most probably takes place between the free base and the alkyl chloride formed from the dissociated hydrogen chloride and the alcohol. The modern view of the second stage of the reaction is that it is more likely to be inter- rather than intra-molecular migration. Hey (loc. cit.) has suggested the following mechanism to explain substitution in the ortho and para positions.

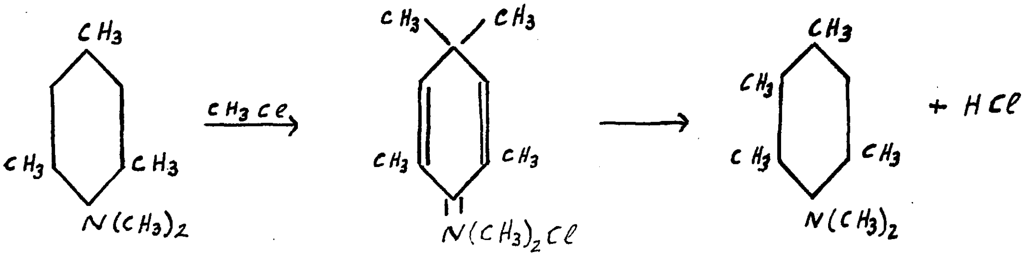


The tertiary amine reacts directly with the alkyl chloride and an intermediate compound with a quinonoid structure is postulated. This intermediate compound loses hydrogen chloride and the final result is that a methyl group has been introduced into the benzene nucleus in a position para to the amino group. The equilibrium indicated below will be upset by the removal of methyl alcohol and the production of primary amines will be favoured.

$$R.N(CH_3)_2.HCl \underset{CH_3OH}{\overset{H_2O}{\rightleftharpoons}} RNH.CH_3.HCl \underset{CH_3OH}{\overset{H_2O}{\rightleftharpoons}} R.NH_2.HCl$$

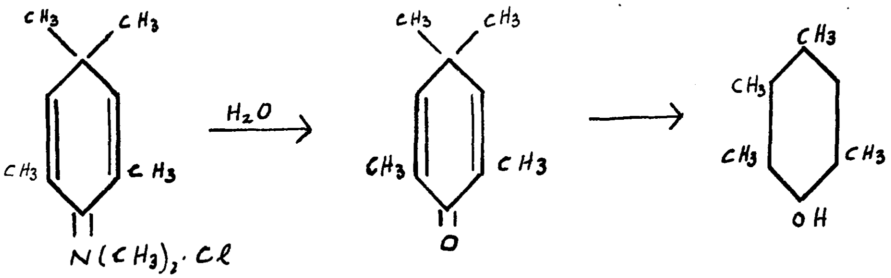
This represents the original primary amine in equilibrium with the secondary and tertiary amines which are formed from it.but, since a similar system in equilibrium must be advanced to explain the production of substituted primary amines from the substituted tertiary amines produced by direct nuclear alkylation, it seems to the present author that, in every case, there should be a certain amount of the original primary amine recovered unchanged. The recovery of unchanged starting material has not been reported by Hey.

The case of meta substitution is considered to be a case of true intra-molecular migration. Meta substitution only occurs when the ortho and para positions to the amino group are occupied and the intermediate product suggested in this case has a quinonoid structure in which two methyl groups are attached to the carbon atom para to the amino group. This intermediate compound on losing hydrogen chloride rearranges to form a compound in which there is a substituent in a position meta to the amino group.



A true intra-molecular rearrangement occurs when free alkyl arylamines are heated with metallic chlorides. (Hickinbottom, J.C.S., 1927, 64; Hickinbottom and Waine, J.C.S., 1930, 1558; Hickinbottom and Preston, J.C.S., 1930, 1566.). The products obtained in this case are different from those obtained by heating the alkylarylamine hydrochloride.

A new observation recorded by Hey (loc. cit.) is the formation of phenol in the Hofmann-Martius reaction. This production of phenols is explained by considering that the quinone-imine, postulated as the intermediate product in meta substitution, is hydrolysed to a quinonoid ketone which rearranges to give a phenol.

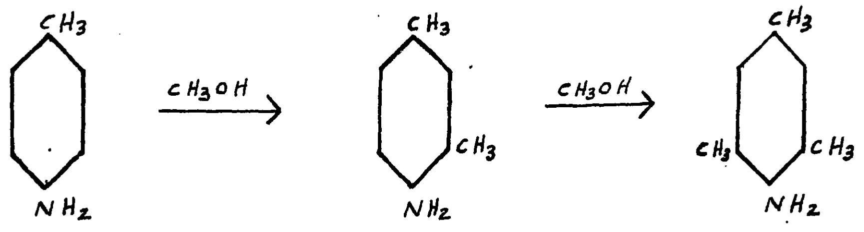


In the present work no phenols have been

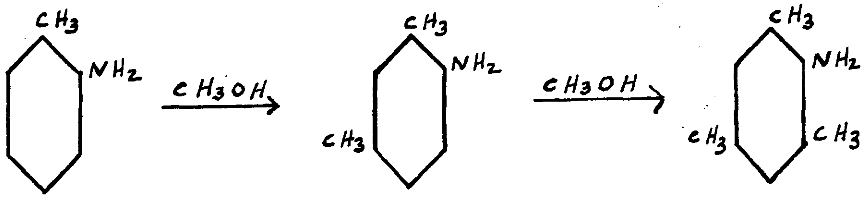
detected/

detected as the presence of this type of compound is unexpected and Hey's paper was published subsequent to the completion of the series of experiments herein described.

The present author has attempted to prepare 1:2-dimethyl-4-amino-benzene from m-toluidine but has not been successful. The primary bases obtained by heating m-toluidine hydrochloride and methyl-alcohol in sealed tubes were converted to benzoyl derivatives. Fractional crystallisation of these derivatives proved the presence of 1:4-dimethyl-2-amino-benzene, mesidine pseudo-cumidine and unchanged m-toluidine. The desired xylidine, 1:2-dimethyl-4-amino-benzene, may have been present but was not isolated. The presence of mesidine must be attributed to some impurity, probably o-and/or p-toluidine. In the case of p-toluidine the position para to the amino group is occupied and substitution will therefore take place ortho to the amino.



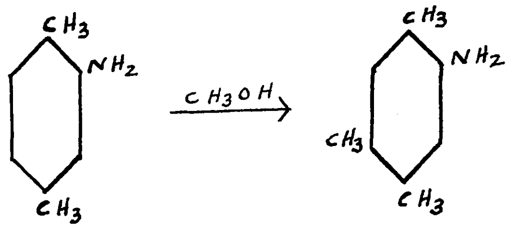
With o-toluidine the methyl group would first enter the position para to the amino and then the second methyl group would occupy the free ortho position.



Since the primary amines produced from m-toluidine proved to be a complex mixture the method was considered to be unsatisfactory for the preparation of xylidines.

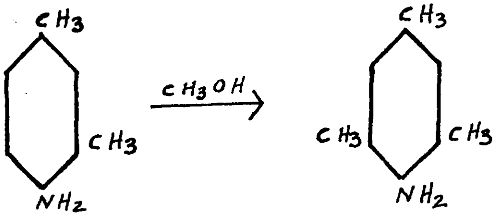
However this method has proved useful for the production of both pseudo-cumidine and mesidine. Starting from the appropriate xylidine in each case it has been found possible to arrange conditions so that only one methyl group is introduced and the primary bases obtained therefore are not such complex mixtures as that obtained from m-toluidine.

Pseudo-cumidine was obtained in yields of about 50% by heating the hydrochloride of p-xylidine (1 mol.) with methyl alcohol (1 mol.) in sealed tubes at a temperature of 280°C.



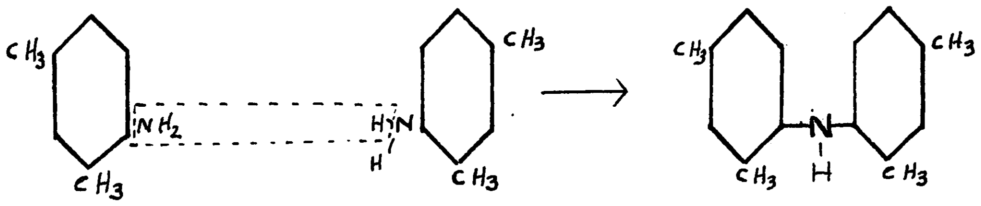
In this case the position para to the amino is unoccupied and substitution therefore takes place at this point. Substances other than primary bases were obtained and among these was an unidentified substance, m.p. 185-195°C. This substance was soluble in dilute hydrochloric acid but the smallness of the amount obtained prevented closer examination.

Mesidine has been prepared by heating the hydrochloride of 1:3-dimethyl-4-amino-benzene with methyl alcohol in sealed tubes at 320°C. When heating was conducted at 280°C. the xylidine was recovered practically unchanged and even at 320°C. the yield of mesidine was 30-35% as compared with 50% yield of pseudo cumidine at the lower temperature. This lowering of the yield and the necessity for a higher reaction temperature must be ascribed to the fact that substitution in a position ortho to the amino does not take place so readily as substitution in the para position. This may be due to the greater ease with which a para quinonoid structure is formed.

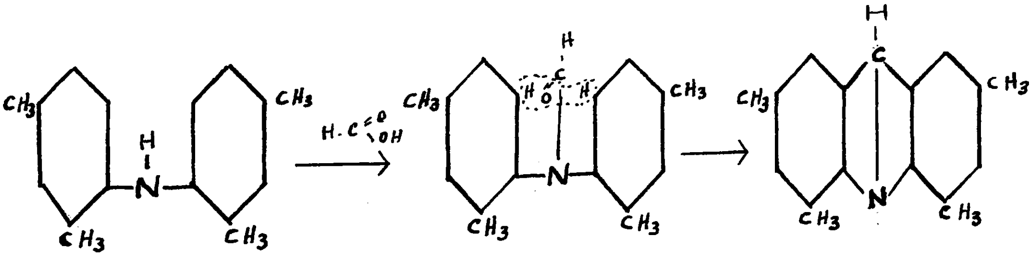


In the preparation of both pseudo cumidine and mesidine the primary bases were separated from secondary and tertiary by Morgan's zincichloride method.

In the production of mesidine the secondary and tertiary bases boiled above 260°C. and these were treated with acetic anhydride in an attempt to separate secondary bases as acetyl derivatives. The product from acetylation was dissolved in alcohol and small yellow needles separated. This substance was further crystallised from alcohol and melted at 118-119°C. Analysis showed it to be a tetra-methyl acridine and a picrate which melted, after crystallisation from benzene, at 210°C. was formed. From this evidence the substance is 1:3:7:9-tetra-methyl acridine, m.p. 120-121°C.; picrate, m.p. 210-211°C. (Senier and Compton, J.C.S., 1907, 91, 1927.). A similar case of the production of a tetra-methyl acridine has been reported by Liebermann and Kardos (Ber., 1914, 47, ii, 1563.) and 1:3:7:9-tetra-methyl acridine has been isolated by Hey (Loc.cit.) No secondary bases were isolated from the acetylated product but taking into consideration the boiling range of this fraction it seems that bases of the diphenylamine type might possibly be present.



From this substituted diphenylamine, indicated above, tetra-methyl acridine can be produced by the intermediate formation of the formyl derivative and subsequent ring closure.



The formyl derivative may be formed by interaction of the diphenylamine and formic acid derived from the methyl alcohol.

An attempt to form p-amino-ethyl benzene by heating aniline hydrochloride with absolute ethyl alcohol in a sealed tube resulted in the production of this substance in a very small amount. It was isolated as the benzoyl derivative but its separation from unchanged aniline proved to be sufficiently difficult to render this method of preparation impracticable.

(2) Preparation of Amines by Ring Methylation.

Experimental.

Ring Methylation of m-Toluidine.

Two quantities of 10 gms. m-toluidine hydrochloride were heated in sealed tubes at 280°C. for two hours with 2 cc. methyl-alcohol in each. The reaction product was a brownish crystalline mass and there was no excess pressure in the tubes. After decomposition of the ~~basic~~ hydrochlorides with warm dilute sodium hydroxide solution the bases were extracted with ether. The ether extract was dried with potassium carbonate. After removal of the ether the distillation was continued and the following fractions were collected :-

(1) 205-230°C. Clear mobile liquid, boiling chiefly at 210°C. Weight 8 gms.

(2) 230-250°C. A very small amount of distillate was obtained.

Above 250°C. decomposition took place and the residue was a dark red oil.

Fraction (1).

The complete fraction was acetylated with acetic anhydride and the acetyl derivative was distilled. No distillate was obtained below 260°C. except a little water. The acetyl derivative remained liquid on cooling and/

and attempts were made by dissolving in alcohol and diluting and cooling to separate a solid. No solid was obtained and the acetyl derivatives were decomposed with concentrated hydrochloric acid and benzoylated. The benzoyl derivatives were solid and were fractionally crystallised from alcohol. The following fractions, arranged in order of increasing solubility, were separated.

(1) Softened at 185°C. melted completely at 200°C.
Benzoyl mesidine, m.p. 204°C. (Hübner, v.Schack, Ber., 10, 1711).

(2) m.p. 169-170°C. Benzoyl pseudo cumidine, m.p. 167°C. (Gudeman, Ber.; 21, 2553).

(3) m.p. 138-140°C. No depression in melting point with benzoyl derivative of 1:4-dimethyl-2-amino-benzene. m.p. of benzoyl derivative of 1:4-dimethyl-2-amino-benzene. 140°C. (Pflug, Ann., 255, 169).

(4) m.p. 114-115°C. Mixed m.p. with m-toluidine benzoyl derivative (m.p. 125°C.) 115-119°C.

Preparation of Mesidine, 1:3:5-trimethyl-2-amino-benzene.

Two quantities of 10 gms. of the hydrochloride of 1:3-dimethyl-4-amino-benzene were heated with 2.5 cc. each methyl alcohol in sealed tubes for one hour at 320°C. On cooling and opening the tubes there was no excess pressure inside. The contents, a thick brown semi-solid material, were treated with dilute warm sodium hydroxide solution and a reddish oil separated. This oil was added to an excess of a 50% aqueous solution of zinc chloride. After vigorous shaking the zincichloride was filtered and dried. The secondary and tertiary bases still adhering to the zincichloride were extracted by boiling petroleum ether (60-80°C.). After petroleum ether treatment the zincichloride was decomposed by concentrated ammonia (0.88 Sp.Gr.) and the bases were extracted with ether. The ether extract was dried with potassium carbonate and the ether was distilled. The resulting bases were distilled and the fraction between 220 and 230°C. was collected (the bulk distilled at 225-226°C.). Weight 7.0 gms. Percentage yield 40..... Mesidine, b.p. 229-230°C.

The secondary and tertiary bases were obtained from the petroleum ether extract from the zincichloride. On distillation only a small amount passed over below 270°C. at/

at which temperature decomposition took place. The residue was a reddish brown very viscous liquid. This liquid was boiled under reflux with acetic anhydride and the product, after washing with sodium carbonate solution, was dissolved in alcohol. After boiling with animal charcoal and filtering pale brown crystals were obtained. Further crystallisation from alcohol gave small, pale yellow needles, m.p. 118-119°C. On analysis this gave N, 6.10%, calculated for $C_{17}H_{17}N$, 5.96%. A picrate was formed by adding an alcoholic solution of this substance to alcoholic picric acid. The picrate was crystallised from alcohol, in which it is not very soluble, and was obtained in orange yellow irragular prisms, m.p. 210-211°C.

Preparation of Pseudo Cumidine, 1:2:4-trimethyl-5-aminobenzene.

Three quantities of 10 gms. p-xylidine hydrochloride were heated in sealed tubes at 280-290°C. for $1\frac{1}{2}$ hrs. with 2.5 cc. of methyl alcohol in each case. The reaction product was a brown crystalline mass and a small amount of liquid collected in the narrow parts of the tubes. There was no excess pressure and no inflammable gas inside the tubes. The products from the three tubes were mixed and warm dilute sodium hydroxide solution was added. The bases separated as an oil which solidified on cooling. This was filtered off from the hydroxide liquor, melted in hot water and zincichlorides were formed by the addition of 35 gms. of zinc chloride in 100 cc. water. The zincichloride, pale brown in colour, was filtered, dried and extracted with boiling petroleum ether. The purified zincichloride was decomposed by concentrated ammonia and the solid bases were filtered off. On crystallisation from aqueous alcohol pale brown needles, m.p. 62-63°C. were obtained. Yield 13.4 gms. Percentage 52...... pseudocumidine m.p. 68°C. (Auwers, Ber., <u>18</u>, 2661).

The secondary and tertiary bases extracted from the zincichloride by petroleum ether were solid and on crystallisation/

crystallisation from alcohol melted at 180-195°C. This substance is soluble in dilute hydrochloric acid and, on reprecipitation by sodium hydroxide, melts at 185-195°C.

Preparation of p-Amino-Ethyl Benzene.

8 gms. aniline hydrochloride were heated in a sealed tube at a temperature of 270-280°C. with 3 cc. absolute alcohol for 1½ hours. A brownish crystalline reaction product was obtained and there was considerable excess pressure inside the tube. An inflammable gas escaped on opening the tube. The product was washed with warm dilute sodium hydroxide solution and the bases were extracted with ether. After distillation of the ether the bases were converted to zincichlorides by treatment with 50% aqueous zinc chloride. The zincichloride, after drying, was extracted with boiling petroleum ether and decomposed with concentrated ammonia. The bases were extracted with ether, dried with potassium carbonate and, after removal of the ether, distilled. The distillation range was 195-220°C., the main bulk passing over between 205 and 220°C. Weight 3 gms. Benzoyl derivatives were formed and fractionally crystallised to give the benzoyl derivative of p-amino-ethyl benzene, m.p. 150-151°C. Pauchsh (Ber., <u>17</u>, 2802) gives m.p. of Benzoyl p-ethyl amino-benzene as 151°C. This initial crystallisation was conducted/

conducted from alcohol and on evaporation of the alcoholic mother liquors the residues obtained were crystallised from benzene. In this way a small amount of benzanilide, m.p. 159-160°C., was isolated.

(3) Preparation of Amino Ethyl Benzenes.

Ethyl Benzene was prepared by the direct ethylation of benzene by ethylene in presence of anhydrous aluminium chloride. This method has been described by Milligan and Reid (J.A.C.S., 1922, 206) and the method used in the present work is essentially the same except that the speed of stirring has been reduced from 10,000 r.p.m. to 1,500 r.p.m. This reduced rate of stirring has not had an adverse effect on the yields of ethyl benzene as yields of the order of 50% theoretical, calculated on the benzene used without deduction for recovered benzene, have been obtained. The only difficulty experienced was of a mechanical nature. The glass stirrer passed through a small water-jacketed condenser and smooth running of this stirrer was only obtained by fixing two small rings of vulcanite inside the condenser inner tube to act as bearings.

Ethyl benzene has also been obtained by the reduction of acetophenone by the Clemmensen method (Ber., 1913, 1837; ibid. 1914, 53). The yields of ethyl benzene obtained by this method were approximately 50% of the theoretical and could not be raised above this figure by any alteration in the time of heating or of the proportions of reacting substances. Clemmensen claims a yield of 80%

ethyl-benzene/

ethyl benzene by the reduction of acetophenone. This reduction method will be discussed in more detail in a later section.

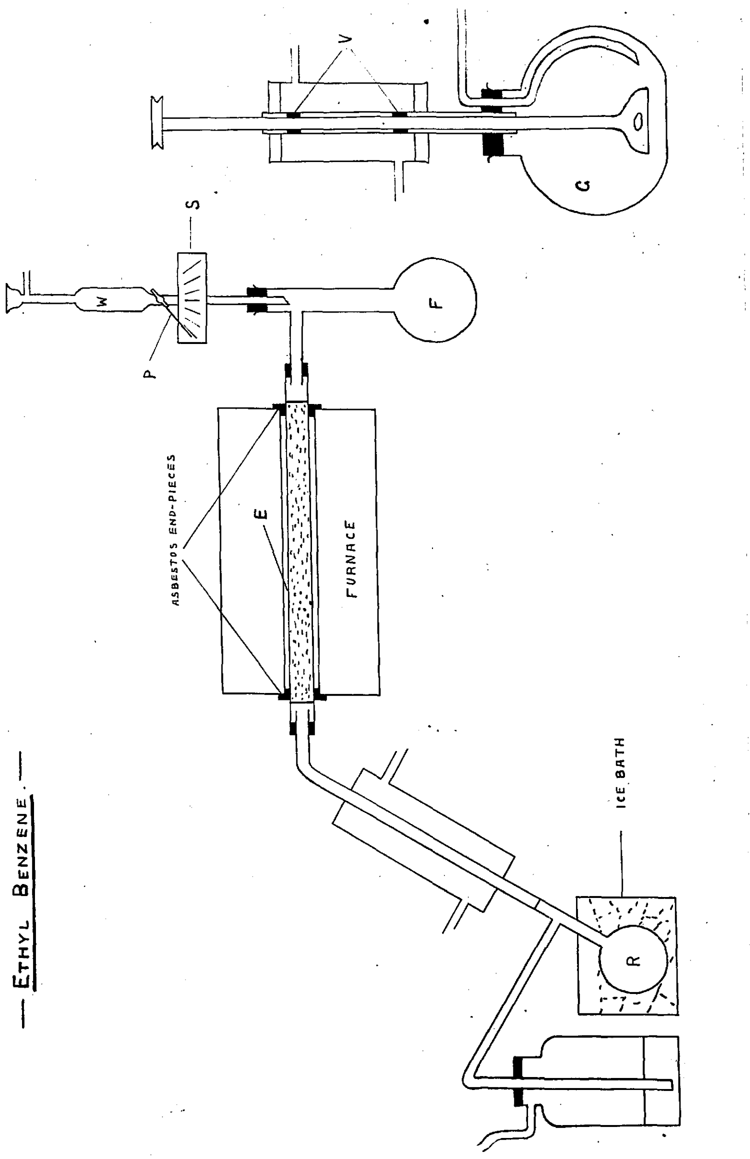
The ethyl benzene was nitrated in the usual way (Beilstein and Kuhlberg, Ann., 1870, 156, 206) but no attempts were made to separate the ortho and para mono-nitro ethyl benzenes thus obtained. This separation has been shown to be difficult by Schultz and Fläckslander (J. pr. 1902, 174, 156) as the boiling points are too close to obtain a satisfactory separation by fractional distillation unless such distillation is conducted on a large scale. (o-nitro ethyl benzene, b.p. 223-224°C.; p-nitro ethyl benzene, b.p. 241-242°C.).

The nitro compounds were reduced by iron filings and hydrochloric acid and the amino compounds were acetylated and fractionally crystallised. According to Pauchsh (Ber., 1884, 17,, 2801) this separation is conducted by leaving the acetyl derivatives in a large volume of water and passing in steam until the liquid becomes milky. In this way the acetyl derivative of p-amino ethyl benzene passes into solution and can be separated from the ortho derivative and unacetylated material. This method is extremely unsatisfactory as the difference of solubility of the two derivatives in water is not sufficiently great to allow of a clean/

a clean separation. A separation was obtained after a prolonged crystallisation from water and petroleum ether. The solubilities of the two acetyl derivatives were investigated. They are both easily soluble in cold ether, alcohol, ethane tetra-chloride, acetone, and benzene and fairly easily soluble in chloroform. The ortho compound is more soluble in water than the para and is less soluble in petroleum ether.

