441. *The Sommelet Reaction. Part III. The Choice of Solvent and the Effect of Substituents.*

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Electron-attracting substituents decrease the rate and the yield of the Sommelet reaction even when electron-releasing substituents are also present. Best conditions are given for the preparation of thirteen aldehydes, including phenolic aldehydes and dialdehydes. 50% Acetic acid solution is introduced as the best solvent for the Sommelet reaction.

AROMATIC aldehydes, substituted by halogens or alkyl or alkoxy-groups, are readily prepared by the Sommelet reaction (cf. Part I, *J.*, 1949, 2700; Part II, *ibid.*, p. 2704). The effect of a nitro-group has been studied by Mayer and English (*Annalen*, 1918, **417**, 63) who failed to prepare *o*- and *p*-nitrobenzaldehyde from the corresponding benzyl chlorides. Graymore (*J.*, 1947, 1118), however, obtained *p*-nitrobenzaldehyde in poor yield from *p*-nitrobenzylmethyleneamine. As no other aldehyde with a strongly electron-attracting group (NO_2, CHO, COMe, SO_2NH_2) appears to have been prepared by the Sommelet method we have decided to study the effect of such substituents.

It soon became apparent that electron-attracting substituents have an unfavourable effect on the Sommelet reaction. It has been shown in Part I (*loc. cit.*) that the reaction of an arylmethyl halide with hexamine proceeds in three steps: (i) a quaternary compound, the hexaminium halide, is formed, (ii) this is hydrolysed to an arylmethylamine, and (iii) the amine is converted into an aldehyde (the Sommelet reaction proper). Our preparative experience indicated that the rate of (i) was decreased by electron-attracting substituents, and this conclusion was confirmed by semi-quantitative rate measurements. A *p*-chloro-substituent has a slight, a *p*-nitro-substituent a pronounced effect. Step (ii) is fast in comparison with the others. The velocity of step (iii) shows very little substituent effect but it is characteristic for negatively substituted aldehydes that yields show a maximum at a definite reaction time and drop off sharply on prolonged heating (cf. Nos. 7 and 8 below, and Table II). The m. p. of the crude product is also decreased, indicating that the aldehyde participates in side reactions. The time of heating is therefore critical in the preparation of aldehydes with electron-attracting groups; with other aldehydes no such difficulty was encountered.

It follows from these facts that, when the hexaminium salt is formed during the Sommelet reaction, the slowness of this step necessitates prolonged heating which reduces the yield and purity of the aldehyde. It is therefore imperative in many cases to prepare and isolate the hexaminium salt first by heating the reactants in chloroform solution which may be done for any length of time without fear of side-reactions.

It was also found that the usual solvent, aqueous ethanol, gave poor yields in many cases. A better reaction medium was therefore sought.

The Choice of Solvent.—Hewett (*J.*, 1940, 297) introduced glacial acetic acid as a solvent for the Sommelet reaction and Badger (*J.*, 1941, 535) prepared the two naphthaldehydes in good yield by this method from the bromomethylnaphthalenes. Very concentrated solutions were employed with a boiling time of only 0·5—1 minute. When we repeated this procedure with 1-chloromethylnaphthalene much of it was recovered unchanged. Ten minutes' heating resulted in the disappearance of the starting material but the yield of aldehyde was poor and decreased further on longer boiling. At the concentration used, the boiling point of the mixture was over 160° and it was apparent that decomposition of the aldehyde occurred. This was confirmed in the case of benzaldehyde: after 1 hour's boiling with hexamine in glacial acetic acid less than one third was recovered. Besides tarry products, benzylamine and benzylmethylamine were formed, *i.e.*, a reversal of the Sommelet reaction had taken place. No such effect was noticed with lower-boiling solvents. Acetic acid should therefore be used with care; the solution should contain at least 5 parts of solvent for each part of hexamine, and boiling be as short as possible.

To carry out the reaction at a lower temperature, 50% acetic acid solution was used as reaction medium. This solvent seems to combine a suitable boiling point with good solvent power and a desirable acidity. The Sommelet reaction [step (iii)] is faster in this medium than, at the same temperature, in aqueous ethanol. In most cases, though not in all, it proved to be the best solvent. It has the disadvantage, however, that it rapidly hydrolyses hexamine, *e.g.* a 70% yield of 1-naphthaldehyde fell to 23% when the solution of hexamine in 50% acetic acid was boiled for 15 minutes before the addition of 1-chloromethylnaphthalene. This can be overcome by the use of excess of hexamine in those cases where the hexaminium salt is formed

TABLE I.

Preparation of aldehydes.