A similar criticism of this method has been made by Day, (J.CS., 1930, 252-256).

From the acetyl derivative the free amines were obtained by hydrolysis with hydrochloric acid and neutralisation of the hydrochloride with sodium hydroxide solution. The hydrochloride of o-amino ethyl benzene is less soluble in dilute hydrochloric acid than is the hydrochloride of the para compound and this may prove to be a more satisfactory method of separating ortho and para amino ethyl benzene.



ETHYL BENZENE.

(3) Preparation of Amino Ethyl Benzenes.

Experimental.

Preparation of Ethyl Benzene by direct Ethylation of Benzene.

In the accompanying sketch the apparatus used is shown diagrammatically. The reaction vessel, G., was a 500 cc. wide necked flask carrying a stirrer and gas inlet tube which was bent to avoid contact with the stirrer. The stirrer was of the Witt type and passed through a small water-cooled condenser. Small vulcanite rings, V, were arranged inside the condenser to serve as bearings for the stirrer. The alcohol was delivered at a constant rate by allowing it to drop from a funnel, W, to the tap of which was attached a glass pointer, P, which recorded on a scale, S. The pressure of the alcohol was kept constant by means of a suitable weir which was so arranged that the pressure of the alcohol was greater than any normal back pressure which might be developed in the apparatus during the experiment.

The tube, E, situated in an electric furnace, was packed with bauxite which had previously been ignited to 850°C. and passed through a 400 mesh sieve. The temperature of the furnace was recorded by a thermocouple (not shown in the sketch) and was maintained at 350°C.

The alcohol flow was so arranged that 36 cc. of absolute alcohol were vapourised per hour in the small flask, F, which was heated in a Woods alloy bath. This rate of alcohol flow gives an approximate yield of 50 gms. ethylene during three hours. Excess alcohol and water were condensed by an outlet condenser and trapped in a small receiving flask, R, cooled in an ice bath. The ethylene was finally dried by passing through a wash bottle containing concentrated sulphuric acid.

116 gms. pure benzene were placed in the reaction flask and 25 gms. anhydrous aluminium chloride were added. The stirrer was started and a speed of stirring of 1,500 r.p.m. was maintained. The benzene was heated to 70-75°C. and the ethylene passed in at the rate of approximately 50 gms. in three hours.

After three hours the reaction mixture was removed from the flask and allowed to stand in a separating funnel. Two layers formed, the top one was almost colourless and the lower one was dark brown and very viscous. This lower layer was discarded and the upper one was washed with dilute hydrochloric acid to remove suspended aluminium hydroxide. It was finally washed with water and dried over anhydrous calcium chloride. On distillation the following fractions were collected.

Fraction 1	80-100°C.	15.6 gms.
Fraction 2	100-150°C.	67.4 gms.
Residue above	150°C.	18.5 gms.

The first two fractions were mixed and carefully fractionated. 74 gms. of ethyl benzene, b.p. 134-136°C., were obtained. This represents a yield of approximately 50% of the theoretical calculated on the benzene used initially without taking into consideration the benzene recovered.

Similar results were obtained from subsequent experiments.

Preparation of Ethyl Benzene by Clemmensen Reduction of Acetophenone.

Experimental.

200 gms. of granulated zinc were washed with dilute hydrochloric acid and then with water and left in contact with 400 cc. of approximately 5% aqueous mercuric chloride over one hour. The liquor was decanted and 300 cc. water and 150 cc. concentrated hydrochloric acid were added. This mixture was heated under reflux on a sand bath until the evolution of hydrogen was vigorous. 50 gms. acetophenone (b.p. 198-201°C.) were added and the heating was continued for eight hours. Occasional additions of concentrated hydrochloric acid were made during this time in order to keep up a brisk evolution of gas. A pale yellow oil formed on the surface and was separated from the acid zinc chloride solution. The yellow oil was dried over anhydrous calcium chloride and distilled at atmospheric pressure. Distillation was continued until the temperature reached 138°C. at which point decomposition with evolution of water took place. The distillate was refractionated and the fraction boiling between 134 and 136°C. was collected. Weight 21 gms. of a clear mobile liquid. Percentage yield of ethyl benzene approximately 50.

Nitration of Ethyl Benzene.

150 gms. of ethyl benzene (b.p. 134-136°C.) were nitrated in a 500 cc. flask fitted with a mechanical stirrer, thermometer and dropping funnel. The acid mixture consisting of 124 gms. of nitric acid (Sp.Gr. 1.41) and 161 gms. of sulphuric acid (Sp.Gr. 1.84) was added at such a speed that the temperature did not rise above 30°C. After the reaction mixture had stood overnight it was heated for three hours on a boiling water bath. The acid layer was run off and the nitro ethyl benzene was washed with dilute sodium hydroxide solution and then with water. It was then dried over anhydrous calcium chloride and distilled. The fraction boiling 220-250°C. was collected. Weight 170 gms. Percentage yield 80.

Reduction of Nitro Ethyl Benzene.

120 cc. water, 200 gms. iron filings and 23 cc. concentrated hydrochloric acid were heated on a water bath to 90-95°C. The temperature was maintained between these limits and 200 gms. of nitro ethyl benzene were added in small quantities. After all the nitro compound had been added the heating was continued until the characteristic smell of the nitro compound had disappeared. The amino ethyl benzene was then steam distilled, separated from the steam distillate and dried over solid potassium hydroxide. Yield 124 gms. Percentage yield 77.

Separation of ortho and para Amino Ethyl Benzene.

77 gms. of the mixed o-and p-amino ethyl benzene were heated on a water bath with 65 gms. of acetic anhydride. The mixture was poured into water and solidified. The solid was not filtered but the liquor was heated by passing in steam. When the liquid became milky it was decanted from the oil. This process was repeated five times and the following fractions were obtained:-

(1) From first three extractions.......... m.p. 50-60°C.
(2) From the fourth and fifth extractions m.p. 52-60°C.
(3) From the sixth extraction............. m.p. 53-73°C.

An oily residue, which solidified to a brownish pink solid, remained.

The three fractions obtained above were mixed and after a prolonged crystallisation from water and petroleum ether (60-80°C.) 6.2 gms. of the acetyl derivative of p-amino ethyl benzene, m.p. 92°C. and 11.5 gms. of the acetyl derivative of o-amino benzene, m.p. 110-111°C., were obtained.

The intermediate fractions from the above fractional crystallisation were separated roughly into the crude para derivative, m.p. 88-94°C., and the crude ortho derivative, m.p. 100-106°C., by fractional crystallisation from water. The solutions were made in water at about/

about 50°C. to avoid separation of oil and were carefully seeded with pure para compound.

The crude para derivative was purified by crystallisation from alcohol and melted at 92°C. (pure, m.p. 94°C.). Total weight obtained 22 gms.

The crude ortho compound was crystallised from benzene and melted at 110-111°C.
Total weight obtained 30 gms.

The melting points of the pure derivatives are those given by Pauchsh (loc. cit.).

These acetyl derivatives were hydrolysed by heating under reflux with hydrochloric acid (50 cc. conc. hydrochloric acid and 50 cc. water) and the resulting hydrochlorides were decomposed with sodium hydroxide solution. The bases were separated and dried over solid potassium hydroxide.

p-Amino Ethyl Benzene.

22 gms. of the acetyl derivative were hydrolysed as above. 7 gms. separated as the hydrochloride and 11 gms. were recovered on neutralisation of the hydrochloride liquor. The total yield, 16 gms., represents an almost quantitative recovery of the base.

o-Amino Ethyl Benzene.

30 gms. of the acetyl derivative were hydrolysed. 20 gms. separated as the hydrochloride and 2 gms. were recovered/

recovered on neutralisation of the hydrochloride liquor. Total yield of base 17 gms., representing 74% recovery.

From consideration of the hydrolysis of these acetyl derivatives it is evident that the hydrochloride of o-amino ethyl benzene is less soluble in hydrochloric acid than is the hydrochloride of p-amino-ethyl benzene and it seems that a separation of the amino-ethyl benzenes as hydrochlorides should be possible. This separation, however, has not been attempted in the present work.

Preparation of Phenols by Diazotisation of Amines.

The method used has been the same in every case. The amine was dissolved in 30% sulphuric acid and the solution was cooled in ice; constant mechanical stirring being maintained. A solution of sodium nitrite was added slowly until the usual end point was indicated with starch-iodide paper. The solution of the diazonium sulphate was decomposed by adding it, in small quantities, to a dilute solution of sulphuric acid containing sodium sulphate through which steam was passing. The boiling point of this solution was approximately 110°C. The phenol was thus removed as soon as it was produced from the diazonium sulphate. When the phenols were liquid they were extracted from the steam distillate with ether and the ether extract was dried over anhydrous sodium sulphate. Solid phenols were filtered off from the steam distillate and crystallised from appropriate solvents.

1:3-Dimethyl-4-hydroxy-benzene.

20 gms. of 1:3-dimethyl-4-amino-benzene were diazotised and gave 13 gms. of the xylenol, b.p. 209-211°C. Percentage yield 65. The product was a pale yellow liquid. Jacobsen (Ber., 11, 24) gives b.p. 211.5°C.

1:4-Dimethyl-2-hydroxy-benzene.

20 gms. of 1:4-dimethyl-2-amino-benzene gave 12 gms. of the crude xylenol. This was crystallised from petroleum ether and was obtained in glistening plates, m.p. 75°C. Yield of pure product 10 gms. Percentage yield 50. Jacobsen (loc. cit.) gives m.p. 74.5°C.

1:2-Dimethyl-4-hydroxy-benzene.

7 gms. of 1:2-dimethyl-4-amino-benzene gave 4 gms. of a crude product which on crystallising from water melted at 61.5 - 62.5°C. Weight 3 gms. Percentage yield 43. Jacobsen (Ber., 17, 161) gives m.p. 62.5°C.

1:3-Dimethyl-2-hydroxy-benzene.

10 gms. of 1:3-dimethyl-2-amino-benzene gave 7.5 gms. of white needles which on crystallising from petroleum ether (40-60°C.) melted at 47-48°C. Weight 6.5 gms. Percentage yield 65. Noelting (Ber., 21, 2829) gives m.p. 49°C.

Mesitol, 1:3:5-Trimethyl-2-hydroxy-benzene.

10 gms. mesidine gave 7.0 gms. mesitol after crystallisation from petroleum ether (40-60°C.), m.p. 70°C. Percentage yield 70. Biedermann, Ledoux (Ber., 8, 250) give m.p. 68-69°C.

Pseudo-Cumenol, 1:2:4-Trimethyl-5-hydroxy-benzene.

10 gms. of pseudo cumidine gave 6.5 gms. of long white needles after crystallisation from petroleum ether (60-80°C.), m.p. 71°C. Percentage yield 65. Wallach, Heusler (Ann., 243, 234) give m.p. 71-72°C.

o-Ethyl Phenol.

17 gms. of o-amino ethyl benzene gave 12 gms. of o-ethyl phenol, a pale yellow liquid, b.p. 202-203°C. Percentage yield 70.

p-Ethyl Phenol.

16 gms. of p-amino ethyl benzene gave 8 gms. of p-ethyl phenol, b.p. 212°C., m.p. 45°C. Percentage yield 50. Bèhal and Choay (Bl. (3), 11, 209) give m.p. 45-46°C., b.p. 218.5-219.5°C.

Section (b)

Preparation of Hydroxy-Aldehydes and Ketones.

Fries Isomerism.

The Fries reaction was introduced by Fries and Fink (Ber., 1908, 41, 4271-4284) who showed that, by heating the chloracetyl derivatives of phenols with aluminium chloride, a change took place whereby o-hydroxy compounds were produced. The yields of o-hydroxy compounds ranged from 90%, in the case of the chloracetyl derivative of p-cresol, to 50% when the corresponding derivative of m-cresol was used. The results obtained by this method were better than when the reaction was carried out in one stage by the interaction of phenol, chloracetyl chloride and aluminium chloride as, in this latter case, more than one chloracetyl group was introduced into the nucleus. The reaction is of general application and has been applied to a number of phenol esters. The acyl groups enter the benzene nucleus in positions either ortho or para to the hydroxyl group. Fries and Witt (Ber., 1914, 47, 3219) considered this reaction to be intra-molecular and this view has been more recently advocated by von Auwers (Auwers and Mauss, Ann, 1928, 464, 293). This is in contradiction to the opinion of Rosenmund and Schnurr (Ann., 1928, 460, 56-98) who contend/

contend that the reaction takes place by the initial formation of an acid chloride which subsequently reacts with the phenol in the presence of aluminium chloride as in the Friedel-Crafts reaction. These workers, therefore consider the reaction to be inter- and not intra-molecular. In support of this suggested mechanism Rosenmund and Schnurr point out that simultaneous Fries treatment of 4-methyl-2-chloro-phenyl acetate and p-tolyl benzoate gives 3-chloro-2-hydroxy-5-methyl benzophenone and 2-hydroxy-5-methyl-acetophenone in addition to 3-chloro-2-hydroxy-5-methyl-acetophenone and 2-hydroxy-5-methyl-benzophenone. If the change were intramolecular then only the last two compounds should be produced. A similar view has been advanced by Skraup and Poller (Ber., 57, 2033) to explain a similar transformation using zinc chloride in place of aluminium chloride. By the action of zinc chloride on m-tolyl acetate at 140-160°C., Skraup and Poller have obtained o-acetyl-m-cresol and a small amount of m-cresol. The para compound (p-acetyl-m-cresol) was not formed at atmospheric temperature and therefore cannot be an intermediate stage in the production of the ortho derivative. With phenyl acetate both the o- and p-hydroxy-ketones are produced when the reaction is carried out using zinc chloride. If the mixture of m-tolyl acetate and zinc chloride at atmospheric temperature is saturated with hydrogen chloride then both o- and p- compounds are obtained.

obtained. As the yield of the p-hydroxy-ketone increases the yield of the ortho decreases. Phenyl acetate saturated with hydrogen chloride in the presence of zinc chloride gives exclusively p-hydroxy-acetophenone. Skraup and Poller believe that the ester undergoes fission, probably into chlorozinc tolyl oxide, $C_6H_4Me.O.ZnCl$, and acetyl chloride in the case of m-tolyl acetate.

Auwers (loc.cit.) states that in repeating Rosenmund and Schnurr's experiment with a mixture of 3-chloro-p-tolyl acetate and p-tolyl benzoate he obtained the products originally isolated and also 3-chloro-p-acetyl tolyl benzoate. This interchange of acyl groups is stated to be quite common when phenol esters of different acids are heated together with aluminium chloride but such interchange does not occur in every case and seems to depend on the nature of the substances concerned. Thus a mixture of phenyl acetate and p-tolyl chloroacetate gave only 2- and 4-hydroxy acetophenone and 2-hydroxy-5-methyl-phenacyl chloride. These products are in agreement with what would be expected from intramolecular arrangement.

Cox (J.A.C.S., 1930, 52, 352) has studied the mechanism of the Fries reaction and has arrived at the conclusion that the rearrangement is intermolecular. The reaction has been conducted in carbon disulphide in the presence of diphenyl ether. From o-tolyl acetate Cox has obtained/

obtained p-acetyl-o-cresol, o-acetyl-o-cresol, cresol, diphenyl ether and p-acetyl diphenyl ether. This production of p-acetyl diphenyl ether points to the initial presence of acetyl chloride and, in this case, the explanation of the interchange of acyl groups given by Auwers does not hold.

In the course of the present work the Fries reaction has been carried out on phenyl acetate, o-, m-, and p-cresyl acetates, phenyl propionate and phenyl-n-butyrate. The general method has been to conduct the reaction by adding the phenol ester (20 gms.) to a suspension of aluminium chloride (25 gms.) in dry carbon disulphide (25 cc.). The final temperature and the time of heating has been varied in individual cases.

In the case of phenyl acetate both o- and p-hydroxy-acetophenone have been obtained by refluxing the carbon disulphide solution for 2½ hours, removing the carbon disulphide and heating the residue at 115-120°C. for 1½ hours. The p-isomer predominates under these conditions. One experiment was conducted at 135-140°C. and, in this case the final heating was continued for 2½ hours. The yield of p-compound obtained was lower than that previously produced but the yield of the o-compound was practically the same as before. This may be due to the fact that the p-hydroxy-acetophenone/

acetophenone may be more easily resinified than o-hydroxy-acetophenone and the continued heating would tend to increase this resinification. The amount of resinified material obtained in this case was greater.

A series of experiments were conducted at lower temperatures and peculiar results were recorded. At 95-100°C. 20 gms. of phenyl acetate gave 2 gms. of p-hydroxy-acetophenone, 1 gm. of unchanged ester and 11 gms. of phenol. The only explanation for this peculiar result is that the aluminium chloride used was known to be of poorer quality than that previously employed. Similar results were obtained using the same aluminium chloride at a temperature of 60°C. and at atmospheric temperature. This production of p-hydroxy-acetophenone agrees with the results obtained by Rosenmund and Schnurr (loc.cit.), who used nitro-benzene as a solvent while Auwers and Jannsen (Ann., 1930, 483, 51) working without any solvent find that mild conditions favour the production of o-hydroxy-ketones. The phenol from the reaction described above was obtained in an almost pure state. When, however, good quality aluminium chloride was used o-hydroxy-acetophenone was produced at 70-80°C. and also at atmospheric temperature. The yield of o-hydroxy-acetophenone in the latter case (at atmospheric temperature) was lower than that at the higher temperature (70-80°C.). The p-hydroxy-ketone was obtained in greater amount at atmospheric temperature/

temperature than at 70-80°C. The amount of phenol isolated using better quality aluminium chloride was much smaller. The explanation of this behaviour may be that the impure aluminium chloride contains free hydrochloric acid which in conjunction with the aluminium chloride reacts in the same way as the zinc chloride in phenyl acetate saturated with hydrogen chloride which gives exclusively p-hydroxy-acetophenone. (Skraup and Poller, loc.cit.) The work of Minaer (J. Russ. Phys. Chem. Soc., 1926, 58,729-36) also seems to favour this view. Minaer obtained a 28% yield of p-hydroxy-acetophenone by the action of dry aluminium chloride on phenyl acetate saturated with hydrogen chloride. The larger amount of phenol obtained when using the impure aluminium chloride may be accounted for if the reaction is intermolecular since it is known that the function of the aluminium chloride in the Friedel-Craft reaction is not strictly catalytic as the yields of Friedel-Craft products increase with an increase in the amount of aluminium chloride.

A similar set of experiments were carried out on o-cresyl acetate. In this series the formation of the p-hydroxy ketone preponderates at atmospheric temperature but the yield of o-hydroxy-ketone does not increase markedly until the temperature reaches 160-165°C. At 155-160°C. with ½ an hour's heating the yield of p-compound was in excess of that produced by heating for 2 hours at 130-135°C. while the yield of the o-compound was practically unchanged. At 160-165°C./

165°C. with one hour's heating the yield of the o-hydroxy ketone was doubled while no para-compound was obtained. This again seems to favour the view of Rosenmund and Schnurr who state that mild conditions favour p-migration while drastic conditions favour o-migration. A sufficiently large number of experiments was not, however, done to justify any dogmatic comment on this matter.

m-Cresyl acetate has also been rearranged under Fries conditions and, although there are three free positions, two ortho and one para, the only hydroxy-ketones obtained were 4-hydroxy-2-methyl-acetophenone and 2-hydroxy-4-methyl-acetophenone. In one of the experiments conducted at ordinary temperature a fraction from the steam distillate boiled at 110-115°C.$_{9mm}$. Anschutz and Scholl (Ann., 379, 342) gives the boiling point of 2-hydroxy-4-methyl-acetophenone as 105-106°C. under 9 mm. pressure. It was thought that the higher boiling fraction might contain the other possible isomer, 6-hydroxy-2-methyl-acetophenone. The oxime of this fraction was prepared but, on fractional crystallisation, the only product obtained was the oxime of 2-hydroxy-4-methyl-acetophenone. The two hydroxy-ketones actually obtained were, as in all other cases, separated by steam distillation since o-hydroxy-ketones are volatile in steam while p-hydroxy-ketones are not. At a temperature of 140°C. the yield of the ortho hydroxy-ketone/

ketone preponderates and as the final temperature is lowered to 100°C. the yield of the ortho compound decreases with a corresponding increase in the para compound. When the reaction is carried out at atmospheric temperature no para compound results after 17 hours and half of the ester is recovered unchanged. When the time is increased to 48 hours the yield of the para compound is small and there is still a considerable amount of unchanged ester. When the reaction is conducted at 47°C. ortho and para compounds are produced in equivalent quantities and m-cresol is also among the reaction products. The m-cresol is separated from the hydroxy-ketone since the sodium salts of o-hydroxy-ketones are relatively insoluble in 5/N sodium hydroxide solution. It appears to be immaterial to the final yield if the aluminium chloride is added all at once or if only half is added at the start and the rest after the reaction has proceeded for half the total time.

The experiments with phenyl acetate using poor quality aluminium chloride suggested the idea, that, if the Fries reaction is intermolecular with the second stage a Friedel-Craft reaction, then a decrease in the amount of aluminium chloride should lead to a decrease in the yield of hydroxy-ketones and favour an increase in the amount of the free phenol. If, on the other hand, the reaction is intra-molecular, then a decrease in the amount of aluminium chloride/

chloride should lead to a decrease in the yield of hydroxy-ketones accompanied by an increase in the amount of free ester.

Experiments on these lines were conducted with m-cresyl acetate. 20 gms. of m-cresyl acetate were treated with 12.5 gms. (half the previous amount) of aluminium chloride in 25 cc. carbon disulphide at 47°C. The yield of p-hydroxy-ketone was decreased but the amount of o-hydroxy-ketone remained the same. The neutral portion, which was obtained in all experiments by rendering the steam distillate alkaline and extracting with ether, was not m-cresyl acetate as it boiled from 210 to 232°C., the temperature rising rapidly from 210°C. (m-cresyl acetate, b.p. 211°C.). This might have been the acetyl derivative of 2-hydroxy-4-methyl-acetophenone as it did not dissolve immediately in dilute sodium hydroxide solution but did so on heating. The hydroxy-ketone, (oxime, m.p. 103°C), was extracted from this alkaline solution after acidification. This ease of hydrolysis seemed suspicious so a larger quantity of m-cresyl acetate was treated under the same conditions. In this experiment the yields of ortho and para hydroxy-ketones were of the same order but the neutral portion definitely contained unchanged ester. The lower boiling fraction, 210-220°C., gave an oxime, m.p. 103°C. (formed by treating with hydroxylamine hydrochloride and potassium/

potassium acetate), showing the presence of 2-hydroxy-4-methyl-acetophenone (oxime, m.p. 103°C.; Auwers, Ber., 1925, 58, B, 26-36). Thus the higher boiling neutral (?) portions from the previous experiment must have been 2-hydroxy-4-methyl-acetophenone, b.p. 245°C. $_{760mm.}$ (Eykmann, C. 1904, i, 1597). It does seem strange however, that only in these two latter experiments was any hydroxy-ketone found in admixture with the recovered ester. This extraction of o-hydroxy-ketone from alkaline solution must be analogous to the extraction of o-substituted phenols. Vavon and Zaharia, (C.r. 1928, 187, 346), have found that the acidity of phenols depends on the nature and position of the substituent groups, those in the ortho position diminishing the acid character to the greatest extent. A similar observation has been made by Sandulesco and Girard (Bull. soc. chim., 1930, 1300) in the case of o-hydroxy-ketones. They found that 90% of o-heptoyl phenol could be extracted from alkaline solution by ether.

Fries reaction was also carried out on p-cresyl acetate, phenyl propionate and phenyl-n-butyrate with the production of 6-hydroxy-3-methyl-acetophenone, o-and p-hydroxy-propiophenone and o- and p-hydroxy-n-butyro-phenone respectively. The reaction conditions were not varied. The method of separation of o- and p-hydroxy-propiophenone used by Hartung, Munch, Miller and Crossley, (J.A.C.S., 1931 4149), who filter off the solid p-hydroxy-ketone from the mixed ketones is not so satisfactory as separation by steam distillation which gives a much purer crude product.

The work in this section has indicated a few abnormalities in the Fries reaction and that these points have not been followed up is due to the fact that, in the present work, the production of hydroxy-ketones rather than an investigation of the reaction mechanism, was the prime object. It is, however, intended to investigate the action of aluminium chloride in carbon disulphide on acetyl chloride and to determine if any additive compound results. Any such additive compound should be capable of producing hydroxy-ketone by interaction with phenol. If such a compound is formed this would account for the continued failure to isolate any acid chloride in the Fries reaction.

Section (b) Experimental.

Fries Reaction.

Preparation of Esters.

Phenyl Acetate.

50 gms. of phenol were placed in a round bottomed flask attached to a reflux condenser and 45 gms. acetyl chloride were added slowly. The reaction started at once but as it was endothermic it was necessary to heat gently. When all the acid chloride had been added the mixture was heated gently until the evolution of hydrogen chloride ceased. The ester was washed with dilute sodium hydroxide solution and was then dried over anhydrous calcium chloride. The fraction boiling between 193 and 195°C. was collected. Weight 64 gms. Percentage yield 92.

The other acetates were prepared in the same manner.

o-Cresyl Acetate.

50 gms. of o-cresol and 38 gms. of acetyl chloride gave 62 gms. of o-cresyl acetate, b.p. 205-207°C. Percentage yield 89.

m-Cresyl Acetate.

50 gms. of m-cresol and 38 gms. acetyl chloride gave 60 gms. of m-cresyl acetate, b.p. 211°C. Percentage yield 86.

p-Cresyl Acetate.

50 gms. of p-cresol and 38 gms. of acetyl chloride gave 65 gms. of p-cresyl acetate, b.p. 211-213°C. Percentage yield 93. The crude ester was pale green in colour but

turned pale yellow on heating and distilled clear.

Phenyl Propionate.

70 grams of propionic acid (b.p. 139-141°C.) were mixed with 89 grams of phenol and 115 grams thionyl chloride was added slowly through a reflux condenser. The flask was heated intermittently by a small flame during the addition of the thionyl chloride. When all the thionyl chloride had been added the heating was continued until no more gas was evolved. The resulting red liquid was distilled and the fraction between 200 and 210°C. was collected. This fraction was a clear liquid which boiled chiefly between 207 and 210°C. Weight 110 grams. Percentage yield 79.

Phenyl-n-Butyrate.

50 grams n-butyric acid, 59 grams phenol and 75 grams thionyl chloride gave 70 grams of phenyl-n-butyrate, b.p. 220-226°C. Percentage yield 70.

Fries Isomerism on Phenyl Acetate.

The results in tabular form are given on the extending page 136.

(1)

25 grams of powdered aluminium chloride were suspended in 25 cc. of dry carbon disulphide and 20 grams of phenyl acetate were slowly added. Hydrogen chloride was evolved and the mixture was refluxed on an oil bath until the evolution of gas had practically ceased. The carbon disulphide was distilled off and the residue, a pale brown honey-combed solid, was heated at 135-140°C. A further evolution of hydrogen chloride commenced and the heating was continued at the same temperature until the gas evolution ceased completely. (about 3 hours heating). The product was left overnight and then the reddish brown reaction mass was decomposed with hydrochloric acid (1 part conc. hydrochloric acid and 1 part water). A reddish oil separated and was steam distilled until the steam distillate gave only a faint colouration with ferric chloride solution. The residue from the steam distillation was filtered while hot through a hot water funnel and on standing deposited crystals. The residue left on the filter was a dark red tar which solidified. The separated crystals were filtered and the filtrate was used to extract the tar from the first filtration.

A further crop of crystals was obtained and this was mixed with first crop and crystallised from water in very pale yellow needles, m.p. 107-108°C. Weight of p-hydroxy-acetophenone 4.4 grams. Percentage yield 22. M.P. given for p-hydroxy-acetophenone 107°C. (Klingel, Ber., 18, 2691).

Steam Distillate.

The steam distillate was made alkaline with sodium hydroxide and extracted with ether...Neutral steam distillate. The sodium hydroxide was neutralised by mineral acid and the liquor was again extracted with ether..Acidic steam distillate. Both distillates were dried over anhydrous sodium sulphate.

Neutral Steam Distillate.

On distillation of the ether there was practically no residue.

Acidic Steam Distillate.

After removal of the ether the residue was distilled and boiled between 190 and 218°C. On redistillation two fractions were collected.

Fraction 1. b.p. 190-205°C.

This fraction gave, on bromination, a bromo derivative, m.p. 90-91°C. This bromo derivative gave no depression of melting point when mixed with tribromo-phenol, m.p.93°C.

Fraction 2. b.p. 205-218°C. Weight 5.5 grams.

This fraction was a pale yellow liquid and boiled chiefly between 210 and 215°C. Tahara (Ber., 25, 1309) gives b.p./

b.p. 213°C. 717 mm. for o-hydroxy-acetophenone.

Percentage yield obtained 27.5.

Phenyl Acetate (2).

The quantities and general conditions were as before but the carbon disulphide suspension was refluxed for 2½ hours and, after the carbon disulphide had been removed, the residue was heated at 115-120°C. for 1½ hours.

Steam Distillation Residue.

From the steam distillation residue 10.5 grams. of a clear crystalline solid mixed with some brown particles was obtained. On standing the crystals seemed to effloresce. On crystallisation from water after boiling with animal charcoal a first crop of thick needles, m.p. 107-108°C., was obtained. On allowing the liquor to stand a further 1.5 gms. crystallised out. This second crop melted first at about 60°C. and completely at 90°C. On being allowed to stand exposed to the air these crystals effloresced and melted at 107-108°C. Total yield 9 grams of p-hydroxy-acetophenone.

Percentage yield 45.

Neutral Steam Distillate.

Practically no residue was obtained on distillation of the ether from extraction of the alkaline steam distillate.

Acidic Steam Distillate.

Distilled and only a very small fraction boiled below 210°C. The fraction 210-220°C. was collected and boiled/

boiled between 213 and 216°C. Weight 5.5 grams. Percentage yield 27.5.......o-hydroxy-acetophenone.

Phenyl Acetate (3).

Conditions and yields similar to (2).

Phenyl Acetate (4).

Quantities as before; carbon disulphide suspension heated under reflux for 2½ hours and the residue after removal of carbon disulphide was heated at 95-100°C. for 1 hour.

Steam Distillation Residue.

2 grams after crystallisation from water, m.p. 107-108°C. The hydrate, which apparently melts between 50 and 60°C., was formed when the substance was crystallised slowly. Percentage yield 10.....p-hydroxy-acetophenone.

Neutral Steam Distillate.

After distillation of the ether there was left a residue of 1 gram of unchanged ester.

Acidic Steam Distillate.

11 grams of a yellow oil which distilled completely between 178 and 185°C...............impure phenol.

Phenyl Acetate (5).

Quantities were as previously. The carbon disulphide suspension was left at ordinary temperature for two days and the carbon disulphide was distilled off under reduced pressure on a water bath heated to about 50°C. The residue was heated at 70-80°C. for 1 hour. On decomposition of the reaction/

reaction product with mineral acid a yellow oil separated and hydrogen sulphide was evolved.

Steam Distillation Residue.

2.5 grams after crystallisation from water, m.p. 106-108°C. Percentage yield 12.5....p-hydroxy-acetophenone.

Neutral Steam Distillate.

This fraction, on removal of the ether, gave less than 1 gram of unchanged ester.

Acidic Steam Distillate.

After distillation of the ether the pale yellow oil which remained was dissolved in 20 cc. warm 5/N sodium hydroxide solution. A sodium salt separated in yellow plates when the solution cooled. This salt was filtered off and decomposed with dilute sulphuric acid. The liberated oil was extracted with petroleum ether and the petroleum ether extract was dried over anhydrous sodium sulphate. On distillation of the solvent the residue distilled between 210 and 215°C. Weight 4 grams. Percentage yield 20...... o-hydroxy-acetophenone.

The liquor from which the sodium salt separated was neutralised and extracted with petroleum ether. The extract was dried over anhydrous sodium sulphate. The solvent was distilled and the residue, 1.5 grams, boiled between 180 and 212°C. .... impure phenol.

Phenyl Acetate (6).

The conditions and the method of working up were the same as in (5) except that the maximum temperature was 60°C.

Steam Distillation Residue.

2 grams after crystallisation from water m.p. 107-108°C. Weight 2 grams. Percentage yield 10 .... p-hydroxy-acetophenone.

Neutral Steam Distillate.

Practically no residue on distillation of the ether.

Acidic Steam Distillate.

7 grams of a pale yellow oil was obtained after distillation of the ether. This was dissolved in 35 cc. of warm 5/N sodium hydroxide solution. On cooling and standing for two days only a very small quantity of crystals separated. These were filtered off and the filtrate was acidified with dilute sulphuric acid. The acidified filtrate was extracted with petroleum ether and the extract dried over anhydrous sodium sulphate. After distillation of the petroleum ether the residue boiled at 180°C. and completely distilled below 210°C. leaving a small brown residue....... chiefly impure phenol.

Phenyl Acetate (7).

The quantities used were as in previous experiments and the carbon disulphide suspension was allowed to stand, protected from atmospheric moisture by a calcium chloride guard tube, for seven days. The product was treated in the usual manner.

Steam Distillation Residue.

2 grams, m.p. 106-107°C. ...... p-hydroxy-acetophenone.

Neutral Steam Distillate.

Practically no unchanged ester.

Acidic Steam Distillate.

Hydrogen sulphide was evolved when the steam distillate was made acid with dilute hydrochloric acid. Residue after distillation of the ether boiled at 180-185°C. and solidified on cooling. Weight 10 grams. ...... phenol.

Phenyl Acetate (8).

The conditions were the same as in (7) except that the reaction was allowed to proceed for 20 hours.

Steam Distillation Residue.

No crystals separated from the filtered steam distillation residue on standing.

Neutral Steam Distillate.

4 grams of a clear liquid, b.p. 192°C., were obtained after distillation of the ether. ...... phenyl acetate/

acetate, (b.p. 193-195°C.).

Acidic Steam Distillate.

The ether was distilled and the residue was dissolved in a slight excess of warm 5/N sodium hydroxide solution. Nothing separated from this solution on standing and it was acidified with dilute hydrochloric acid. The acidified solution was extracted with petroleum ether and the extract was dried over anhydrous sodium sulphate. On distillation of the petroleum ether the residue boiled at 178-183°C. and solidified on cooling. Weight 5 grams. ...... phenol.

Phenyl Acetate (9) Rosenmund's Method.

24 grams of powdered aluminium chloride were suspended in 50 grams of dry nitro-benzene. A slight reaction took place with the liberation of heat and the suspension was cooled before 25 grams of phenyl acetate in 50 grams of nitro-benzene were added. The mixture was allowed to stand at atmospheric temperature for 24 hours. At the end of this period the bulk of the aluminium chloride had disappeared. The reaction product was decomposed by pouring it into water. A dark red liquid separated and was steam distilled.

Steam Distillation Residue.

The residue from the steam distillation was filtered hot but no crystals separated on cooling.

Steam Distillate.

The steam distillate was made alkaline and the nitro-benzene was separated. The steam distillate was then acidified and extracted with ether, A brown oil was left after removal of ether from this extract and this oil was dissolved in a slight excess of warm 5/N sodium hydroxide solution. No crystals separated from this solution which was then acidified and extracted with petroleum ether. The extract was dried over anhydrous sodium sulphate and the petroleum ether was distilled. The residue boiled at 180-185°C. and solidified on cooling. Weight 4 grams. ....phenol.

Phenyl Acetate (10) Rosenmund's Method.

The method used was essentially the same as previously but the quantities of the reacting substances were only half the former amounts. The aluminium chloride was of better quality than that used in the preceeding experiments.

Steam Distillation Residue.

3 grams, 103-105°C. ..... p-hydroxy-acetophenone.

Steam Distillate.

The steam distillate was separated from the nitro benzene by making alkaline and it was then acidified. An ether extraction was conducted and the ether extract was dried over anhydrous sodium sulphate. On distillation of the ether about 3.5 grams of a red liquid was left. This was treated with a concentrated aqueous solution of semi-carbazide/

semi-carbazide hydrochloride and potassium acetate to which had been added a small amount of alcohol. A solid semi-carbazone separated and was filtered off. After crystallisation from alcohol the semi-carbazone melted at 217°C. Analysis gave N (micro) 21.62%. Calculated for $C_9H_{11}O_2N_3$ 21.76%.

.. .. .. o-hydroxy-acetophenone semi-carbazone.

The filtrate from the semi-carbazone preparation was brominated and gave 2 grams of a bromo derivative which, on crystallisation from dilute alcohol, melted at 83-85°C. Mixed m.p. with tribromo-phenol (m.p. 92°C.) 86-88°C.

Fries on Phenyl Acetate.

PHENYL ACETATE

No.	Temp. °C.	Time hrs.	Ortho		Para		Unchanged Ester gms.	Phenol gms.
			b.p. °C.	Wt. Gms.	m.p. °C.	Wt. Gms.		
1	135-140	about 2½	210-215	5.5	107-108	4.4	-	-
2	115-120	1½	213-216	5.5	107-108	9.0	-	-
3	115-120	1½	213-216	5.5	107-108	8.5	-	-
4	95-100	1		-	107-108	2.0	1.0	11.0
5	70-80	1	210-215	4.0	107-108	2.0	Less than 1 gram	1.5
6	60	1		-	107-108	2.0	-	7.0
7	7 days at atmos.			-	106-107	2.0	-	10.0
8	20 hrs.at atmos.			-		-	4.0	5.0
9	24 hrs. at atmos.			-		-	-	4.0
10	24 hrs.at atmos.			abt. 1.5	103-105	3.0	-	- 1.0

Fries on o-Cresyl Acetate.

The results in tabular form are given on the extending page 142.

(1)

The general conditions and method of working up the products were the same as in the case of phenyl acetate. The carbon disulphide suspension was refluxed for 2½ hours after the addition of 20 grams m-cresyl acetate. The carbon disulphide was removed on a water bath under reduced pressure and the residue was heated at 135-140°C. for 1½ hours.

Steam Distillation Residue.

The steam distillation residue was filtered hot and the crystals which separated on cooling were recrystallised from water after boiling with animal charcoal. White prisms, m.p. 106-107°C. Weight 8.5 grams. Percentage yield 42.5.

..... 4-hydroxy-3-methyl-acetophenone, m.p. 104°C. (Klingel, Ber., 18, 2699,).

Neutral Steam Distillate.

Practically no unchanged ester was recovered.

Acidic Steam Distillate.

The residue, after distilling off the ether, was fractionated under a pressure of 11 mm.

Fraction (1). Up to 105°C. 2 grams, pale yellow liquid.

Fraction(2). 105-110°C. 4 grams, pale yellow liquid.

..... 2-hydroxy-3-methyl-acetophenone, b.p. 106-107°C. 10.5mm. Anschütz and Scholl (Ann., 379, 342).

o-Cresyl Acetate (2)

The same quantities of reacting substances, i.e. 20 grams ester, 25 grams aluminium chloride and 25 cc. carbon disulphide, were treated under the same conditions as in (1) and the following yields were obtained.

4-hydroxy-3-methyl-acetophenone, 7 grams, m.p. 107-108°C.

2-hydroxy-3-methyl-acetophenone, 105-110°C. 11mm. 4.5 grams.

2 grams boiling up to 105°C. 11 mm. were also obtained.

o-Cresyl Acetate (3)

The same quantities as before were used and the final heating was conducted at 130-135°C. for two hours. Three such experiments were conducted and the portion non-volatile in steam was worked up separately in each case. The three steam distillates were mixed.

Steam Distillation Residue.

(a) 8.0 grams, m.p. 104-105°C.

(b) 8.0 grams, m.p. 105°C. 4-hydroxy-3-methyl-acetophenone.

(c) 10.0 grams, m.p. 106-107°C.

Neutral Steam Distillate.

Practically no unchanged ester.

Acidic Steam Distillate.

The mixed acidic steam distillates were extracted with ether and the extract was dried over anhydrous sodium sulphate. The ether was distilled and the residue was fractionated under 11mm. pressure.

Fraction (1) Up to 105°C. 3.0 grams,

Fraction (2) 105-110°C. 12.0 grams..... 2-hydroxy-3-methyl-acetophenone.

o-Cresyl Acetate (4).

The final heating was conducted at a temperature of 155-160°C. for half an hour.

Steam Distillation Residue.

From the hot filtered solution 12 grams solid separated on cooling. On recrystallisation from water this yielded 10 grams, m.p. 106-107°C. .... 4-hydroxy-3-methyl-acetophenone.

Acidic Steam Distillate.

Fraction (1) Up to 105°C. 11mm. 2 grams.

Fraction (2) 105-110°C. 11mm. 4 grams. ..... 2-hydroxy-3-methyl-acetophenone.

o-Cresyl Acetate (5).

The residue, after refluxing in carbon disulphide for two and a half hours, was heated at 160-165°C. for one hr.

Steam Distillation Residue.

The residue from steam distillation was filtered hot but no crystals separated from the filtrate. The residue from this filtration was a very tarry material.

Acidic Steam Distillate.

9.5 grams, b.p. 105-110°C. 11mm. ...... 2-hydroxy-3-methyl-acetophenone.

During steam distillation hydrogen sulphide was evolved.

o-Cresyl Acetate (6).

50 grams powdered aluminium chloride were suspended in 50 cc. dry carbon disulphide and 40 grams o-cresyl acetate were added. The mixture was refluxed gently for 7 hours and the carbon disulphide was distilled off under reduced pressure on a water bath at a temperature of 45°C. The residue was decomposed by the addition of water when a vigorous reaction with evolution of hydrogen sulphide ensued.

Steam Distillation Residue.

24 grams of crude material which yielded, on crystallisation from water, 20 grams, m.p. 107-108°C. .... 4-hydroxy-3-methyl-acetophenone.

Neutral Steam Distillate.

The neutral steam distillate was distilled under atmospheric pressure and boiled between 205-220°C. Weight 4.0 grams. Hydrogen sulphide was evolved towards the end of the distillation. This fraction probably contains unchanged o-cresyl acetate.

Acidic Steam Distillate.

Fraction (1) up to 105°C. 11mm. 5 grams.

Fraction (2) 105-110°C. 11mm 5 grams .... 2-hydroxy-3-methyl-acetophenone.

The table given on page 142 shows the results obtained in the series of experiments conducted on o-cresyl acetate. In all the experiments with the exception of No 6. 20 grams of the ester were used. In No. 6. double the quantity of all reacting substances was employed. No. 6. was the only experiment in which any considerable quantity of unchanged ester was recovered. In all cases o-cresol was present in the fraction boiling below 105°C. at 11mm. pressure. This substance was positively identified as the dibromo derivative.

Fries on o-Cresyl Acetate.

o-CRESYL ACETATE

No.	Temp. °C.	Time hrs.	Ortho		Para	
			b.p. °C.11mm.	Wt. Gms.	m.p. °C.	Wt. Gms.
1	135-140	1½	105-110	4.0.	106-107	8.5
2	135-140	1½	105-110	4.5	107-108	7.0
3	130-135	2	105-110	12.0	(a) 104-105 (b) 105 (c) 106-107	8.0 8.0 10.0
4	155-160	½	105-110	4.0	106-107	10.0
5	160-165	1	105-110	9.5		-
6	47	7	105-110	5.0	107-108	20.0

m-Cresyl Acetate (1). (Table on Page 152.)

25 grams of powdered aluminium chloride were suspended in 25cc. of dry carbon disulphide and 20 grams of m-cresyl acetate were slowly added. A vigorous reaction took place and the mixture was gently refluxed for 2½ hours. The carbon disulphide was removed by heating on a water bath and the residue, a very viscous material light brown in colour, was heated at 140°C. for 1½ hours. The resulting product was decomposed with water and steam distilled.

Steam Distillation Residue.

The residue from the steam distillation was filtered while hot and the crystals which separated on cooling were recrystallised from water after boiling with animal charcoal. White prisms, m.p. 126-127°C. Weight 2.5 grams. Percentage Yield 12.5. M.P. given in literature for 4-hydroxy-2-methyl-acetophenone, 128°C. (Eykman, C. 1904, i, 1597).

Acidic Steam Distillate.

After distillation of the ether a very pale yellow oil remained and was distilled under 9mm. pressure. Fraction, b.p. 105-108°C. was collected. Weight 12 grams. Percentage yield 60. This fraction boiled chiefly between 105 and 106°C. There was a very small amount of an orange yellow residue which solidified. Anschütz and Scholl, (Ann., 379, 342)

(Ann., 379, 342), give b.p. of 2-hydroxy-4-methylacetophenone as 105-106°C. $_{9mm.}$

m-Cresyl Acetate (2) and (3).

Two experiments were conducted using the same quantities of materials as in (1) and, while the initial heating was the same, the final temperature was maintained at 120°C. for 1½ hours.

Steam Distillation Residue.

(2) 4.0 grams, m.p. 127-128°C.
(3) 3.5 grams, m.p. 126-127°C. 4-hydroxy-2-methyl-acetophenone.

Acidic Steam Distillate.

(2) 11.0 grams, b.p. $_{767}$ 232-42°C.
(3) 11.5 grams, b.p. $_{9}$ 100-109°C. 2-hydroxy-4-methyl-acetophenone.

In (3) there was a small amount of residue which solidified.

m-Cresyl Acetate (4).

The quantities were as before and the final heating was conducted at 100°C. for 1½ hours.

Steam Distillation Residue.

5.0 grams, m.p. 127-128°C. .... 4-hydroxy-2-methyl-acetophenone.

Acidic Steam Distillate.

10.5 grams, b.p. 100-108°C. $_{9mm.}$ 2-hydroxy-4-methyl-acetophenone.

m-Cresyl Acetate (5).

The final heating was conducted at 140°C. for 5 minutes/

Steam Distillation Residue.

1.0 grams, m.p. 127.5°C. 4-hydroxy-2-methyl-

Acidic Steam Distillate.

12.0 grams, b.p. 100-108°C. 9mm. 2-hydroxy-4-methyl-

m-Cresyl Acetate (6).

The initial refluxing was carried on for 1 hour and the final heating for 1 hour at 160°C.

Steam Distillation Residue.

3.0 grams, m.p. 124-126°C. 4-hydroxy-2-methyl-

Acidic Steam Distillate.

Fraction (1)	105-110°C.	9mm.	12 grams.	2-hydroxy-4-methyl-
Fraction (2)	110-115°C.	9mm.	2.5 grams.	

There was a small residue which solidified.

m-Cresyl Acetate (7).

After the addition of the m-cresyl acetate to the suspension of aluminium chloride in carbon disulphide the mixture was allowed to stand for 17 hours at atmospheric temperature. The carbon disulphide was removed as completely as possible by reduction of the pressure at atmospheric temperature. The residue was decomposed with water and steam distilled.