Aldehyde.	Halogenomethyl compound,		Hexaminium salt^{a} (g.).	Hexamine (g.).	Solvent,		Time of heating (hrs.).	M. p.,		Crude yield^{b,c} (%).
		g.				c.c.		crude.	pure.	
1. 1-Naphthaldehyde	1-$C_{10}H_7{\cdot}CH_2Cl$	50	—	79	50% AcOH	235	2	1—2·5°	2·5°^{d}	82^{e}
		10	—	8·5	AcOH	30	$\frac{1}{6}$	—		30^{e}
		10	—	10^{f}	60% EtOH	60	3	—		72^{e}
2. *p*-Nitrobenzaldehyde	*p*-$NO_2{\cdot}C_6H_4{\cdot}CH_2Cl$	—	20	—	50% AcOH	100	1	105	106	59
3. *o*-Nitrobenzaldehyde	*o*-$NO_2{\cdot}C_6H_4{\cdot}CH_2Cl$	—	10	—	50% AcOH	50	2	36—38	44	36 (17)
4. *m*-Nitrobenzaldehyde	*m*-$NO_2{\cdot}C_6H_4{\cdot}CH_2Cl$	—	10	—	50% AcOH	50	2	51—52	58	45 (35)
5. 2 : 4-Dinitrobenzaldehyde	2 : 4-$(NO_2)_2C_6H_3{\cdot}CH_2Cl$	—	10	—	50% AcOH	50—80	1—2	—	—	0
6. *p*-Sulphamylbenzaldehyde^{g}	*p*-$NH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}CH_2Cl$^{h}	—	10	1·6	50% AcOH	33	5	102—104	118	21 (0)
		10	—	7·8^{i}	50% AcOH	50	5	113—114		19 (0)
7. 3-Nitro-4-hydroxybenzaldehyde	3 : 4 : 1-$NO_2{\cdot}C_6H_3(OH){\cdot}CH_2Cl$^{a}	10	—	10	AcOH	100	$\frac{1}{4}$	139—141	144·5	70 (66)
		10	—	10	50% AcOH	100	$1\frac{1}{2}$	139—141		41
8*a*. 5-Nitrosalicylaldehyde	3 : 6 : 1-$NO_2{\cdot}C_6H_3(OH){\cdot}CH_2Cl$^{j}	10	—	10^{k}	AcOH	100	1	122—123	126	57 (45)
		10	—	10	50% AcOH	125	2	122—123		37
8*b*.	3 : 6 : 1-$NO_2{\cdot}C_6H_3(OAc){\cdot}CH_2Cl$^{l}	—	10	—	50% AcOH	135	$1\frac{1}{2}$	122—124		34 (24)
9. 3-Chloro-4-hydroxybenzaldehyde	4 : 3 : 1-$OH{\cdot}C_6H_3Cl{\cdot}CH_2Cl$^{m}	—	10	—	AcOH	25	$\frac{1}{4}$	115—120	139 (lit.)	22 (10)
10. 3 : 5-Dichlorosalicylaldehyde	2 : 3 : 5 : 1-$OH{\cdot}C_6H_2Cl_2{\cdot}CH_2Cl$^{m}	—	20	—	AcOH	50	1	92—94	95	66
		10	—	10	AcOH	45	1	88—92		55 (51)
11*a*. 4-Hydroxy*iso*phthalaldehyde	2 : 1 : 5-$OH{\cdot}C_6H_3(CHO){\cdot}CH_2Cl$^{a}	10	—	10	50% AcOH	55	1	108—109	113	63 (55)
11*b*.	4 : 1 : 3-$OH{\cdot}C_6H_3(CHO){\cdot}CH_2Cl$^{a}	10	—	10	60% EtOH	150	$3\frac{1}{2}$	105—108		30 (0)
		10	—	10	50% AcOH	100	1	106—107		25 (0)
12. 2-Methoxy-5-acetylbenzaldehyde^{o}	2 : 5 : 1-$MeO{\cdot}C_6H_3(COMe){\cdot}CH_2Cl$^{a}	10	—	10	60% EtOH	35	4	137—140^{n}	144	28 (0)
13. Terephthalaldehyde	*p*-$C_6H_4(CH_2Cl)_2$	—	10^{p}	3·6	50% AcOH	85	2	114	116	34
14. Phthalaldehyde	*o*-$C_6H_4(CH_2Br)_2$	—	10	—	50% AcOH	30—50	$\frac{1}{4}$—2	—	—	0
15. 2 : 5-*Dimethoxyterephthalaldehyde*	2 : 5 : 1 : 4-$(MeO)_2C_6H_2(CH_2Cl)_2$^{q}	—	10	—	50% AcOH	50	1	206	207	32 (29)
		—	10	—	AcOH	50	$\frac{1}{4}$	204—206		28 (25)