Steam Distillation Residue.

No crystals were deposited after the filtrate from the steam distillation residue had been allowed to stand for several days.

Steam Distillation Residue.

1.0 grams, m.p. 127.5°C. 4-hydroxy-2-methyl-

Acidic Steam Distillate.

12.0 grams, b.p. 100-108°C. 9mm. 2-hydroxy-4-methyl-

m-Cresyl Acetate (6).

The initial refluxing was carried on for 1 hour and the final heating for 1 hour at 160°C.

Steam Distillation Residue.

3.0 grams, m.p. 124-126°C. 4-hydroxy-2-methyl-

Acidic Steam Distillate.

Fraction (1)	105-110°C.	9mm.	12 grams.	2-hydroxy-4-methyl-
Fraction (2)	110-115°C.	9mm.	2.5 grams.	

There was a small residue which solidified.

m-Cresyl Acetate (7).

After the addition of the m-cresyl acetate to the suspension of aluminium chloride in carbon disulphide the mixture was allowed to stand for 17 hours at atmospheric temperature. The carbon disulphide was removed as completely as possible by reduction of the pressure at atmospheric temperature. The residue was decomposed with water and steam distilled.

Steam Distillation Residue.

No crystals were deposited after the filtrate from the steam distillation residue had been allowed to stand for several days.

Neutral Steam Distillate.

The ether extract of the alkaline steam distillate was dried over anhydrous calcium chloride and the ether was distilled. The residue boiled at 210-211°C. Weight 10 grams. ..... m-cresyl acetate (b.p. 211°C.).

Acidic Steam Distillate.

5 grams, b.p. 100-107°C. $_{9mm.}$ 2-hydroxy-4-methyl-

m-Cresyl Acetate (8).

This was conducted in exactly the same manner as (7) only the mixture was allowed to stand for 48 hours.

Steam Distillation Residue.

1.5 grams, m.p. 126-127°C. 4-hydroxy-2-methyl-

Neutral Steam Distillate.

9.0 grams, b.p. 211°C. .... m-cresyl acetate.

Acidic Steam Distillate.

Fraction (1) up to 100°C. $_{9mm.}$ 2.5 grams.

Fraction (2) 100-107°C. $_{9mm.}$ 3.5 grams. 2-hydroxy-4-methyl-

Fraction (1) with bromine water gave a bromo derivative which, after crystallisation from dilute alcohol, melted at 80-82°C. ..... tribromo m-cresol, m.p. 84°C.

Formation of Oximes.

(a) From fraction, b.p. 100-107°C. $_{9mm.}$ from (8)

A portion of this fraction was dissolved in alcohol and hydroxylamine hydrochloride followed by potassium/

potassium acetate was added. The solution was heated gently and diluted largely with water. The crude oxime separated and was washed with water. Crystallised from alcohol in fine needles, m.p. 104°C. (Oxime of 2-hydroxy-4-methyl-acetophenone, m.p. 103°C. Auwers, Ber., 1925, 58, 43).

(b) From Fraction, b.p. 105-110°C. $_{9mm.}$ from (6). The oxime formed in the same manner melted at 102-103°C.

(c) From Fraction, b.p. 110-115°C. from (6) The oxime from this fraction melted at 100-102°C.

m-Cresyl Acetate (9).

25 grams powdered aluminium chloride were suspended in 25 cc. of dry carbon disulphide and 20 grams of m-cresyl acetate were added slowly. The mixture was gently refluxed for 2 hours. The carbon disulphide was distilled off and a semi-solid, pale yellow in colour, was left. On addition of water violent decomposition took place and the oil which separated was steam distilled. The steam distillation residue was filtered while hot and on cooling separated crystals, m.p. 126-128°C. Weight 4.5 grams. The steam distillate was worked up in the usual manner.

Neutral Steam Distillate.

On distillation of the ether 1 gram of unchanged ester, b.p. 210°C, was left.

Acidic Steam Distillate.

The pale yellow oil obtained on evaporation of the ether was dissolved in warm 5/N sodium hydroxide solution. Sodium salts separated and were filtered off. The separated sodium salt was decomposed with dilute hydrochloric acid and extracted with ether. The ether extract was dried over anhydrous sodium sulphate and the ether distilled. The residue was distilled under 9mm. pressure. The chief fraction boiled between 107 and 109°C. and was a pale yellow liquid. Weight 4.5 grams. 2-hydroxy-4-methyl-acetophenone. There was a small amount of high boiling residue which solidified.

The filtrate from the sodium salts gave, on acidification 2 grams of liquid boiling below 210°C. chiefly m-cresol.

m-Cresyl-Acetate. (10).

In this case the general conditions were the same as in (9) but the aluminium chloride was added in two quantities. 12.5 grams were added initially and refluxed for two hours. Then another 12.5 grams aluminium chloride were added and the refluxing continued for another 2 hours.

The steam distillation residue gave 4 grams of crystals, m.p. 120-125°C., which, on recrystallisation from water melted at 126-127°C. Weight 4 grams. 4-hydroxy-2-methyl-acetophenone.

Neutral Steam Distillate.

Practically no residue remained on the evaporation of the ether.

Acidic Steam Distillate.

Insoluble Sodium Salts.

These were decomposed with dilute hydrochloric acid, extracted with ether and the ether extract was dried over anhydrous sodium sulphate. On distillation of the ether the residue boiled between 107 and 109°C. at 9mm pressure. Weight 4 grams. 2-hydroxy-4-methyl-acetophenone.

Soluble Sodium Salts.

The liquid obtained from the sodium hydroxide liquor was distilled at atmospheric pressure. 2.5 grams, b.p. 200-205°C. A small amount of this liquid was brominated with bromine water and the bromo derivative was crystallised from alcohol and melted at 80-81°C. (tribromo-m-cresol, m.p. 84°C.).

m-Cresyl Acetate (11).

In this case the procedure was the same as in the preceding experiment except that only 12.5 grams aluminium chloride was used and the refluxing was continued for 5 hours.

The steam distillation residue gave 1 gram of crystals m.p. 126-127°C. 4-hydroxy-2-methyl-acetophenone.

Neutral Steam Distillate.

On removal of the ether 2 grams of a pale yellow oil remained. This liquid distilled between 210 and 232°C.

Towards the end of the distillation hydrogen sulphide was evolved. This liquid hydrolysed easily with sodium hydroxide solution and the hydrolysis product gave a semi-carbazone which, on crytallisation from alcohol, melted at 228-230°C. Auwers, (Ber., 1925, 58, 36-51) gives the m.p. of the semi-carbazone of 2-hydroxy-4-methyl-acetophenone as 233°C.

Acidic Steam Distillate. Insoluble Sodium Salts.

4.5 grams clear colourless liquid, b.p. 107-109°C. at 9mm. .... 2-hydroxy-4-methyl-acetophenone.

Soluble Sodium Salts.

5.5 grams boiling between 200-208°C. The temperature remained constant at 201°C. while the bulk of this fraction distilled. .... m-cresol.

m-Cresyl Acetate (12).

The conditions were the same as in (11) but double the quantities of reactants were employed.

Steam Distillation Residue.

2.0 grams, m.p. 126-127°C. ..... 4-hydroxy-2-methyl-acetophenone.

Neutral Steam Distillate.

17 grams of a light brown liquid. Distilled at atmospheric pressure.

Fraction (1)	210-220°C. clear liquid	10 grams.
Fraction (2)	220-234°C. very pale yellow	6 grams.

Fraction (1) was redistilled and 6 grams boiled at 210-215°C., 2 grams at 215-225°C. while a small amount of residue remained.

An oxime was formed from fraction 210-215°C. and melted at 103°C. on crystallisation from alcohol. This shows the presence of 2-hydroxy-4-methyl-acetophenone, oxime, m.p. 103°C. From the boiling point this fraction was considered to contain unchanged m-cresyl acetate, b.p. 211°C.

Acidic Steam Distillate. Insoluble Sodium Salts.

4 grams, b.p. 107-109°C. at 9mm. ..... 2-hydroxy-4-methyl-acetophenone.

Soluble Sodium Salts.

10 grams. Distilled at atmospheric pressure. 7 grams distilled between 200 and 204°C. ... m-cresol.

Fries on m-Cresyl Acetate.

m-CRESYL ACETATE

No.	Temp. °C.	Time Hrs.	Ortho		Para		Unchanged Ester Gms.	m-cresol gms.
			b.p. °C. 9mm.	Wt. Gms.	m.p. °C.	Wt. Gms.		
1	140	1½	105-108	12	126-127	2.5	-	-
2	120	1½	232-242 767	11	127-128	4.0	-	-
3	120	1½	100-109	11.5	126-127	3.5	-	-
4	100	1½	100-108	10.5	127-128	5.0	-	-
5	140	5 mins	100-108	12.0	127-128	1.0	-	-
6	160	1	105-110	12.0	124-126	3.0	-	-
7	Atmos	17	100-107	5.0		-	10.0 b.p 210-11	-
8	Atmos	48	100-107	3.5	126-127	1.5	9.0 b.p.211	-
9	47	2	107-109	4.5	126-128	4.5	1.0 b.p.210	2.0
10	47	2	107-109	4.0	126-127	4.0	-	2.5
11	47	5	107-109	4.5	126-127	1.0	2.0 b.p.210-32	5.5
12	47	5	107-109	4.0	126 127	2.0	17.0	7.0 200-204°C.

p-Cresyl Acetate.

25 grams of powdered aluminium chloride were suspended in 25 cc. dry carbon disulphide and 20 grams of p-cresyl acetate were added slowly. The mixture was refluxed gently for 2½ hours and then left overnight. The carbondisulphide was removed under reduced pressure and the residue, a brown viscous looking mass, was heated at 135-140°C. for 1½ hours. The resulting product was decomposed with water and steam distilled. The steam distillate was a pale yellow liquid which solidified on standing. This distillate was filtered and a pale yellow solid, which was pressed free from a small amount of oil, was obtained. The solid was crystallised from methyl alcohol and melted at 48°C. Weight 15 grams. Percentage yield 75. m.p. of 2-hydroxy-5-methyl-acetophenone 50°C. (Rosenmund and Schnurr, Ann., 1928, 460, 56).

The filtrate from the steam distillate was made alkaline and extracted with ether. This ether extract contained practically no unchanged ester. The distillate was acidified and again extracted with ether . The ether was evaporated and the residue benzoylated. A benzoate, m.p. 71-72°C. after crystallisation from alcohol, mixed m.p. with p-cresol benzoate (m.p. 72°C) 71-72°C., was obtained.

Similar experiments conducted under the same conditions gave very similar results.

Phenyl Propionate.

25 grams of powdered aluminium chloride were suspended in 25cc. dry carbon disulphide and 20 grams of phenyl proponiate were gradually added. A violent reaction took place and when this had ceased the mixture was gently refluxed for 2½ hours. The carbon disulphide was distilled off and the residue was heated at 135-140°C. till hydrogen chloride ceased to be evolved. The product on decompositiion with water gave an oil which partly solidified. This was steam distilled and the residue was filtered while hot.

Steam Distillation Residue.

Pale yellow needles separated from the steam distillation residue on cooling and, after filtering these off, the liquor was used to extract the residue from the original filtration. A second crop of crystals was thus obtained and the mixed crystals were recrystallised from dilute alcohol. Pale yellow needles, m.p. 146-147°C. Weight 5.0 grams. Percentage yield 25. m.p. of p-hydroxy-propiophenone 148°C. (Hartung, Munch, Miller and Crossley, J.A.C.S., 1931, 53, 4149).

Neutral Steam Distillate.

The ether was distilled and a small amount of unchanged phenyl propionate remained.

Acidic Steam Distillate.

The residue after distillation of the ether was redistilled/

redistilled at 5mm. pressure and the following fractions were collected.

Fraction (1)	up to 90°C.	2 grams.
Fraction (2)	90-100°C. (chiefly at 95°C.)	6 grams.

Fraction (1) gave, on bromination, a bromo derivative which after crystallisation from alcohol melted at 89-90°C. Tribromo-phenol, m.p. 94°C.

Fraction (2) is o-hydroxy-propiophenone as has been proved by reduction to o-propyl phenol. Hartung, Munch, Miller and Crossley (loc. cit.) give b.p. of o-hydroxy-propiophenone as 110-115°C. at 6mm. This observation may possibly be a typographical error in the American Journal since the boiling point of o-hydroxy-propiophenone at 5mm. pressure has been calculated by the Clausius-Clapeyron equation and has been found to be 93°C. The data used were the boiling points at other pressures given in the literature. Fischer, Slimmer (C. 1902, ii, 214, Ber., 36, 2586) give b.p. 115°C.$_{15mm.}$ and Petschck and Simonis, (Ber., 1913, 46, 2014) give b.p. 150°C.$_{80mm.}$

Further experiments under the same conditions gave similar results.

Phenyl n-Butyrate.

25 grams of powdered aluminium chloride were suspended in 25 cc. dry carbon disulphide and 20 grams of phenyl-n-butyrate were added slowly. The mixture was refluxed for 2½ hours and the carbon disulphide was then distilled off. The heating was continued at 135-140°C. for 2 hours. The product was decomposed with water and steam distilled.

Steam Distillation Residue.

5 grams, m.p. 90-91°C., after crystallisation from water. p-hydroxy-n-butyrophenone, m.p. 91°C. (Perkin J.C.S., 1884, 55, 548).

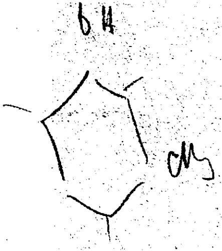
Neutral Steam Distillate.

No unchanged phenyl-n-butyrate was recovered.

Acidic Steam Distillate.

The ether extract was dried over anhydrous sodium sulphate and the ether was distilled. The residue was distilled under 14mm. pressure. A small amount boiled 120°C. and the fraction, b.p. 120-124°C., was collected. Weight 7 grams, pale yellow liquid. Percentage Yield 35. Coulthard, Marshall and Pyman (J.C.S., 1930, 280-291) give b.p. of o-hydroxy-n-butyrophenone as 124-126°C. 14mm.

The conditions were not varied for subsequent experiments and very similar results were obtained.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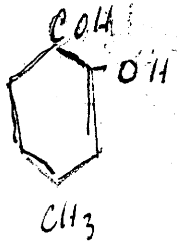
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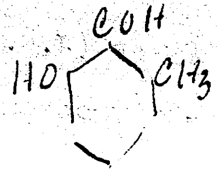
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Reimer-Tiemann Hydroxy-Aldehyde Synthesis.

In order to prepare 1:2-dimethyl-3-hydroxy-benzene which was not prepared from the corresponding xylidine since this substance had not been isolated from the xylidine mixtures investigated, the Reimer-Tiemann reaction has been applied to m-cresol. The standard Reimer-Tiemann procedure was first employed and the the modification of Sen and Ray (J. Ind. Chem. Soc., 1932, 9, 173-179) was tried. In this latter case a chloroform-alcohol mixture is used and it is claimed that this increases the yield of hydroxy-aldehydes. In practice it was found that the yields of hydroxy-aldehydes were increased to some extent but the greatest advantage of the method is that a greater proportion of the m-cresol can be recovered since less resinification takes place.

Reimer-Tiemann treatment of m-cresol results in the formation of three hydroxy-aldehydes, 2-methyl-6-hydroxy-, 4-methyl-2-hydroxy- and 2-methyl-4-hydroxy-benzaldehyde. The latter is separated from the two former since it is non-volatile in steam, a property common to all hydroxy-aldehydes in which the hydroxyl is para to the carbonyl group.

The two hydroxy-aldehyde which are steam volatile have been separated by Anselmino (Ber., 1917, 50, i, 395) by the formation of anils. He describes the anil of 4-methyl-2-hydroxy-benzaldehyde as a solid, m.p. 93°C., while the anil of 6-hydroxy-2-methyl-benzaldehyde is stated to be a/

a liquid. It has now been shown that the anil of 6-hydroxy-2-methyl-benzaldehyde is a solid, m.p. 51.5°C. and the m.p. of the anil of 4-methyl-2-hydroxy-benzaldehyde has been confirmed as 93°C. The anil of 6-hydroxy-2-methyl-benzaldehyde is much more soluble in aniline than is the anil of the isomeric hydroxy-aldehyde and it seems, that what has been previously described as the pure anil, has been a solution of the anil in aniline. In the first experiment in which the steam volatile hydroxy-aldehydes were treated with an equivalent amount of aniline an anil, which completely solidified, was obtained. This anil could not be separated by fractional crystallisation from alcohol. In subsequent experiments a slight excess of aniline was used and the almost pure anil of 4-methyl-2-hydroxy-benzaldehyde, m.p. 92-93°C., separated on cooling the mixed anils. The liquid portion obtained by filtering off the solid anil was washed with dilute acetic acid to remove excess aniline. On removal of the excess aniline the residue solidified and on crystallisation from alcohol melted at 51.5°C.

Experimental. Reimer-Tiemann on m-Cresol.

100 grams of sodium hydroxide were dissolved in 300 cc. of water and to this solution 40 grams of m-cresol were added. This solution was cooled and placed in a litre flask fitted with a reflux condenser and a thermometer dipping into the liquid. 60 grams of chloroform were added in small quantities at a time. The flask was shaken frequently and the temperature was not allowed to rise above 65°C. When all the chloroform had been added the temperature was raised to 80°C. for a few minutes and the reaction product was allowed to stand overnight. A yellow solid separated (sodium salts of hydroxy-aldehydes). The residual chloroform was removed on a water bath and the remaining liquor was acidified with dilute sulphuric acid. A red oil separated and was steam distilled. The steam distillation residue was filtered while hot and on cooling separated crystals. These were crystallised from water after boiling with animal charcoal. Glistening white plates, m.p. 106-107°C. Weight 3.0 grams. Percentage yield 7.0 calculated on 34 grams m-cresol since 6 grams were recovered. Tiemann, Schotten (Ber., 11, 700, 773) give m.p. 110°C. for 2-methyl-4-hydroxy-benzaldehyde.

The steam distillate was extracted with ether and the ether extract was shaken with a concentrated aqueous solution of sodium meta-bisulphite. A solid bisulphite compound/

compound separated and was filtered off and dried. Weight 15 grams. From the aqueous-ether filtrate from the bisulphite compound 6 grams m-cresol were recovered. The bisulphite compound was decomposed by sodium carbonate solution and the hydroxy-aldehydes were extracted with ether. The ether extract was dried over anhydrous sodium sulphate and on distillation of the ether 5 grams of a reddish oil remained. This was mixed with 4 grams of aniline and a small crystal of iodine was added. This mixture was heated on a water bath and on cooling solidified. The solid product was crystallised from alcohol and melted at 60°C. Further crystallisation of the final crops from the first crystallisation gave needles, m.p. 43-45°C. These solids were mixtures of the anils from the two o-hydroxy-aldehydes.

Reimer-Tiemann.

Modification of Sen and Ray (Loc.cit.)

50 grams of sodium hydroxide were dissolved in 300 cc. of water and 40 grams of m-cresol were added together with 50 grams of ethyl alcohol. The mixture was contained in the same apparatus as previously and 60 grams of chloroform in 100 grams ethyl alcohol were added slowly with constant shaking. The temperature was maintained at 50°C. The mixture was left overnight and the alcohol chloroform mixture was removed on a water bath under reduced pressure. The residual liquor was acidified and steam distilled. The

steam/

steam distillation residue was filtered hot and separated crystals which on recrystallisation from water melted at 104-106°C. Weight 6.5. grams. Percentage Yield of 2-methyl-4-hydroxy-benzaldehyde 21. This yield was calculated on 24 grams m-cresol since 16 grams were recovered.

The steam distillate was extracted with ether and the ether extract was shaken with a concentrated solution of sodium meta-bisulphite. The solid bisulphite compound was filtered off and dried. Weight 15 grams. This bisulphite was decomposed by heating with sodium carbonate solution and the hydroxy-aldehydes were extracted with ether. The ether extract was dried over anhydrous sodium carbonate and the ether was distilled. Weight 7 grams. This was heated with 6 grams aniline and a crystal of iodine and on cooling partially solidified. The solid was filtered off and recrystallised from alcohol, yellow needles, m.p. 92-93°C. .... 4-methyl-2-hydroxy-benzaldehyde. Weight 3 grams, corresponding to approximately 2 grams of the hydroxy-aldehyde. Percentage yield 6.6.

The liquid anil from the above filtration was washed with dilute acetic acid and solidified. The solid was crystallised from alcohol and separated in small yellow needles, m.p. 51.5°C. This anil gave on analysis N 6.60%. Calculated for $C_{14}H_{13}ON$, N 6.62%. This anil on decomposition with dilute sulphuric acid gave an oil, which, on crystallisation from very dilute alcohol separated in small needles, m.p. 31°C. Anselmino (loc.cit.) gives m.p. of 6-hydroxy-2-methyl-benzaldehyde as 32°C.

The weight of anil, m.p. 51.5°C. obtained was 5 grams and this corresponds to 3.2 grams of the hydroxy-aldehyde. Percentage yield 10.6.

A number of similar Reimer-Tiemann reactions were conducted on m-cresol and similar yields were obtained.

Gattermann Hydroxy-Aldehyde Synthesis.

The Gattermann method has been used to prepare 4-hydroxy-2-methyl-benzaldehyde from m-cresol. The actual Gattermann procedure has not been employed but advantage has been taken of the modifications suggested by Adams and Levine (J.A.C.S., 1923, 45, 2375; 1924, 46, 1518), who use zinc cyanide and generate the hydrogen cyanide in situ. In the original method Adams and Levine used ether as a solvent but in the work described in the experimental part of this present paper a very poor yield was obtained using ether. Benzene, suggested by Adams and Levine in their latter paper, has been found to be much more efficient than ether. Ether, however, has been used with success by Malkin and Nierenstein (J.A.C.S., 1931, 53, 239) in preparing the hydroxy-aldehyde from phloroglucinol.

In one of the experiments described in the experimental part of this work a crystalline by product has been obtained. This substance contains nitrogen and gives, on analysis, results agreeing with the formula $C_{17}H_{17}O_2N$. It melts at 235°C. with slight decomposition, dissolves in sodium hydroxide solution and is precipitated unchanged from alkaline solution by acid, reduces alkaline potassium permanganate solution and does not reduce Fehlings solution. On boiling this substance with concentrated hydrochloric acid no decomposition is effected and it is similarly inert to 50%/

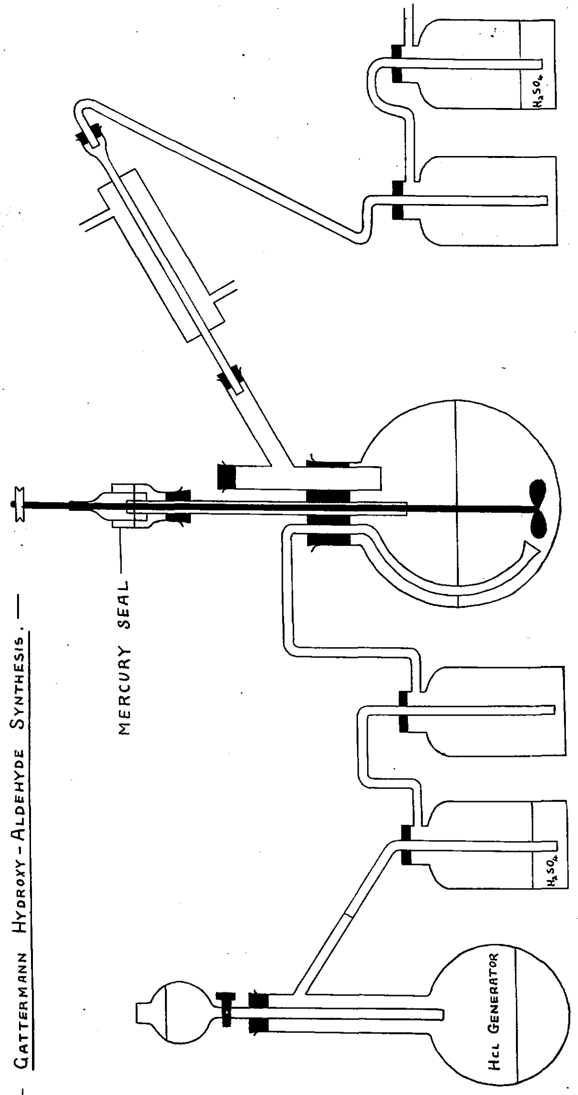
50% sulphuric acid. Concentrated sulphuric acid dissolves it producing a light brown solution probably due to sulphonation. The nitrogen seems to be bound in a ring structure and to possess no basic properties but the structure of the substance has not been elucidated. It is felt, however, that this substance may be of value in deciding whether the intermediate product in the Gattermann reaction is the aldimine hydrochloride, $C_6H_4(OH).CH:NH.HCl$, formerly suggested or if it is of the type of the chloromethylene derivative, NH:CH.NH:CHPh, recently proposed by Hinkel, Ayling and W.H.Morgan (J.C.S., 1932, 2793) to explain the formation of benzaldehyde from benzene in the Gattermann reaction.

Normal Gattermann procedure has been regarded as producing exclusively p-hydroxy-aldehydes but Kiewiet and Stephen (J.C.S., 1931, 84) have prepared an ortho-substituted methoxy-benzaldehyde by the action of anhydrous hydrogen cyanide and hydrogen chloride on m-methoxy phenol. The reaction was carried out at 0°C. and therefore cannot be regarded as a normal Gattermann reaction in which the usual temperature is 40°C.

The present work has shown that o-substituted hydroxy-aldehydes are produced in small quantity under normal Gattermann conditions. From m-cresol the three possible/

possible hydroxy-aldehydes, 2-methyl-6-, 2-methyl-4- and 4-methyl-2-hydroxy-benzaldehyde, have been obtained. The o-substituted hydroxy-aldehydes are present in only small amount and have been separated from the p-hydroxy-aldehyde by steam distillation and from one another by formation of the anil (4-methyl-2-hydroxy-benzaldehyde) and the phenylhydrazone (2-methyl-6-hydroxy-benzaldehyde). When the amount of zinc cyanide is reduced the production of o-substituted hydroxy-aldehydes seems to be favoured.

GATTERMANN HYDROXY-ALDEHYDE SYNTHESIS.



Experimental. Gattermann Hydroxy-Aldehyde Synthesis.

m-Cresol (1)

The apparatus finally used is shown in the accompanying sketch. The reaction vessel was a large round bottomed flask, fitted with a mercury seal stirrer, a delivery tube and a Y tube. One limb of the Y tube was attached to a condenser. In the flask there was a solution of 20 grams m-cresol in 200 cc. dry ether and to this was added 35 grams of zinc cyanide. Dry hydrogen chloride was passed through the delivery tube and the stirrer was started. After 2 hours the hydrogen chloride in-flow was decreased and the stirring was continued for another ½ hour. A semi solid mass formed at the bottom of the flask and the ether was decanted off. The residue was decomposed with water and steam distilled. The steam distillate was extracted with ether and the ether extract was shaken with a concentrated solution of sodium meta-bisulphite. Only a very small amount of solid bisulphite compound separated and was discarded after filtration. The ether layer was separated from the filtrate and the ether was distilled off. In order to estimate the amount of unchanged m-cresol the residue from the ether extract was heated in a steam oven with 15 cc. concentrated sulphuric acid for 1¼ hours. The sulphonic acid was then added to a large flask and cooled before the addition of 90 cc. of concentrated/

concentrated nitric acid. The nitro compound was poured into 40 cc. of water and the flask was washed with another 40 cc. of water. The derivative was filtered and dried. Weight 17 grams, m.p. 102-104°C. This is equivalent to 8 grams of m-cresol.

The residue from the steam distillation was filtered while hot and on standing crystals separated. These were recrystallised from water and gave 1 gram of pale yellow plates, m.p. 105-106°C. ..... 2-methyl-4-hydroxy-benzaldehyde.

m-Cresol (2).

The apparatus used was as before except that provision was made for heating the large flask on a water bath. 20 grams of m-cresol were dissolved in 70 cc. of sodium dried benzene and placed together with 50 grams of zinc cyanide in the large flask. A rapid stream of dry hydrogen chloride was passed in for ½ an hour. At the end of this time the gas stream was decreased and a small quantity of powdered anhydrous aluminium chloride was added. through the free limb of the Y tube. 25 grams of aluminium chloride were thus added and the temperature was gently raised to 40°C. during 2½ hours. A pink mass formed and was allowed to stand overnight. It was then decomposed by heating under reflux with 200 cc. of 10% hydrochloric acid. A reddish brown benzene layer was formed and steam distilled. The steam/

steam distillation residue was filtered while hot and the crystals which separated on cooling were recrystallised from water. Weight 7.0 grams, m.p. 108-109°C. Percentage yield 28. ..... 4-hydroxy-2-methyl-benzaldehyde.

The steam distillate was washed with dilute sodium hydroxide solution and the benzene was separated. The alkaline solution was acidified and extracted with ether. The ether extract was shaken with a concentrated solution of sodium meta-bisulphite but no solid bisulphite compound separated.

m-Cresol (3).

The same quantities of reacting products were treated in the same way. From the steam distillation residue liquor crystals were obtained, which after recrystallisation, melted at 107-108°C. Weight 7.5 grams. Percentage yield 30. ..... 4-hydroxy-2-methyl-benzaldehyde.
The tarry residue left from the original filtration of the steam distillation residue was dissolved in alcohol. This alcoholic solution separated yellow crystals which, after further crystallisation from alcohol, melted at 235°C. (slight decomposition). Weight 3.5 grams. This substance is soluble in dilute sodium hydroxide solution, does not reduce Fehlings solution but reduces alkaline potassium permanganate very easily. Analysis gave C 76.21; 76.46: H 6.4; 6.66; N 5.09; 5.20. Calculated for $C_{17}H_{17}O_2N$ C 76.39; H 6.36; N 5.24.

The steam distillate was shaken up and the benzene layer was separated and dried over anhydrous sodium sulphate. The benzene was distilled and the residue started to boil at 205°C. The fraction 205-214°C. was collected. This fraction boiled mainly between 208 and 210°C. Weight 2.5 grams, pale yellow liquid. The latter portion of the distillate solidified in the condenser and was crystallised from alcohol. It separated in flat needles, m.p. 60°C. .....2-hydroxy-4-methyl-benzaldehyde. Anselmino (loc.cit) gives the m.p. of this hydroxy-aldehyde as 60-61°C.

The bulk of the distillate was heated on a water bath with 2 grams of aniline and a small crystal of iodine. On cooling a solid anil separated and was filtered off and crystallised from alcohol. 2 grams, m.p. 90-91°C. The anil of 2-hydroxy-4-methyl-benzaldehyde melts at 93°C. The liquid obtained from the filtration of the anil was washed with dilute acetic acid and a small amount of solidewas obtained. This was crystallised from alcohol and melted at 45°C. thereby showing that it was probably the impure anil of 2-hydroxy-6-methyl-benzaldehyde (m.p. 51.5°C.).

m-Cresol (4).

The procedure in this case was the same as in (3) except that only 15 grams of zinc cyanide was used instead of 50 grams. The filtrate from the steam distillation residue gave/

gave 3.0 grams of crystals, m.p. 107-108°C. Percentage Yield 12. 4-hydroxy-2-methyl-benzaldehyde.

The tarry residue left from the original filtration did not yield the substance, m.p. 235°C., obtained in (3) but gave another substance which was much more soluble in alcohol. This substance did not melt below 277°C. and is soluble in dilute sodium hydroxide solution. The alkaline solution turns violet on heating and acid precipitates the substance unchanged.

The steam distillate was shaken up and the benzene layer was separated and dried over anhydrous sodium sulphate. The benzene was removed and the distillation was continued. The following fractions were collected.

Fraction (1).	198-205°C.	Weight 1.0 grams.
Fraction (2).	205-215°C.	Weight 5.0 grams.

Fraction (1).

This fraction was heated with aniline and a small crystal of iodine. On cooling a solid anil separated, m.p. after crystallisation from alcohol 92°C. .... anil of 2-hydroxy-4-methyl-benzaldehyde. The liquid obtained from the filtration of the solid anil was washed with dilute acetic acid and finally with ether. This ether extract was washed with water and added to a similar extract obtained from Fraction (2).

Fraction (2).

This fraction was heated on a water bath with 4 grams aniline and a small crystal of iodine. A solid anil separated on cooling and was filtered off. The aniline liquor was washed with dilute acetic acid and a solid, m.p. 85°C. mixed with liquid separated. This solid was filtered and mixed with that previously obtained. The mixed solids were crystallised from alcohol. Pale yellow needles, m.p. 91-92°C. Weight 5 grams. This corresponds to 3.2 grams of 2-hydroxy-4-methyl-benzaldehyde, (anil, m.p.93°C.). Percentage yield 13.

The portion of the anil which still remained liquid was extracted with ether, washed with dilute acetic acid and mixed with the similar extract from fraction (1). The ether was evaporated and the residue was treated with phenylhydrazine in glacial acetic acid. A solid phenylhydrazone, mixed with oil separated and was filtered and pressed. On crystallisation from alcohol pale yellow needles, m.p. 169-170°C. were obtained. Analysis gave N 12.50% Calculated for $C_{14}H_{14}ON_2$ N 12.39%. Anselmino (loc.cit.) gives m.p. of phenylhydrazone of 2-hydroxy-6-methyl-benzaldehyde as 172°C.

Preparation of Zinc Cyanide.

52 grams of sodium cyanide were dissolved in 100 grams of water and magnesium chloride solution was added. The precipitated magnesium hydroxide and carbonate were filtered off. The filtrate was added slowly with cooling to a solution of 62 grams of zinc chloride in 60 cc. of aqueous alcohol. The zinc cyanide was precipitated and filtered. It was washed with alcohol and ether and dried in a desiccator.

Estimation.

0.1817 grams of zinc cyanide were dissolved in 60 cc. N sodium hydroxide solution and titrated with N/10 silver nitrate solution until a permanent precipitate formed.

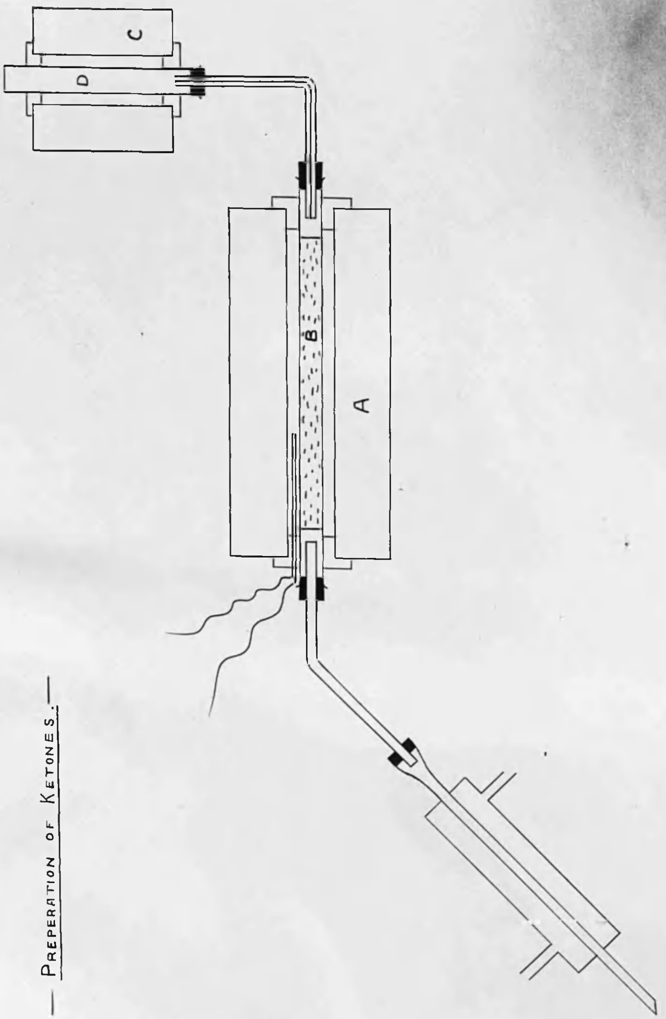
Volume of N/10 $AgNO_3$ = 15.1 cc.

$$\% \text{ Purity of } Zn(CN)_2 = \frac{15.1 \times 11.7 \times 100}{1000 \times 0.1817}$$

$$= 97.2$$

Preparation of Ketones.

Propiophenone and n-butyro-phenone were prepared with the anticipation of obtaining m-propyl and m-n-butyl phenol from these substances by nitration, reduction, diazotisation followed by Clemmensen reduction. The failure of the Clemmensen reduction with m-hydroxy-acetophenone prevented the above schemebeing put into operation. The ketones mentioned were prepared by the method of Sabatier and Maihle (C.r., 1914, 158, 830-835). A mixture of the requisite fatty acid and benzoic acid was passed through a tube packed with calcium carbonate heated to 470°C. An attempt was made to prepare iso-butyro-phenone but proved unsuccessful due to the tube becoming blocked. The reason for this may be that calcium iso-butyrate is more stable than calcium n-butyrate and therefore does not decompose at the temperature used. Higher temperatures than that stated caused decomposition of the benzoic acid.



— PREPERATION OF KETONES. —

Preparation of Ketones. Experimental.

The apparatus used is shown in the accompanying sketch and consisted of an electric furnace, A, containing a glass combustion tube, B, about 80 cms. long. A delivery vessel, D, was fitted with a capillary delivery tube and surrounded by an electric heater, C. The remainder of the apparatus is self explanatory.

Preparation of Propio-phenone.

The combustion tube was packed with precipitated calcium carbonate and a thin nichrome wire extended almost the entire length of the tube to prevent complete choking. 15 grams of benzoic acid were dissolved in 30 grams of propionic acid (b.p.139-141°C.) and were passed through the furnace, which was at a temperature of 470°C., in 40 minutes. The total distillate was mixed with another 5 grams of propionic acid and repassed through the tube. A pale yellow liquid was obtained and was dried over anhydrous calcium chloride. On distillation a fraction boiling up to 150°C. was collected. Weight 10 grams. On redistillation this gave 8 grams boiling between 100 and 102°C. ... Propione.

The higher boiling fraction was washed with sodium carbonate solution and extracted with ether. The ether extract was dried over anhydrous calcium chloride and distilled. A fraction was collected, b.p. 208-210°C. This was a very/

very pale yellow liquid. Weight 9 grams. Percentage yield 55. ..... Propio-phenone.

Experiments repeated under the same conditions gave similar yields.

Preparation of n-Butyro-phenone.

50 grams of benzoic acid were dissolved in 100 grams of n-butyric acid (b.p. 158-159°C.) and were passed through the tube packed with calcium carbonate at a temperature of 470°C. The product was distilled and the fraction up to 180°C. was collected. This fraction was redistilled and only a very small amount boiled below 150°C. This points to the absence of butyrone (b.p. 144°C.). The main bulk boiled between 155 and 160°C. and was thus very probably unchanged n-butyric acid. The residue above 170°C. was added to the original high boiling fraction. This fraction was washed with dilute sodium hydroxide solution and extracted with ether. The ether extract was dried over anhydrous calcium chloride and distilled. The fraction boiling between 222 and 225°C. (butyro-phenone) was collected. This fraction was a very pale yellow liquid. Weight 22 grams. Percentage yield 40. This yield was calculated on 45 grams of benzoic acid since 5 grams of benzoic acid were recovered from the sodium hydroxide washings.

Preparation of iso-Butyro-Phenone.

This preparation was carried out in exactly the same manner as previously. After running for a few minutes the tube became completely choked. Impure calcium carbonate was substituted for the precipitated calcium carbonate previously employed but again the tube choked. A mixture of ferric oxide and precipitated calcium carbonate was tried but without success.

Preparation of m-Hydroxy-Acetophenone.

Acetophenone was nitrated and gave good yields of m-nitro-acetophenone. (Rupe, Braun and Zembruski, Ber., 34, 3522; G.T.Morgan and Moss, J.S.C.I., 1923, 461 T.).

In the original literature sufficient emphasis is not placed on the necessity for the very vigorous stirring which is required during the reaction. The temperature must be maintained below 5°C. otherwise the production of o-nitro-acetophenone and m-nitro-benzoic acid predominates. It has been found that a much better crude product is obtained if the sulphuric acid is added to the acetophenone with constant stirring and cooling. Quantities of 10 grams of acetophenone have been used since with greater amounts unduly large reaction vessels are required to prevent loss by splashing during the rapid stirring. Using quantities of the order indicated yields of m-nitro-acetophenone of 75-85% of the theoretical amount have been obtained.

Reduction of the m-nitro-acetophenone by iron filings and acetic acid (Rupe, Braun and Zembruski; G.T. Morgan and Moss, loc.cit.) proved to be rather unsatisfactory as the yields obtained were from 50-60% of the theoretical. The comparatively poor yields were due to difficulty being experienced in obtaining a solution of the base free from iron. The published method effects this purpose by precipitating the iron as basic ferric acetate but in in all the attempts made in the present work this acetate was found difficult to filter and still seemed to contain some of the base probably as an iron complex.

A much better method for the reduction of m-nitro-acetophenone is the procedure of Camps (Arch. d. Pharm., 1902, 240, 1). This reduction is effected by tin and hydrochloric acid and as the bulk of the base separates as a complex stanni-chloride the yields were much better.

The diazotisation of m-amino-acetophenone has been conducted in the usual manner and the yields of m-hydroxy-acetophenone obtained on decomposition of the diazonium compound have been satisfactory. (Biginelli, Gazz., 24, 1, 440).

Preparation of m-Hydroxy-Acetophenone. Experimental.

m-Nitro-Acetophenone.

10 grams of acetophenone were mixed with between 50 and 60 grams of concentrated sulphuric acid (Sp. Gr. 1.84). During the addition of the acetophenone the sulphuric acid was stirred gently and cooled by an ice salt mixture. When the temperature of the mixture had fallen below 5°C. a mixture of 8.5 grams of concentrated nitric acid (Sp.Gr. 1.40) and 30 grams of concentrated sulphuric acid was added gradually. The addition of the mixed acids was so regulated that the temperature did not rise above 5°C. Throughout this addition the mixture was vigorously stirred by a double blade stirrer driven by an electric motor. After the addition of all the acid the yellow oil thus produced was stirred for a further 10 minutes and then poured slowly and with constant stirring into ice water. A yellow solid separated and was filtered and washed with water. One crystallisation from aqueous alcohol after boiling with animal charcoal gave yellow needles, m.p. 80°C. m.p. of m-nitro-acetophenone, 80-81°C. (Buchka, Ber., 10, 1714). Weight 9.5 grams. From the mother liquor a further 1.5 grams was obtained by evaporating the alcohol, rendering the aqueous residue alkaline and extracting with ether. The total yield of 11 grams corresponds to a percentage yield of 79.

A series of similar experiments were conducted and similar yields of m-nitro-acetophenone were obtained.

Reduction of m-Nitro-Acetophenone.

10 grams of m-nitro-acetophenone in suspension in 20 cc. of water were added gradually to 15 grams of granulated tin and 100 cc. of concentrated hydrochloric acid. The mixture was heated with constant stirring on a water bath. A yellow liquid formed and on cooling a white crystalline solid separated. This complex stanni-chloride was decomposed with a concentrated solution of sodium hydroxide and m-amino-acetophenone separated as an oil. This oil solidified on standing. The liquor from which the stanni-chloride separated was concentrated and concentrated sodium hydroxide was added. More m-amino-acetophenone separated and was mixed with the bulk obtained from the solid stanni-chloride. The combined yield was crystallised from aqueous alcohol after boiling with animal charcoal. Pale yellow plates, m.p. 97-98°C. Weight 7.2 grams. Percentage yield 90. m-Amino-acetophenone melts at 99.5°C. (Rupe, Braun and Zembruski, loc.cit.).

Diazotisation of m-Amino-Acetophenone.

10 grams of m-amino-acetophenone were dissolved in 100cc. of water and 44 grams of concentrated sulphuric acid added. A 10% aqueous solution of sodium nitrite was added slowly at such a rate that the temperature did not rise

above 5°C. When the usual end point was obtained with starch iodide paper the addition of the nitrite was stopped. The reaction mixture was heated to 50°C., nitrogen was evolved and the temperature then rose of its own accord. A reddish tar separated, solidified and was filtered off. The liquor was concentrated and a white solid separated. This was mixed with the tar and crystallised from water after boiling with animal charcoal. Colourless needles were obtained, m.p. 95°C. Weight 6.5 grams. Percentage yield 65. The m.p. of m-hydroxy-acetophenone is given as 92-93°C. by Biginelli (loc.cit.) and as 95°C. by Rupe and Majewski (Ber., 1900, 33, 3407).

Clemmensen Reduction.

The Clemmensen reduction method (Clemmensen, Ber., 1913, ii, 1837; 1914, i, 53), using amalgamated zinc and hydrochloric acid, has proved of considerable value as a means of reducing aromatic aldehydes and aromatic-aliphatic ketones to the corresponding hydrocarbons. It has also been applied to the reduction of hydroxy-aldehydes and ketones and has opened up a new and convenient method of preparing phenols. It has been used for this purpose in the present work.

The first hydroxy-ketone which was subjected to this reduction in the present investigation was m-hydroxy-acetophenone. This hydroxy ketone did not react normally and its behaviour will be discussed later. Before concluding that the abnormal results were due to some property of the m-hydroxy-acetophenone it was decided to test the correctness of the reduction procedure by using acetophenone, the reduction of which has been described by Clemmensen. He claims to have obtained yields of ethyl benzene of the order of 85% theoretical and has suggested a mechanism for the reduction. Styrene is always present in the ethyl benzene and is accounted for by Clemmensen by supposing that the reaction takes place in two stages.

The first stage results in the formation of styrene as follows :-

$$C_6H_5.CO.CH_3 + H_2 = C_6H_5.CH:CH_2 + H_2O$$

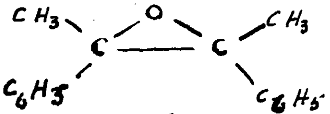
and the styrene then undergoes further reduction to ethyl benzene.

The yields of ethyl benzene which have been obtained are not so good as those reported by Clemmensen and have never exceeded 50% of the theoretical. A number of interesting by-products, which throw some light on the course of the reaction, have been obtained. These by-products are in agreement with the reaction mechanism suggested by Steinkopf and Wolfram (Ann., 1922-3, 430, 124). This reaction mechanism will be discussed later.

The reduction product obtained from acetophenone was an oil which was separated from the acid-zinc-chloride liquor and distilled under reduced pressure. The lower boiling portions yielded ethyl benzene and styrene which was identified by its bromo derivative, styrene di-bromide.

The higher boiling fractions on repeated distillation under reduced pressure yielded residues (1 and 2) which are probably polymerisation products of styrene. From the liquid portion a fraction which solidified was obtained. This was shown to be acetophenone pinacol. The other liquid fractions were analysed and analysis showed/

showed that the fraction, b.p. 136-139°C. $_{\text{2mm.}}$ (2C.) had the molecular formula $C_{16}H_{16}O$. Two substances of this formula are possible from the reduction of acetophenone.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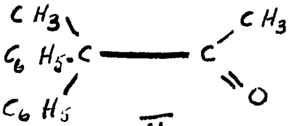
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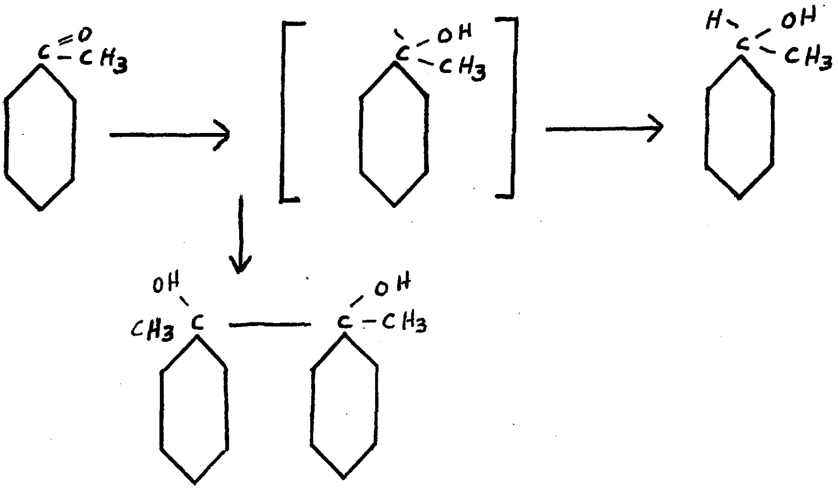
1) is derived from acetophenone pinacol by dehydration and 11) is derived from this latter substance by pinacolone transformation. The liquid isolated gives a semi-carbazone and therefore seems to have formula 11).

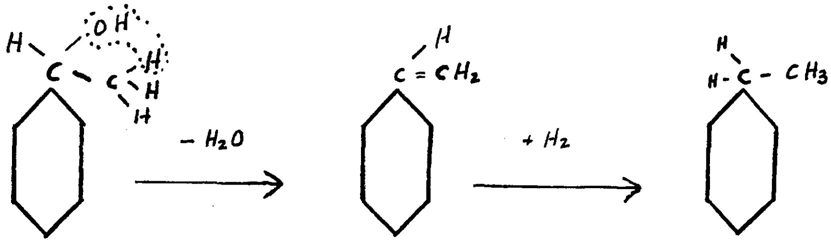
A second liquid fraction, b.p. 145-147°C. $_{\text{2mm.}}$ (3C) was isolated and analysed. This substance has the molecular formula $C_{14}H_{14}O$ but its structure has not been investigated.

The occurrence of a pinacolone among the reduction products of acetophenone might be regarded as strange since this substance contains a carbonyl group which should undergo further reduction. The reduction of acetophenone pinacolone has been shown not to occur under Clemmensen conditions (Hall and Bruce, J.A.C.S., 1930, 52, 347) but benzophenone pinacolone is reduced under these conditions (Steinkopf and Wolfram, loc. cit.).

The products obtained in this reduction are very similar to those obtained by Steinkopf and Wolfram(loc.cit.) who definitely proved the presence of polymers of styrene and α chlor-ethyl benzene. These authors did not obtain any substance corresponding to the liquid $C_{14}H_{14}O$ obtained in the present work. The mechanism of this reaction is considered by Steinkopf and Wolfram to take place in two stages though it seems to the present author that the first stage is probably enolisation and the fact that reduction takes place in acid solution would favour this view. Lapworth (J.C.S., 1903, 1121). Mayer (Ann., 1911, 380, 212). No evidence of enolisation is advanced in this present paper so the mechanism of Steinkopf and Wolfram will now be considered. The first stage is said to be the rupture of the oxygen-carbon double bond with the addition of hydrogen to the oxygen. This semi-pinacol may then unite with another such unit to give a true pinacol or it may be reduced to a carbinol. With acetophenone the first stage is as follows:-



The second stage is a dehydration of the carbinol produced with the formation of an unsaturated hydrocarbon which is then further reduced to a saturated hydrocarbon.



This dehydration of the carbinol has not been proved by Steinkopf and Wolfram. The present author, however, has heated methyl phenyl carbinol with hydrochloric acid and zinc chloride and has obtained styrene under these conditions which are those occurring in the Clemmensen reduction. An ether, $\alpha\cdot\alpha$ -diphenyl diethyl ether, previously obtained by Wuyts (Bull. soc.chim. Belgique, 30, 30-41) has also been obtained from methyl phenyl carbinol by this dehydration. That such an ether has not been found among the reduction products of acetophenone is not surprising since the amount of methyl phenyl carbinol present at any time must be small.

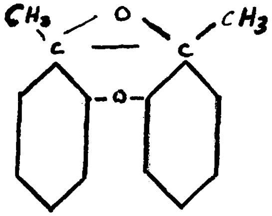
The Clemmensen method has been applied with success to the reduction of the hydroxy-ketones from the Fries rearrangement of phenyl acetate, o-, m-, and p-cresyl acetate, phenyl propionate and phenyl-n-butyrate. The yields of phenols/

phenols from p-hydroxy-ketones have in all cases been greater than those obtained from the corresponding o-hydroxy-ketones. This observation is in agreement with the work of Sandulesco and Girard (Bull. soc.chim., 1930, 1300) who found that, using normal Clemmensen conditions, the reduction of o-heptoyl phenol gave a yield of only 15% n-heptyl phenol while the corresponding p-hydroxy-ketone gave a 75% yield of the phenol.

The by products obtained were, with the exception of two cases, gelatine-like materials from which no crystallisable substances were isolable.

One of the exceptions referred to occurred in the reduction of o-hydroxy-acetophenone, which, in addition to o-ethyl phenol, gave a crystalline substance, m.p. 100-101°C. This substance on analysis gave results which agreed with the molecular formula $C_{16}H_{14}O_2$. The insolubility of this substance in dilute warm sodium hydroxide solution points to the absence of hydroxyl groups. Alkaline potassium permanganate is readily reduced by this substance but the reduction of Fehlings solution only takes place on prolonged heating.

The following two formulae are suggested for this substance. (See overleaf).



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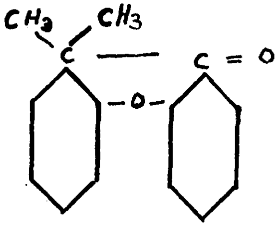
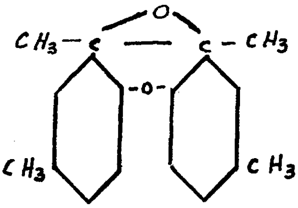


II

Another crystalline substance, m.p. 137-139°C., has been obtained by the reduction of o-hydroxy-acetophenone. In this case the reduction was carried out in glacial acetic-hydrochloric acid solution. (Sandulesco and Girard, loc. cit.). This substance is also insoluble in sodium hydroxide solution, reduces alkaline potassium permanganate easily and Fehlings solution on heating. The reduction of Fehlings solution appears to proceed more rapidly than with the substancemelting at 100-101°C. The analysis also agrees with the formula $C_{16}H_{14}O_2$. It will be noticed that substance (1) can be transformed into substance (2) by a pinacolone transformation. The fact that a substance of the type suggested for formula (1) should not undergo complete transformation under the conditions of the reduction may be due to the stability of the ethylene oxide linkage reported by Lucas and Legagneur (Bull. soc. chim., 45, 718, 1930). In neither case, however, has the structure of the isolated solid been positively established.

Crystalline solids have also been obtained in the reduction of 6-hydroxy-3-methyl-acetophenone by ordinary Clemmensen methods. One of these substances melted at 200-201°C. while the other melted at 153°C. Both, on analysis, gave results agreeing with the formula $C_{18}H_{18}O_2$. Both are insoluble in dilute sodium hydroxide solution and the substance m.p. 200-201°C., does not reduce alkaline potassium permanganate but reduces Fehlings solution on warming, while substance, m.p. 153°C., reduces cold alkaline potassium permanganate but does not reduce Fehlings solution even on heating. Two formulae are again suggested.



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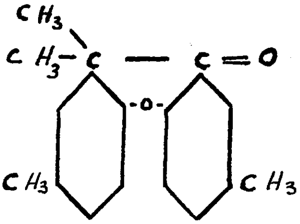
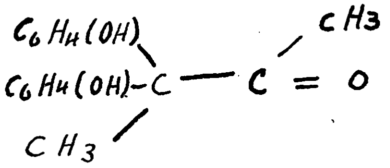


II

Clemmensen reduction has proved to be singularly ineffective in the reduction of m-hydroxy-acetophenone. This substance when reduced by ordinary Clemmensen procedure gives only a trace of m-ethyl phenol. The bulk of the product obtained was non volatile in steam and on cooling separated as a dark brown semi solid material. When a mixture of glacial acetic acid and hydrochloric acid was used/

used in place of the normal hydrochloric acid-water mixture, a non steam volatile crystalline product was isolated. A small amount of m-ethyl phenol was also produced. The crystalline product, which melted at 159-160°C. gave, on analysis, results corresponding to $C_{16}H_{16}O_3$. This compound is soluble in sodium hydroxide solution and reduces Fehlings solution on heating. It may possibly be the pinacolone from m-hydroxy-acetophenone.



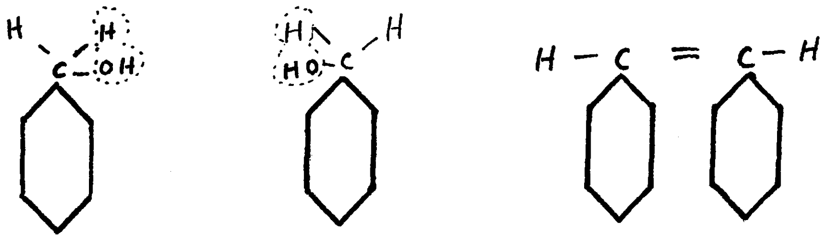
This structure has not been proved but it is intended to investigate this substance more fully in order to determine whether or not it will elucidate the behaviour of m-hydroxy-acetophenone on reduction. That the abnormality of the reduction occurs in the initial stage has been shown by the fact that m-methoxy phenyl methyl carbinol under Clemmensen conditions is converted to m-methoxy ethyl benzene. This again is probably a case of dehydration followed by reduction. The suggestion that the difficulty of reduction may be due to the orientation of the molecule of m-hydroxy-acetophenone is strengthened by the fact that substituent groups in the benzene nucleus have a marked effect on the reduction/

reduction of the carbonyl group in aliphatic-aromatic ketones. Day (J.C.S., 1930, 252-256) failed to obtain more than a 19% yield of p-ethyl-amino-benzene by the reduction of p-amino-acetophenone. The corresponding hydroxy-acetophenone is easily reduced to p-ethyl phenol in good yield. The orientation of the substituent groups also plays an important part. This has been shown by the work of Sandulesco and Girard (loc.cit.) already mentioned. Another possible explanation of the behaviour of m-hydroxy-acetophenone might be that the unsaturated hydrocarbon, m-hydroxy-styrene, polymerises much more readily than do the corresponding o-and p- hydroxy-styrene. The enhanced tendency to polymerisation possessed by a substance of the type of m-hydroxy-acetophenone is shown by the production of gelatine-like material in the reduction of m-methoxy-phenyl methyl carbinol. Such a product was not obtained when methyl phenyl carbinol was dehydrated. It will, however, be necessary to study the reduction of m-hydroxy-acetophenone by other reducing agents to determine whether or not the difficulty experienced is due to an inherent difficulty of reduction or to a tendency to polymerisation which is aggravated by Clemmensen conditions.

The reduction of m-methoxy-and m-amino-acetophenone has been attempted but the sole product in both cases has been/

been a non crystallisable gelatine-like material.

The Clemmensen reduction has also been applied to hydroxy-aldehydes but the results have been poor with the hydroxy-aldehydes used. The reduction of benzaldehyde has been used as a test of reduction conditions. The reduction of benzaldehyde by ordinary Clemmensen conditions produced only a small amount of toluene. The bulk of the product was a liquid, boiling at 200-210°C., which has not been investigated. A solid residue from the distillation of the above mentioned liquid gave, on crystallisation, stilbene, m.p. 123°C. This substance could be obtained from benzyl alcohol which is considered by Steinkopf and Wolfram to be the initial reduction product. Benzyl alcohol on dehydration would produce an unsaturated residue which might be expected to unite with another such residue to produce stilbene.



Benzaldehyde has also been reduced using a glacial acetic-hydrochloric acid mixture. In this case more toluene no stilbene and an unknown liquid fraction were produced.

2-Methyl-4-hydroxy-benzaldehyde has been reduced to 1:2-dimethyl-4-hydroxy-benzene. The yield was poor and no crystallisable substances were obtained from the residue. The anil of 2-methyl-3-hydroxy-benzaldehyde has also been reduced and has yielded 1:2-dimethyl-3-hydroxy-benzene. The yield in this case was slightly better than that obtained from the previous hydroxy-aldehyde but still was not good. The reason for using the anil and not the hydroxy-aldehyde was that, since the aldehyde is a low melting solid and has not been obtained in sufficient quantity to be purified by distillation, the anil was more convenient.

The use of difficultly hydrolysable derivatives of hydroxy-aldehydes might serve to indicate whether the poor yield of primary products obtained in the reduction of hydroxy-aldehydes is due to polymerisation or condensation of the aldehydes or their reduction products. In this case the aldehyde would be present in only small amount at any time and would then most probably be reduced without polymerisation or condensation.

Clemmensen Reduction. Experimental.

Acetophenone.

400 grams of granulated zinc were washed with dilute hydrochloric acid and then with water and left in contact with 800 cc. of approximately 5% aqueous mercuric chloride for 12 hours. The liquor was decanted and 400 cc. of concentrated hydrochloric acid and 800 cc. of water were added. This mixture was heated under reflux condenser on a sand bath and when a brisk evolution of hydrogen had commenced 100 grams of acetophenone (b.p. 200°C.) were added. The heating was continued for 7 hours and at the end of 4 hours an additional 100 cc. of concentrated hydrochloric acid was added. The acid-zinc chloride liquor, on the surface of which floated a greenish oil, was decanted from the residual zinc and extracted with ether. The ether extract was dried over anhydrous calcium chloride and the ether was distilled. The residue was heated on a water bath under a pressure of 70 mm. and a clear mobile liquid distilled. Weight 39 grams. The pressure was then reduced to 3mm. and a further 4 grams distilled. This fraction was added to the main bulk of low boiling distillate which was fractionated. The fraction 134-136°C. was collected (ethylbenzene). Weight 40 grams, A small fraction boiled at 136-145°C. This decolourised bromine and/

and gave a small amount of a bromo derivative, which when crystallised from aqueous alcohol melted at 72°C. Styrene dibromide, m.p. 74-74.5°C. (Zincke, Ann., 216, 288) b.p. 139-141°C. (Anschütz, Ann., 235, 328).

The high boiling residue from this first distillation was a reddish brown very viscous material which was dissolved in benzene. Absolute alcohol added to this benzene solution produced no precipitation. This precipitation was attempted because in earlier experiments a solid had been obtained by this means. The alcohol and benzene were distilled off and the residue was distilled under 3mm. pressure. Distillation commenced at 110°C. and the temperature rose rapidly to 155°C. and then more slowly to 175°C. where it remained constant for a short time. Above this point the temperature rose steadily to 200°C. and then rapidly to 220°C. where decomposition started. The distillate was a pale yellow slightly viscous oil. Weight 34 grams. .... Distillate (1). The residue from this distillation solidified on cooling .... Residue (1).

Distillate (1)

This distillate was redistilled under 2 mm. pressure and the following fractions were collected.

Fraction (1). 50-100°C., boiled chiefly 70-75°C., pale yellow liquid. Weight 1.5 grams.

Fraction (11) 100-150°C., boiled chiefly 140-145°C., pale yellow liquid, slightly viscous. Weight 24.5 gms.

Fraction (111). 150-175°C., very viscous, pale yellow. Weight 6.0 grams.

Residue (11). Solidified, dissolved in acetone and added to residue (1).

Fraction (1).

This fraction contained halogen in small amount. A semi-carbazone was formed by addition of a concentrated solution of semi-carbazide hydrochloride and potassium acetate in aqueous alcohol. The semi-carbazone after crystallisation from alcohol melted at 196-198°C. ..... Acetophenone semi-carbazone. The halogen containing compound may be α-chlor-ethyl benzene, b.p. 195°C. (with decomp.).(Schramm, M.8, 102.)

Fraction (11).

This fraction decolourised acid potassium permanganate solution. It was redistilled under 2mm. pressure and the following fractions were collected.

Fraction 1A. Up to 135°C., clear liquid. Weight 16 grams.

Fraction 2A. 135-140°C., clear liquid. Weight 7.0 grams.

Fraction 3A. 139-140°C. clear liquid. Weight 1.5 grams.

A small amount of a very viscous residue was left and solidified on standing. This was added to Fraction (111)

Fraction (111).

This fraction almost completely solidified on standing. The solid was filtered off and washed with petroleum/

petroleum ether (60-80°C.). The solid thus separated melted at 117-119°C. and crystallised from petroleum ether in flat hexagonal plates, m.p. 122°C. Weight 1.2 grams. Acetophenone pinacol, m.p. 122°C. (Lucas and Legagneur, Bull. soc. chim., 1929, (lV) 45, 718-34).

Fractions 1A and 2A were mixed and redistilled under 2mm. pressure to give the following fractions.

Fraction 1B	120-135°C.
Fraction 2B	135-138°C.
Fraction 3B	138-139°C.
Fraction 4B	139-150°C.

A pale yellow residue remained.

Fractions 1B and 2B were mixed and redistilled under 2mm. pressure and gave the following fractions.

Fraction 1C.	105-136°C.	clear mobile liquid.	4.0 grams.
Fraction 2C.	136-139°C.	clear mobile liquid.	2.5 grams.

A small amount of pale yellow residue remained.

Fraction 3B. and 4B were mixed and redistilled under 2mm. pressure and gave the following fraction.

Fraction 3C.	145-147°C.	6.5 grams.

This fraction was not so mobile as the lower fractions and had a smell of a different character. The residue from this final fractionation solidified and was added to the original <u>fraction 111</u>.

Fraction 2C. b.p. 136-139°C. $_{2mm.}$

This fraction was a clear liquid when distilled but on standing it turned yellow and after a very long time partly solidified. The solid portion melted at **41-42°C.** Acetophenone pinacolone, m.p. 41°C.; semi-carbazone, m.p. 175°C. (Parry, J.C.S., 1915, 115,).

The following results were obtained using the liquid before it had solidified. It does not give the iodoform reaction or the sodium nitroprusside test for the $CH_3.CO.C.$ grouping. A small amount was added to an aqueous solution of semi-carbazide hydrochloride and potassium acetate to which had been added a small quantity of alcohol. The mixture was warmed slightly and after standing overnight a semi-carbazone, m.p. 160-164°C., separated. This was recrystallised from alcohol, m.p. 172-173°C. N (found micro.) 14.68%

Calculated for $C_{17}H_{19}ON_3$ 14.95%.

Analysis of Fraction 2C.

% C.	85.33;	85.34;	85.41
% H.	7.40;	7.20;	7.44

Molecular Weight (Freezing point method in benzene) 222.6

Calculated for $C_{16}H_{16}O$

% C	85.72	
% H	7.14	Molecular weight 224.

This fraction is therefore acetophenone pinacolone.

Analysis of Fraction 3C. b.p. 145-147°C. $_{2mm.}$

% C 84.89; 84.84

% H 7.20; 7.13

Molecular Weight (Freezing point method in benzene)

193.6; 192.0; 195.9

Calculated for $C_{14}H_{14}O$

% C 84.89

% H 7.07 Molecular weight 198.

Preparation of Methyl Phenyl Carbinol.

A mixture of 30 grams methyl iodide and 50 cc. of absolute ether was made and about 20 cc. of this were added to 5 grams of dry clean magnesium ribbon contained in a flask fitted with a reflux condenser. When the reaction had ceased the rest of the ether solution of methyl iodide was added in small quantities. After the addition of all the iodide the mixture was heated gently to complete the reaction. The flask was then cooled in ice water and 22 grams of freshly distilled benzaldehyde in 50 cc. of absolute ether was cautiously added in small quantities with constant shaking. After standing overnight sufficient dilute hydrochloric acid was added to dissolve the precipitate. The ether layer was separated and washed with sodium carbonate solution and then with sodium meta-bisulphite solution. It was finally dried over anhydrous potassium carbonate. After distillation of the ether the residue was distilled under reduced pressure. The fraction boiling at 95-100°C. at 10mm. pressure was collected. Weight 10 grams. Percentage yield 40.

Preparation of Styrene from Methyl Phenyl Carbinol.

10 grams of methyl phenyl carbinol were heated under reflux on a water bath for 4 hours with 20 grams of zinc chloride in 50 cc. of water and 15 cc. of concentrated hydrochloric acid. The liquid was extracted with ether and the ether extract was dried over anhydrous potassium carbonate. The residue after distillation of the ether was fractionated under 8mm. pressure. A fraction boiling below 80°C. was collected. This was a clear liquid which decolourised bromine. Weight 2 grams. It was brominated in carbon disulphide and the crude bromo derivative melted at 69-70°C., recrystallised from aqueous alcohol, m.p. 72-73°C. Styrene-di-Bromide, m.p. 74-74.5°C. (Zincki, loc.cit.)

The next fraction b.p. 80-110°C. was small and was discarded. The residue above 110°C. was a yellow liquid which was diluted largely with alcohol but nothing was precipitated. This treatment was applied as it was thought that this liquid might contain polymers of styrene. The alcohol was distilled off and the residue was again distilled under reduced pressure. A fraction was collected boiling at 150°C. under 15mm. pressure. This was a clear mobile liquid which did not decolourise bromine at ordinary temperature, formed no compound with acetic anhydride and did not react with semi-carbazide hydrochloride. Weight 5 grams. Found %C 84.96; %H 7.97. Calculated for $C_{16}H_{18}O$, %C 84.96; %H 7.97.

Reduction of o-Hydroxy-acetophenone.(1)

50 grams of amalgamated zinc were prepared in the same manner as previously. This zinc was heated under reflux on a sand bath with 90 cc. of concentrated hydrochloric acid and 180 cc. of water. When the evolution of hydrogen was brisk 10 grams of the hydroxy-ketone were added and the heating was continued for 1½ hours. Small quantities of concentrated hydrochloric acid were added at intervals in order to maintain a brisk reaction. A pale yellow oil separated from the acid layer which was decanted from the residual zinc and steam distilled. The steam distillate was a colourless oil and the last traces of the distillate solidified in the condenser. This solid, which was only obtained in small quantities was recrystallised twice from alcohol and was obtained in feathery needles, m.p.100-101°C.

The steam distillate was extracted with petroleum ether and the extract was dried over anhydrous sodium sulphate. On distillation of the petroleum ether the residue boiled at 200-203°C. Weight 4 grams. o-Ethyl phenol, b.p.$_{756}$ 206.5-207-5°C. (Béhal and Choay, Bl. (3) <u>11</u>, 210).

The residue from the steam distillation was a substance which resembled gelatine in appearance. This substance was not further investigated.

The solid, m.p. 100-101°C., gave on micro-analysis, the following result. %C 80.65; %H 5.89. Calculated for $C_{16}H_{14}O_2$ %C 80.67; %H 5.88.

Other reductions conducted on the same lines gave very similar results.

Reduction of o-Hydroxy-acetophenone (2).

50 grams of amalgamated zinc were prepared and were heated under reflux on a sand bath for 5½ hours with 10 grams of the hydroxy-ketone, 100 cc. of concentrated hydrochloric acid and 100 cc. of glacial acetic acid. The liquor turned pink in colour at first and then became clear when an oil separated on the surface. Small quantities of concentrated hydrochloric acid were added during the heating. On cooling needle shaped crystals separated from the oil and were filtered off. These recrystallised from alcohol in long rectangular plates, m.p. 137-138°C.

The liquor which had been decanted from the residual zinc was extracted with benzene and the benzene extract was mixed with water and steam distilled. The steam distillate was shaken up and the benzene layer was separated and dried over anhydrous sodium sulphate. After distillation of the benzene the residue boiled between 200 and 203°C. Weight 4.5 grams. ...... o-ethyl phenol.

A small amount of high boiling residue was obtained from the distillation of o-ethyl phenol. This residue was dissolved in alcohol and the alcoholic solution was diluted with water. A solid m.p. 130-136°C. separated and was recrystallised from alcohol, m.p. 137-139°C.

The residue from the steam distillation was again a gelatine-like substance.

The solid m.p. 137-139°C., gave, on micro-analysis, the following result. %C 80.44; %H 5.99. Calculated for $C_{16}H_{14}O_2$ %C 80.67; %H 5.88

Reduction of m-Hydroxy-acetophenone (1).

50 grams of zinc were amalgamated in the usual way and heated under reflux on a sand bath with 90 cc. of concentrated hydrochloric acid and 180 cc. of water. When the reaction was vigorous 10 grams of m-hydroxy-acetophenone were added and the heating was continued for 8 hours. An oil separated and was decanted from the residual zinc. Steam distillation gave a very small steam distillate which had a phenolic odour. This steam distillate was extracted with ether and the ether extract was dried over anhydrous sodium sulphate. On evaporation of the ether the residue was a reddish liquid. Weight about 0.5 grams. This liquid was benzoylated and the benzoyl derivative separated as a yellow oil which partly solidified after standing in an ice-chest for over a week. The solid portion was filtered and was obtained in the form of glistening plates, m.p. 117-118°C. (Unidentified). The oily residue after the removal of the solid completely solidified and melted at 45-50°C. This was recrystallised from alcohol and melted at 52.5°C. The benzoate of m-ethyl phenol melts at 52.5°C. (Béhal and Choay, loc. cit.).

The residue from the steam distillation was extracted with ether and on removal of the ether a dark green sticky mass was left. This residue was heated under reflux with

concentrated/

concentrated hydrochloric acid and again steam distilled. A very small amount of steam distillate was obtained and this was brominated by the addition of a small quantity of bromine. A bromo derivative separated and was crystallised from alcohol after boiling with animal charcoal. It separated in long needles, m.p. 77-78°C. (unidentified).

A number of similar experiments were conducted but in every case only a very small amount of steam distillate was obtained.

Reduction of m-Hydroxy-acetophenone (2).

50 grams of zinc were amalgamated in the usual way and were heated under reflux with 10 grams of m-hydroxy-acetophenone, 100 cc. of concentrated hydrochloric acid and 100 cc. of glacial acetic acid for 10 hours. The liquor turned brown then red and finally yellow and on cooling it became red again and separated a thick oil. This oil and zinc chloride solution were decanted from the residual zinc and diluted largely with water. A red sticky material separated and was extracted with ether. The ether was allowed to evaporate and a thick liquid containing solid material remained. The solid was filtered off and the filtrate was again dissolved in ether and benzene was added to the ether solution. This precipitated solid material which was added to that previously obtained and crystallised from/

from ether, m.p. 158-160°C. Weight 3 grams.

The ether and benzene were removed from the residue which was steam distilled. Only a very small amount of steam distillate collected and this was extracted with ether. The residue, after removal of ether, was benzoylated but the benzoyl derivative remained liquid.

Reduction of m-Hydroxy-acetophenone (3).

The quantities used and the initial procedure were the same as in (2). The separated oil and zinc chloride solution were decanted from the residual zinc and extracted with benzene. This benzene extraction left a red liquor which was extracted with ether and the ether extract was dried with anhydrous sodium sulphate. After evaporation of the ether a red liquid was left from which a solid separated. This solid was filtered off and crystallised from ether, m.p. 158-160°C.

The benzene extract was steam distilled and the benzene layer of the steam distillate was separated and dried with anhydrous sodium sulphate. The benzene was evaporated and the residue, less than 1 gram, was benzoylated. The benzoyl derivative was crystallised from alcohol and melted at 50-52°C. ...... m-ethyl phenol.

The residue from the steam distillation separated white crystals on standing, m.p. 158-160°C. These were mixed/

mixed with the solid from the ether extract. Total weight 2 grams.

Solid, m.p. 158-160°C.

The solids obtained from (2) and (3) were mixed and crystallised from dilute acetic acid. Small white prisms were obtained, m.p. 159-160°C. Micro-analysis gave % C, 74.54; % H, 6.39. Calculated for $C_{16}H_{16}O_3$ % C, 74.96; % H, 6.25. (probably m-hydroxy-acetophenone pinacol).

Reduction of p-Hydroxy-acetophenone.

(1) 50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams p-hydroxy-acetophenone were heated on a sand bath for 1 hour. The phenol was extracted from the steam distillate with petroleum ether and solidified on evaporation of the petroleum ether. Weight 3.0 grams, m.p. 43-44°C. .... p-ethyl phenol, m.p. 45-47°C. (Beilstein, Kuhlberg, Ann., 156, 211).

The residue from the steam distillation was a resinous semi-plastic mass.

(2) 50 grams amalgamated zinc, 260 cc. water, 130 cc. concentrated hydrochloric acid and 15 grams of p-hydroxy-acetophenone were heated on a boiling water bath for $1\frac{1}{2}$ hours. Yield 5.0 grams, m.p. 44-45°C. ...... p-ethyl-phenol.

The residue was as before.

Reduction of o-Hydroxy-Propiophenone.

100 grams of amalgamated zinc, 360 cc. water, 180 cc. of concentrated hydrochloric acid and 20 grams of o-hydroxy-propiophenone were heated on a sand bath for 12 hours. Yield 10 grams, b.p. 105-106°C.$_{12mm.}$ ..... o-propyl phenol, b.p. 100-101°C.$_{10mm.}$ (Vavon and Anziani, Bull. soc.chim.,(4) 47, 1638, 1927).

Reduction of p-Hydroxy-Propiophenone.

100 grams amalgamated zinc, 360 cc. water, 180 cc. concentrated hydrochloric acid and 20 grams of p-hydroxy-

p-hydroxy-propiophenone were heated on a sand bath for 1 hour. Yield 12 grams, b.p. 226-227°C. .... p-propyl phenol, b.p. 228°C.$_{748mm.}$ (Clemmensen, Ber., 1914, i, 53)

A small amount of unchanged hydroxy-ketone, m.p. 147-148°C. was recovered.

Reduction of o-Hydroxy-Butyrophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid were heated on a sand bath for 12 hours with 12 grams of o-hydroxy-butyrophenone. Yield 9 grams, b.p. 115-117°C. $_{14mm.}$ Read and Mullen, (J. A. C. S., 1928, 50, 1763) give b.p. 113-115°C.$_{14mm.}$ for o-n-butyl phenol.

Reduction of p-Hydroxy-Butyrophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 6 grams p-hydroxy-butyrophenone were heated on a sand bath for 14 hours. Yield 4 grams, b.p. 125-126°C. $_{10mm.}$ Read and Mullen (loc. cit.) give b.p. 121-123°C.$_{14mm.}$ for p-n-butyl phenol.

Reduction of 4-Hydroxy-3-Methyl-Acetophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams of the hydroxy-ketone were heated on a boiling water bath for 1½ hours. Yield 6 grams, b.p. 220°C. $_{760mm.}$ b.p. of 2-methyl-4-ethyl phenol 218-220°C. (Vavon and Paira, C. 1930, ii, 235);

b.p. 220-222°C. (Auwers and Mauss, Ann., 460, 240-277).

Reductions conducted in a similar manner gave almost identical yields.

Reduction of 4-Hydroxy-2-Methyl-Acetophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams of the hydroxyketone were heated on a water bath for 1½ hours. Yield 5.5 grams, b.p. 232-233°C. 758mm. b.p. of 3-methyl-4-ethyl phenol 230-233°C. (Vavon and Paira, loc. cit.).

Reduction of 6-Hydroxy-3-Methyl-Acetophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams of the hydroxyketone were heated on a sand bath for 1 hour. Yield 5.5 grams, b.p. 218-222°C. 759mm. 2-ethyl-4-methyl phenol, b.p.215-219°C. (Vavon and Paira, loc. cit.).

Four reductions using the same quantities and the same conditions were conducted. The steam distillates were mixed and extracted with petroleum ether. On distillation of the petroleum ether after drying with sodium sulphate 29 grams of a pale yellow oil were left. This was distilled and the fraction 222-224°C. was collected. Weight 22 grams.

The higher boiling residue was further distilled. Above 225°C. the temperature rose slowly to 234°C. and then more rapidly to 240°C. above which temperature decomposition took place.

The distillate was a pale yellow oil. The semi-carbazone of the fraction, b.p. 225-240°C., was made and crystallised from alcohol in pale yellow feathery needles, m.p. 211°C. Semi-carbazone of 6-hydroxy-3-methyl-acetophenone, m.p. 212°C. (Anschütz and Scholl, Ann., 379, 342). The remainder of the distillate was dissolved in warm 5/N sodium hydroxide solution and a sodium salt separated. This salt on decomposition with dilute hydrochloric acid gave a solid, m.p. 47°C., unchanged 6-hydroxy-3-methyl-acetophenone. Weight 2.5 grams. The filtrate from the sodium salt was neutralised with dilute hydrochloric acid and extracted with petroleum ether. The petroleum ether extract was dried with sodium sulphate and the petroleum ether was distilled. The residue boiled at 208-216°C. Weight 3 grams. This was probably an impure sample of 2-ethyl-4-methyl phenol (b.p. 215-219°C.).

The residues from the steam distillations were extracted with ether and mixed. On partial evaporation of the ether a solid separated and was filtered off. This solid melted at 148-150°C. and was crystallised from alcohol in which it was not very soluble. From the alcohol solution a mixture of long needles and plates separated. This alcohol solution after filtration and concentration gave small plates, m.p. 145°C. The mixed crystals first obtained were recrystallised from alcohol and long needles, m.p. 200-201°C., were/

were isolated. The solid, m.p.145°C., on recrystallisation from dilute alcohol melted at 153°C.

Solid, m.p. 200-201°C.

Micro-Analysis. % C, 81.41; % H, 6.91

Calculated for $C_{18}H_{18}O_2$ % C, 81.21; % H, 6.77

Solid, m.p. 153°C.

Micro-Analysis. % C, 80.81; % H, 6.71

Calculated for $C_{18}H_{18}O_2$ % C, 81.21; % H, 6.77

Reduction of 2-Hydroxy-4-Methyl-Acetophenone.

50 grams of amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams of the hydroxy ketone were heated on a sand bath for 20 hours. Yield 5 grams, m.p. 41-42°C. Crystallised from petroleum ether, m.p. 42-43°C. Weight 4.5 grams. 6-ethyl-3-methyl phenol, m.p. 43-44°C. (Auwers, Bundesmann and Wieners, Ann., 447, 162-196, 1926).

Other reductions conducted under the same conditions yielded similar results.

Reduction of 2-Hydroxy-3-Methyl-Acetophenone.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydroxhloric acid and 10 grams of the hydroxy-ketone were heated for 12 hours on a sand bath. Yield 7 grams, b.p. 208-210°C. $_{750mm.}$ Auwers (Ann., 447, 180, 1926) gives b.p. of 2-methyl-6-ethyl phenol as 212-214°C.

Reduction of 4-Hydroxy-o-Toluylaldehyde.

50 grams amalgamated zinc, 180 cc. water, 90 cc. concentrated hydrochloric acid and 10 grams of the hydroxyaldehyde were heated for 12 hours on a sand bath. The yield was about 1 gram of a brownish red liquid with a phenolic odour. This was converted to phenoxyacetate by warming with solid sodium hydroxide and mono-chlor-acetic acid. The crude phenoxyacetate, weight 2 grams, m.p. 150-153°C., crystallised from benzene in small white glistening needles, m.p. 160-161°C. Phenoxyacetate of 1:2-dimethyl-4-hydroxy-benzene, m.p. 162.5°C. (Gluud and Breuer, C. 1919, i, 626).

Reduction of the Anil of 2-Hydroxy-6-Methyl-Benzaldehyde.

50 grams of amalgamated zinc, 180 cc. water, and 90 cc. of concentrated hydrochloric acid were heated under reflux on a sand bath. 10 grams of the anil were added in small quantities and the heating was continued for 5 hours. Yield 1.5 grams, m.p. 72-73°C. 1:2-dimethyl-3-hydroxy-benzene, m.p. 75°C. (Töhl, Ber., 18, 2562).

Part 3.

Preparation of Derivatives.

Since this work was initially an attempt to separate individual phenols from a complex mixture the derivatives here prepared were those which were considered to be of value in achieving this object. In selecting derivatives two properties were considered of prime importance; ease of preparation and hydrolysability with liberation of the original phenol. For these reasons the derivatives which have been selected have been the p-nitro-benzoates, 3:5-dinitro-benzoates and phenoxyacetates. The first two are comparatively easily hydrolysed but the latter require to be heated under pressure with caustic alkali. p-Nitro-benzoates were selected because these derivatives have been found to be exceedingly useful for the separation of dihydric phenols (Gray and Cruikshanks, Proc. Chem. Soc., 1914, 30, 303.)

p-Nitro-Benzoates.

The general method employed in the preparation of these derivatives has been to add a pyridine solution of the acid chloride to a solution of the phenol in pyridine. This mixed solution was allowed to stand overnight and in the majority of cases a solid separated. The pyridine was removed by washing with dilute sulphuric acid and the solid product/

product was filtered off, washed with sodium carbonate solution and then with water and crystallised from an appropriate solvent. Some of the higher phenols, however, did not form p-nitro-benzoates by this method. The derivatives of these phenols were therefore prepared by using chloroform as a solvent. The method used in this case has been to suspend the acid chloride in chloroform and add the phenol. The solution of the acid chloride was completed by heating to boiling and, after standing for a short time, the chloroform was distilled off. The residue was washed with dilute warm sodium hydroxide solution then with water and was finally crystallised from a suitable solvent. When cold sodium hydroxide solution was used a sticky product resulted probably due to contamination with unchanged acid chloride. The superiority of the chloroform over the pyridine method seems to depend on the reactivity of the hydroxyl group. When the pyridine method is used with higher homologues of phenol the acid chloride seems to react with the pyridine in preference to the phenol. That pyridine forms addition compounds with acid chlorides has been shown by Minunni (Gazz., <u>22</u>, 213-217) who obtained, by the interaction of benzoyl chloride and pyridine, a compound to which he ascribes the formula, $C_6H_5.N.Cl.C;O.C_6H_5$

PHENOL

1 gram phenol gave 2.1 grams of a p-nitrobenzoate. m.p. of crude product 127-128°C. Recrystallised from alcohol in very pale yellow saw toothed plates, m.p. 129°C. Raiford (J.A.C.S., 1924, 46, 2052) gives m.p.129°C.

o-Cresol.

1 gram o-cresol gave 2.0 grams of a p-nitrobenzoate. m.p. of crude product 93-94°C. Recrystallised from alcohol in very pale yellow needles, m.p. 94°C. Hänggi (Helv. chim. acta., 1921, 4, 23-25) gives m.p. 92-93°C.

m-Cresol.

1 gram of m-cresol gave 2.0 grams of a p-nitrobenzoate. Crude product melted at 87-88°C. Recrystallised from alcohol in white flakes, m.p. 88.5°C. Hänggi (loc.cit.) gives m.p. 85-85.5°C.

p-Cresol.

1 gram of p-cresol gave 2.0 grams of a p-nitrobenzoate. Crude product, m.p. 97-98°C. Recrystallised from alcohol in very pale yellow plates, m.p. 98°C. Hänggi (loc.cit.) gives m.p. 96.5-97.5°C.

1:2-Dimethyl-3-Hydroxy-Benzene. X

0.5 grams of this xylenol gave 1 gram of a p-nitro-benzoate. Crude, m.p. 121-122°C. Recrystallised from alcohol in pale yellow needles, m.p. 124-125°C. N(found micro) 5.28%. Calculated for $C_{15}H_{13}O_4N$, 5.16%.

1:2-Dimethyl-4-Hydroxy-Benzene.

1 gram of this xylenol gave 1.5 grams of p-nitrobenzoate. Crude product, m.p. 125-127°C. Recrystallised from alcohol in pale yellow plates, m.p. 127-128°C. N (found) 5.18%. Calculated for $C_{15}H_{13}O_4N$ 5.16%.

1:3-Dimethyl-5-Hydroxy-Benzene.

1 gram of this xylenol gave 1.7 grams of p-nitrobenzoate. Crude product, m.p. 107-108°C. Recrystallised from alcohol in small, very pale yellow plates, m.p. 109°C. N (found) 5.20%. Calculated for $C_{15}H_{13}O_4N$ 5.16%.

1:3-Dimethyl-4-Hydroxy-Benzene.

1 gram of this xylenol gave 1.5 grams of p-nitrobenzoate. Crude product, m.p. 110-111°C. Recrystallised from alcohol in pale yellow needles, m.p. 112-113°C. N (found) 5.19%. Calculated for $C_{15}H_{13}O_4N$ 5.16%.

1:3-Dimethyl-2-Hydroxy-Benzene.

1 Gram of this xylenol gave 1.0 grams of p-nitrobenzoate. Crude product, m.p. 98-99°C. Recrystallised from alcohol in pale yellow prisms, m.p. 99-100°C. N (found) 5.17%. Calculated for $C_{15}H_{13}O_4N$ 5.16%.

o-Ethyl Phenol.

1 gram of o-ethyl phenol gave 1.0 grams of p-nitrobenzoate. Crude product, m.p. 55°C. Recrystallised from alcohol in pale yellow plates, m.p. 56-57°C. Vavon and Mitchovitch (Bull. soc. chim., 1929, (lV) 45, 961-972) give m.p. 56-57°C.

p-Ethyl Phenol.

1 Gram of p-ethyl phenol gave 1.5 grams of p-nitro-benzoate. Crude product, m.p. 77-79°C. Recrystallised from alcohol in small, very pale yellow needles, m.p. 80°C. Vavon and Mitchovitch (loc. cit.) give m.p. 80-81°C.

o-n-Propyl Phenol. X

1 gram of o-n-propyl phenol gave 1.5 grams of p-nitro-benzoate. Crude product was liquid and solidified on cooling to -20°C., m.p. 37-39°C. Recrystallised from alcohol in very pale yellow plates, m.p. 39-40°C. N (found) (micro) 5.02%. Calculated for $C_{16}H_{15}O_4N$ 4.91%.

p-n-Propyl Phenol. X

1 gram of p-n-propyl phenol gave 2.0 grams of p-nitro-benzoate. Crude product, m.p. 78-80°C. Recrystallised from alcohol in very pale yellow needles, m.p. 82-82.5°C. N (found) 4.84%. Calculated for $C_{16}H_{15}O_4N$ 4.91%

o-n-Butyl Phenol. X

The p-nitro-benzoate of this phenol was liquid but solidified after standing for a considerable time. As this substance has not yet been analysed its preparation is not claimed.

p-n-Butyl Phenol. X

0.5 grams of p-n-butyl phenol gave 1.0 grams of p-nitro-benzoate. Crude product, m.p. 66-68°C. Recrystallised from alcohol in pale yellow needles, m.p. 68-69°C.

Read and Mullen (J.A.C.S., 1928, 50, 1763) give m.p. 67-68°C.

Mesitol, 1:3:5-Trimethyl-2-Hydroxy-Benzene.

1 gram of mesitol gave 1.5 grams of p-nitro-benzoate. Crude product, m.p. 110-115°C. Recrystallised from alcohol in pale yellow flakes, m.p. 115-117°C. N (found) 4.89%. Calculated for $C_{16}H_{15}O_4N$ 4.91%.

pseudo-Cumenol, 1:2:4-Trimethyl-5-Hydroxy-Benzene.

1 gram of pseudo-cuminol gave 2.0 grams of p-nitrobenzoate. Crude product, 114-116°C. Recrystallised from alcohol in small pale yellow needles, m.p. 116-117°C. N (found) 5.00%. Calculated for $C_{16}H_{15}O_4N$ 4.91%.

Thymol.

1 gram of thymol gave 1.0 grams of p-nitro-benzoate. Crude product, m.p. 65-67°C. Recrystallised from alcohol in very pale yellow plates, m.p. 69.5°C. N (found) 4.69%. Calculated for $C_{17}H_{17}O_4N$ 4.68%.

3-Methyl-4-Ethyl Phenol.

1 gram of this phenol gave 1.5 grams of p-nitrobenzoate. Crude product, m.p. 110-112°C. Recrystallised from alcohol in pale yellow plates, m.p. 117.5°C. Vavon and Paira (C. 1930, ii, 235) give m.p. 116°C.

2-Ethyl-4-Methyl Phenol.

1 gram of this phenol gave 1.0 grams of p-nitrobenzoate. Crude product, m.p. 94-96°C. Recrystallised from alcohol in very pale yellow plates, m.p. 97-98°C. Vavon and Paira (loc.cit.) give m.p. 95-96°C.

2-Methyl-4-Ethyl Phenol. X

1 gram of this phenol gave 1.5 grams of p-nitrobenzoate. Crude product, m.p. 63-65°C. Recrystallised from alcohol in very pale yellow plates, m.p. 70°C. Vavon and Paira (loc.cit.) give m.p. 70-71°C.

3-Methyl-6-Ethyl Phenol.

1 gram of this phenol gave 1.5 grams of p-nitrobenzoate. Crude product, m.p. 87-89°C. Recrystallised from alcohol in pale yellow plates, m.p. 89.5-90°C. N (found) 5.00%. Calculated for $C_{16}H_{15}O_4N$ 4.91%.

1:4-Dimethyl-2-Hydroxy-Benzene.

1 gram of this xylenol gave 1.1 grams of p-nitrobenzoate. Crude product, m.p. 84-86°C. Recrystallised from alcohol in pale yellow needles, m.p. 87°C. N (found) 5.20%. Calculated for $C_{15}H_{13}O_4N$ 5.16%.

The derivatives marked thus, X, were prepared by the chloroform method.

3:5-Dinitro-Benzoates.

The general method used for the preparation of 3:5-dinitro-benzoates has been the same as with the p-nitro-benzoates. 1 gram of the phenol was dissolved in 20 cc. dry pyridine and 2.5 grams of the acid chloride was added. In this case, however, very little action took place at ordinary temperature and it was necessary to heat under reflux condenser for 1 hour to complete the reaction. The yields obtained from phenol, the cresols and xylenols were, in the main, good but the crude products were discoloured, usually dark red. o-Ethyl phenol, o-propyl phenol and mesitol were found to give very poor yields by this method. The pyridine method has been used by Phillips and Keenan (J.A.C.S., 1931, 53, 1924). In the preparation of the remaining 3:5-dinitro-benzoates chloroform was used as a solvent and the method of working was the same as described under p-nitro-benzoates. The chloroform method has been found to be much superior to the pyridine as the yields were better and the crude product was much improved in quality.

Phenol.

1 gram of phenol gave 1.0 grams of a 3:5-dinitro-benzoate. Crude product m.p. 135-140°C. Recrystallised from alcohol, in pale yellow plates, m.p. 145°C. Phillips and Keenan (loc.cit.) give m.p. 145.8°C.

o-Cresol.

1 gram of o-cresol gave 1.5 grams of 3:5-dinitrobenzoate. Crude product, m.p. 130-132°C. Recrystallised from alcohol in pale yellow flat needles, m.p. 137-138°C. Phillips and Keenan (loc.cit.) give m.p. 138.4°C.

m-Cresol.

1 gram of m-cresol gave 1.0 grams of 3:5-dinitrobenzoate. Crude product, m.p. 159-160°C. Recrystallised from alcohol in small, pale yellow needles, m.p. 164°C. Phillips and Keenan (loc.cit.) give m.p. 165.4°C.

p-Cresol.

1 gram of p-cresol gave 1.0 grams of 3:5-dinitrobenzoate. Crude product, m.p. 185-186°C. Recrystallised from alcohol in small, pale yellow plates, m.p. 187°C. Phillips and Keenan (loc.cit.) give m.p. 188.6°C.

1:2-Dimethyl-3-Hydroxy-Benzene.

0.5 grams of this xylenol gave 1.0 grams of a 3:5-dinitro-benzoate. Crude product m.p. 139-140°C. Recrystallised from alcohol in almost colourless needles, m.p. 142°C. N (found) 9.00%. Calculated for $C_{15}H_{12}O_6N_2$ 8.86%.

1:2-Dimethyl-4-Hydroxy-Benzene. X

1 gram of this xylenol gave 1.0 grams of 3:5-dinitro-benzoate. Crude product m.p. 178-180°C. Recrystallised from alcohol in small white needles. m.p. 181°C. Phillips and Keenan (loc.cit.) give m. p. 181.6°C.

1:3-Dimethyl-5-Hydroxy-Benzene.

1 gram of this xylenol gave 1.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 190-191°C. Recrystallised from alcohol in very pale yellow needles, m.p.194-195°C. Phillips and Keenan (loc.cit.) gave m.p. 195.4°C.

1:3-Dimethyl-4-Hydroxy-Benzene.

1 Gram of this xylenol gave 1.2 grams of 3:5-dinitro-benzoate. Crude product, m.p. 158-162°C. Recrystallised from alcohol in small white plates, m.p. 164°C. Phillips and Keenan (loc.cit.) give m.p. 164.6°C.

1:3-Dimethyl-2-Hydroxy-Benzene.

1 gram of this xylenol gave 1.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 154-156°C. Recrystallised from alcohol in small, very pale yellow crystals, m.p. 157-158°C. Phillips and Keenan (loc.cit.) give m.p. 158.8°C.

1:4-Dimethyl-2-Hydroxy-Benzene.

1 gram of this xylenol gave 1.3 grams of 3:5-dinitro-benzoate. Crude product, m.p. 133-134°C. Recrystallised from alcohol in small, very pale yellow needles, m.p.137°C. Phillips and Keenan (loc.cit.) give m.p.137.2°C.

o-Ethyl Phenol. X

1 gram of o-ethyl phenol gave 2.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 102-103°C. Recrystallised from alcohol in white plates, m.p. 107°C. Vavon and Mitchovitch (Bull. soc.chim., 1929, (IV) 45, 961-972) give m.p. 108°C.

p-Ethyl Phenol.

1 gram of p-ethyl phenol gave 1 gram of 3:5-dinitrobenzoate. Crude product, m.p. 129-130°C. Recrystallised from alcohol in small white plates, m.p. 132°C. Vavon and Mitchovitch (loc.cit.) give m.p. 132-133°C.

o-n-Propyl Phenol. X

1 gram of o-n-propyl phenol gave 1.5 grams of 3:5-dinitro-benzoate. Crude product, m.p. 74-76°C. Recrystallised from alcohol in very pale yellow plates, m.p. 78-78.5°C. N (Found) 8.53%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%.

p-n-Propyl Phenol. X

1 gram of p-n-propyl phenol gave 2.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 115-117°C. Recrystallised from alcohol in pale yellow plates, m.p. 120°C. N (found) 8.53%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%.

o-n-Butyl Phenol. X

1 gram of o-n-butyl phenol gave 1.5 grams of 3:5-dinitro-benzoate. Crude product, m.p. 75-80°C. Recrystallised from alcohol in pale yellow needles, m.p. 80-81°C. N (found) 8.22%. Calculated for $C_{17}H_{16}O_6N_2$ 8.13%

p-n-Butyl Phenol. X

1 gram of p-n-butyl phenol gave 1.5 grams of 3:5-dinitro-benzoate. Crude product, m.p. 84-86°C. Recrystallised from alcohol in very pale yellow plates, m.p. 89-89.5°C. N (found) 8.10%. Calculated for $C_{17}H_{16}O_6N_2$ 8.13%.

Mesitol.

1 gram mesitol gave 2.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 160-165°C. Recrystallised from alcohol in small white plates, m.p. 171°C. N (found) 8.49%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%.

pseudo-Cumenol.

1 gram of pseudo-cumenol gave 1 gram of 3:5-dinitro-benzoate. Crude product, m.p. 130°C. Recrystallised from alcohol in small very pale yellow plates, m.p. 133°C. N (found) (micro) 8.70%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%.

Thymol. X

1 gram thymol gave 1.5 grams of 3:5-dinitro-benzoate. Crude product, m.p. 96-98°C. Recrystallised from alcohol in flat needles, m.p. 102.5°C. Phillips and Keenan (loc.cit.) give m.p. 103.2°C.

3-Methyl-4-Ethyl-Phenol. X

1 gram of this phenol gave 2.0 grams of 3:5-dinitro-benzoate. Crude product, m.p. 122-125°C. Recrystallised from alcohol in small, pale yellow needles, m.p. 129°C. Vavon and Paira (loc.cit.) give m.p. 128°C.

2-Ethyl-4-Methyl Phenol. X

1 gram of this phenol gave 1.5 grams of 3:5-dinitrobenzoate. Crude product, m.p. 130-133°C. Recrystallised from alcohol in small, pale yellow needles, m.p. 138°C. Vavon and Paira (loc.cit.) give m.p. 136-137°C.

2-Methyl-4-Ethyl Phenol. X

1 gram of this phenol gave 2.5 grams of 3:5-dinitrobenzoate. Crude product, m.p. 139-140°C. Recrystallised from alcohol in small yellow plates, m.p. 141°C. N (found) 8.51%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%. Vavon and Paira (loc.cit.) give m.p. 137-138°C.

3-Methyl-6-Ethyl Phenol.

1 gram of this phenol gave 2.0 grams of 3:5-dinitrobenzoate. Crude product, m.p. 113-115°C. Recrystallised from alcohol in pale yellow needles, m.p. 116.5-117°C. N(found) 8.60%. Calculated for $C_{16}H_{14}O_6N_2$ 8.49%.

The derivatives marked thus, X, were prepared by the chloroform method.

Phenoxy-Acetates.

For the preparation of phenoxy-acetates the modification of the general method suggested by Brüchner (Zeits. für. ang.chem., 41, 37, 1043, 1928) was used.

The phenol (1 gram) was mixed with finely powdered sodium hydroxide (2 grams) and powdered monochlor-acetic acid (1 gram) was added. Very gentle heating was necessary to start reaction which then proceeded vigorously of its own accord. This reaction was carried out under reflux condenser. The resulting product was dissolved in 15 cc. warm water and allowed to cool. In some cases a sodium salt separated. The sodium salts were decomposed with dilute mineral acid. The precipitated phenoxy-acetate was filtered off and crystallised from a suitable solvent. With the less acidic phenols a better yield was obtained by the method of Fischer (Ges. abh. z. Kenntnis d. Kohle, ii, 236, 1918) who heated the phenol in solution in sodium hydroxide with monochlor acetic acid for three hours.

Phenoxy-Acetates.

Phenol.

1 gram phenol gave 1.1 grams phenoxy-acetate. Crystallised from water in stout white needles, m.p. 99°C. Hantzsch (Ber., 1886, 19, 1296) gives m.p. 98-99°C.

o-Cresol.

1 gram o-cresol gave 1.2 grams o-cresoxy-acetate. Crystallised from water in needles, m.p. 151-152°C. Oglialoro and Cannone (Gazz. chim. ital., 1888, 18, 511) give m.p. 151-152°C.

m-Cresol.

1 gram m-cresol gave 1.0 grams m-cresoxy-acetate. Crystallised from water in small white plates, m.p.103°C. Oglialoro and Forte (Gazz. chim. ital., 1890, 20, 508) give m.p. 102°C.; Koelsch (J.A.C.S., 1931, 53, 304) gives m.p. 102-103°C.

p-Cresol.

1 gram p-cresol gave 1.0 grams p-cresoxy-acetate. Crystallised from water in white needles, m.p. 135-136°C. Gabriel (Ber., 1881, 14, 923) gives m.p. 135-136°C.

1:2-Dimethyl-3-Hydroxy-Benzene.

0.5 grams of this xylenol gave 1.0 grams of xylenoxy-acetic acid. Crystallised from benzene in small plates, m.p. 187°C. Brüchner (Zeits. für ang. chem., 1928, 41, 37,1043) gives m.p. 187°C.

1:2-Dimethyl-4-Hydroxy-Benzene.

1 gram of this xylenol gave 1.0 grams of xylenoxy-acetate. Crystallised from benzene in small white needles, m.p. 160-161°C. Gluud and Breuer (C. 1919, i, 626) give m.p. 162.5°C.

1:3-Dimethyl-5-Hydroxy-Benzene.

1 gram of this xylenol gave 1.1 grams of xylenoxy-acetic acid. The crude product crystallised from water melted at 82-84°C. which corresponds approximately with the m.p. given in the literature. (Schutz, Buschmann, Wissebach, Ber., 1923, 56, ii, 1967) and others, viz:- 85-86°C. Recrystallisation of this product from a petroleum ether-benzene mixture yielded rectangular plates, m.p. 110°C. (found. C 66.71%, H 6.67%; $C_{10}H_{12}O_3$ requires C 66.67%, H 6.67%) The pure product melting at 110°C., after crystallisation from water gave needles, m.p. 82-83°C. which lost 9.0% by weight when dried at 103°C. and yielded a residue which melted at 110°C. It appears therefore that the xylenoxy-acetic acid, m.p. 85-86°C., described in the literature is the hydrate $C_{10}H_{12}O_3.H_2O$ (water 9.1%) and that the anhydrous substance melts at 110°C.

A note recording this work was sent to the Chemical Society almost simultaneously with the appearance of the publication of Schneider and Shohan (Bur. Mines, Report of Investigations No. 2969, 10, 1929) giving the m.p. of this xylenoxy/

xylenoxy acetic acid as 111°C. The present author's work was not published and the hydrate reported therein has now been confirmed by Albright (J.A.C.S, 1933, 55, 1736).

1:3-Dimethyl-4-Hydroxy-Benzene.

1 gram of this xylenol gave 0.9 grams of the xylenoxy acetic acid. Crystallised from water in small needles, m.p. 140.5°C. Gluud and Breuer (loc.cit.) give m.p. 141.6°C.

1:3-Dimethyl-2-Hydroxy-Benzene.

1 gram of this xylenol gave 1.2 grams of the xylenoxy acetic acid. Crystallised from benzene in small lustrous plates, m.p. 139.5°C. Brüchner (loc.cit.) gives m.p. 139.5oC.

1:4-Dimethyl-2-Hydroxy-Benzene.

1 gram of this xylenol gave 1.0 grams of xylenoxy acetic acid. Crystallised from water in small needles, m.p. 116°C. Gluud and Breuer (loc.cit.) give m.p. 118°C.

o-Ethyl Phenol.

1 gram of o-ethyl phenol gave 1.0 grams of the phenoxy-acetate. Crystallised from benzene in small needles, m.p. 139-140°C. Brüchner (loc.cit.) gives m.p. 140-141°C.

p-Ethyl Phenol.

1 gram of p-ethyl phenol gave 1.2 grams of the phenoxy-acetate. Crystallised from petroleum ether (60-80°C) in regular hexagons, m.p. 96-97°C. Brüchner (loc.cit.) gives m.p.96°C.

o-n-Propyl Phenol.

1 gram of o-n-propyl phenol gave 1.3 grams of the phenoxy-acetate. Crystallised from petroleum ether (60-80°C.) in small needles, m.p.100-101°C. (found C 68.21%; H 7.30%. Calculated for $C_{11}H_{14}O_3$ C 68.02%; H 7.22%.)

p-n-Propyl Phenol.

1 gram of p-n-propyl phenol gave 1.0 grams of the phenoxy-acetate. Crystallised from petroleum ether (60-80°C.) in small needles, m.p. 91°C. (found C 68.30%; H 7.21%. Calculated for $C_{11}H_{14}O_3$ C 68.02%; H 7.22%.)

o-n-Butyl Phenol.

1 gram of o-n- butyl phenol gave 1.1 grams of the phenoxy-acetate. Crystallised from benzene in small needles, m.p. 105°C. Sandulesco and Girard (Bull. soc. chim., 1930, 1300) give m.p. 105.5°C.

p-n-Butyl Phenol.

0.5 grams of p-n-butyl phenol gave 0.5 grams of the phenoxy-acetate. Crystallised from petroleum ether (60-80°C.) in small needles, m.p. 82-83°C. (Found, micro. C 69.31%; H 7.79%. Calculated for $C_{12}H_{16}O_3$ C 69.23%; H 7.69%).

Mesitol.

1 gram of mesitol gave 1.0 grams of the phenoxy-acetate. Crystallised from water in needles, m.p. 149-150°C. (Found, micro. C 67.90%; H 7.13%. Calculated for $C_{11}H_{14}O_3$ C 68.02%; H 7.22%.)

pseudo-Cumenol.

1 gram of pseudo-cumenol gave 1.0 grams of the phenoxy-acetate. Crystallised from benzene in small needles, m.p. 129-130°C. (Found, micro. C 68.11% H 7.13%. Calculated for $C_{11}H_{14}O_3$ C 68.02% H 7.22%.

Thymol.

1 gram of thymol gave 1.2 grams of the phenoxyacetate Crystallised from benzene in small diamond shaped crystals, m.p. 147-149°C. Koelsch (loc.cit.) gives m.p. 148-149°C.

3-Methyl-4-Ethyl Phenol.

1 gram of this phenol gave 1.2 grams of the phenoxyacetate. Crystallised from benzene in small needles, m.p. 131-132°C. Vavon and Paira (C.1930, ii, 235) give m.p. 131-132°C.

2-Ethyl-4-Methyl Phenol.

1 gram of this phenol gave 1.0 grams of the phenoxyacetate. Crystallised from benzene in fine needles, m.p.132-132.5°C. Vavon and Paira (loc.cit.) give m.p. 132-133°C.

2-Methyl-4-Ethyl Phenol.

1 gram of this phenol gave 1.1 grams of the phenoxyacetate. Crystallised from water in needles, m.p. 125-126°C. Vavon and Paira (loc.cit) give m.p. 125-126°C.

3-Methyl-6-Ethyl Phenol.

1 gram of this phenol gave 1.0 grams of the phenoxyacetate. Crystallised from benzene in flat hexagons, m.p. 96°C. (Found, micro. C 67.85% H 7.24%. Calculated for

Calculated for $C_{11}H_{14}O_3$ C 68.02% H 7.22%.

6-Ethyl-2-Methyl Phenol.

1 gram of this phenol gave 1.5 grams of the phenoxyacetate. Crude product melted at about 115°C. Recrystallised from benzene and finally from petroleum ether (60-80°C.) in white plates, m.p. 149-150°C. The micro-analysis on this product did not agree with the calculated figures and therefore the identity of this substance is not definitely established.

With the exception of thymol and 1:3-dimethyl-5-hydroxy-benzene which was obtained from Schuchardt, all the phenols have been prepared. 6-Ethyl-2-methyl phenol which was prepared has evidently not been obtained in a state of purity as no satisfactory derivatives have been obtained from this phenol. The micro analysis recorded in this work were done by Dr. A. Schoeller.

Solubilities of Phenoxy-Acetates.

Phenol	m.p. °C.	Water	Alcohol	Benzene	Pet. Ether	$CHCl_3$	CS_2	Acetone	Na Salt in alkali
Phenol	99	easily in boiling	easily	easily in warm	not easily in boiling	easily	easily in warm	easily	easily
o-cresol	151 152	not easily in boiling	easily	not very in boiling	not easily in boiling	easily	easily in cold	easily	easily
p-cresol	135 136	easily in warm	easily	easily in warm	not easily in boiling	easily	easily	easily	not easily
m-cresol	103	easily in warm	easily	easily in warm	not easily in boiling	easily	easily	easily	not easily
1:3:2 xylenol	139.5	easily in boiling	easily	easily in warm	not easily in boiling	easily	easily in warm	easily	not easily
o-ethyl	139 140	easily in boiling	easily	easily in warm	not easily in boiling	easily	easily in warm	easily	easily
1:3:4 xylenol	140.5	easily in warm	easily	easily in warm	not easily in boiling	easily	easily	easily	easily
1:4:2 xylenol	116	easily in warm	easily	easily in warm	slightly in boiling	easily	easily in warm	easily	not easily
1:2:3 xylenol	187	not easily in boiling	easily	not easily in boiling	not easily in boiling	easily	easily in warm	easily	not easily
p-ethyl	96 97	easily in warm	easily	easily in cold	not easily in boiling	easily	easily	easily	not easily
1:3:5 xylenol	111	easily in boiling	easily	easily in warm	not easily in boiling	easily	easily in warm	easily	not easily
mesitol	149 150	not easily in boiling	easily	easily in warm	not easily in boiling	easily	easily	easily	easily
2-ethyl-4-methyl	132 132.5	easily in boiling	easily	easily in warm	fairly in boiling	easily	easily	easily	easily
4-ethyl-2-methyl	125 126	not easily in boiling	easily	not easily in boiling	not easily in boiling	easily	easily in warm	easily	not easily
6-ethyl-3-methyl	96	not easily in boiling	easily	easily in boiling	not easily in boiling	easily	easily	easily	not easily
1:2:4 xylenol	160 161	not easily in boiling	easily	not easily in boiling	not easily in boiling	easily	not very in warm	easily	not easily
o-n-propyl	100 101	easily in boiling	easily	easily in warm	fairly in boiling	easily	easily	easily	easily
4-ethyl-3-methyl	131 132	easily in boiling	easily	easily in warm	not easily in boiling	easily	easily	easily	not easily
p-n-propyl	91	easily in warm	easily	easily in warm	fairly in boiling	easily	easily	easily	not easily
thymol	147 149	not easily in boiling	easily	easily in warm	not easily in boiling	easily	easily	easily	easily
pseudo cumenol	129 130	not easily in boiling	easily	not easily in boiling	not easily in boiling	easily	easily	easily	not easily
o-n-butyl	105	easily in boiling	easily	easily in warm	fairly easily in boiling	easily	easily	easily	easily
p-n-butyl	82 83	easily in warm	easily	easily in warm	fairly easily in boiling	easily	easily	easily	not easily

The derivatives given in this table are arranged in order of increasing boiling point of the phenols from which they are derived. The boiling points taken are those given in Beilstein. The temperature implied by the word 'warm' is approximately 60°C.

Discussion of Derivatives.

The solubilities (shown in preceding tables) of the derivatives prepared were determined in a rough way by taking approximately the same amounts of derivatives and solvents in each case. It will be seen that, while excellent for identifying individual phenols, the p-nitro- and 3:5-dinitro-benzoates are not of much value as a means of separation. In the case of the p-nitro-benzoates all the derivatives prepared are readily soluble in benzene, chloroform, ether and carbon disulphide and not very soluble in cold alcohol and petroleum ether (60-80°C.). The solubilities of the 3:5-dinitro-benzoates are very similar in character to those of the p-nitro-benzoates, but as a class the 3:5-dinitro-benzoates are less soluble in alcohol. With the exception of the derivative of 1:3-dimethyl-5-hydroxy-benzene all are easily soluble in cold acetophenone. Differences in solubilities in alcohol exist but are not sufficiently great to allow of a clean separation being obtained by fractional crystallisation.

The phenoxy-acetates, on the other hand, are much more useful. A preliminary separation as the sodium salts is possible. The solubilities of the sodium salts given in the table are those observed during the preparation of the derivatives. It will be noticed that where there is only/

only one substituent group in the phenol the sodium salts of the ortho substituted phenoxy-acetates are more easily soluble in alkali than thos of the corresponding para-substituted phenoxy-acetates. There is also a difference in the solubilities of the free acids in water and benzene. Of the three cresoxy acetic acids the o-cresoxy acetate is the most insoluble in water and benzene while p-cresoxy acetate is less soluble in water and benzene than m-cresoxy acetate. This difference in solubilities has been noted by Lederer (Zeits, ang. chem., 1895, 114) and used by Gluud and Breuer (Ges. Abh.z. Kenntnis d. Kohle, 1918, 2, 236) and others as a means of separation.

The xylenoxy acetates as a class are only slightly soluble in cold water while in boiling water the derivatives of the o-xylenols are the least soluble, the derivatives of the m-xylenols being less soluble than those of the p-xylenol. The difference in solubilities is such that only a very rough separation might be expected by fractional crystallisation from water. These xylenoxy acetates are not readily soluble in cold benzene but all, except the two ortho xylenoxy acetates, are easily soluble in warm benzene. A separation of the two o-xylenols from the others is therefore possible by this means.

The phenoxy acetate of o-ethyl phenol is less soluble/

soluble in water and benzene than the corresponding derivative of p-ethyl phenol but the difference is not sufficiently great to give a really good separation.

The derivatives from o- and p-propyl phenol have very similar solubilities though the phenoxyacetate from o-n-propyl phenol is less soluble in water and benzene than that from p-n-propyl phenol. The difference is not marked.. These observations also apply to the o- and p-n-butyl phenol derivatives.

The two trimethyl phenols, mesitol and pseudocumenol, gave phenoxy acetates which do not differ much in solubility. The sodium sals of the phenoxy acetate of pseudo-cumenol is less soluble in dilute alkali than is the sodium salt of the phenoxy acetate of mesitol.

Among the ethyl-methyl phenols investigated the sodium salts of the phenoxyacetates of 3-methyl-4-ethyl, 2-methyl-4-ethyl and 3-methyl-6-ethyl phenol are relatively insoluble in dilute alkali. The phenoxy acetate of 2-methyl-4-ethyl and 3-methyl-6-ethyl phenols are less soluble in water and benzene than the other but the difference does not seem to be sufficiently great to give a clean separation by fractional crystallisation.