a. Preparation given in Experimental Section. *b*. The yields are based in all cases on chloromethyl compounds, not on hexaminium salts. *c*. The figure in parentheses indicates the amount which crystallised out of the reaction mixture. The rest was obtained by extraction with ether (3, 4, 6, 9, 12), ethyl acetate (7, 8, 10), or chloroform (11, 15). *d*. The m. p. (33—34°) given by Stephen (*J.*, 1925, **127**, 1877) is erroneous. Repeated purification through the bisulphite compound and by distillation failed to raise the m. p. above 2·5°. The semicarbazone had the m. p. given by Stephen (222°). *e*. The aldehyde was extracted with ether and distilled; b. p. 160—163°/18 mm. *f*. More hexamine (5 g.) was added after 1·5 hours' boiling. *g*. Burton and Hu, *J.*, 1948, 603. *h*. Angyal and Jenkin, *Aust. J. Sci. Res.*, *A*, 1950, in press. *i*. Formaldehyde (3·4 c.c.; 40%) was added. *j*. Buehler, Kirchner, and Diebel, *Org. Synth.*, 1940, **20**, 59. *k*. The intermediate 3-nitro-6-hydroxybenzylmethyleneamine has a low solubility and separates after a short time. To avoid bumping, the yellow precipitate was dissolved by the addition of concentrated hydrochloric acid (15 c.c.) as soon as it appeared. *l*. Jacobs and Heidelberger, *J. biol. Chem.*, 1915, **20**, 659. *m*. Buehler, Brown, Holbert, Fulmer, and Parker, *J. Org. Chem.*, 1941, **6**, 902. *n*. Recrystallised from ethanol. *o*. Gray and Bonner, *loc. cit.* *p*. The hexaminium salt was added to the boiling solution in small portions during 0·5 hour. *q*. Wood and Gibson, *J. Amer. Chem. Soc.*, 1949, **71**, 393.

TABLE II. p-*Nitrobenzaldehyde from* 20 *g. of* p-*nitrobenzylhexaminium chloride.*

Solvent,		Time (mins.).	Yield (g.).	M. p. (crude).	Solvent,		Time (mins.).	Yield (g.).	M. p. (crude).	Solvent,		Time (mins.).	Yield (g.).	M. p. (crude).
	c.c.					c.c.					c.c.			
AcOH	20	2	2·6	98—99°	AcOH	50	20	4·0	97—98	50% AcOH	200	30	3·5	105
AcOH	20	30	2·7	95—98	AcOH	100	10	4·0	105	50% EtOH	60	60	2·2	105
AcOH	50	10	5·9	103	50% AcOH	100	60	6·3	105	Water	250	60	2·4	105

rapidly. When this formation is slow, the hexaminium salt can be prepared in chloroform and then heated in 50% acetic acid solution; hydrolysis is then no disadvantage because it is not hexamine itself but its hydrolysis products which react in step (iii).

Thus, the procedure which is most likely to give good results in yet untried cases is to prepare the hexaminium salt in chloroform and then heat it with 50% acetic acid solution.

The Effect of Substituents.—Details of the preparation, and yields, of fifteen aldehydes are summarised in Table I. Where the hexaminium salt was isolated, this is indicated in the table by showing the amount of this salt used in the reaction. The conditions given in the table represent for each aldehyde (except Nos. 3 and 4 for which the optimum conditions were not ascertained) the highest yield obtained from at least ten runs in which the solvent, the concentration, and the time of heating were varied. In some cases the conditions giving the best yield in another solvent are also given for comparison.

The effect of varying conditions on the yield is shown in Table II for *p*-nitrobenzaldehyde. Runs made without isolating the hexaminium salt gave low yields and impure product. The by-products were, as usual, *p*-nitrobenzylamine and *p*-nitrobenzylmethylamine.

1-Naphthaldehyde has been prepared several times previously by the Sommelet reaction (Mayer and Sieglitz, *Ber.*, 1922, **55**, 1846; Anderson and Short, *J.*, 1933, 485; Coles and Dodds, *J. Amer. Chem. Soc.*, 1938, **60**, 853; Rupe and Brentano, *Helv. Chim. Acta*, 1936, **19**, 586; Ruggli and Preuss, *ibid.*, 1941, **24**, 1350; Badger, *loc. cit.*; Price and Voong, *J. Org. Chem.*, 1949, **14**, 115). It is included here because of the thorough study we made of the reaction conditions, resulting in greatly improved yield. It was found that methylation to 1-(methylaminomethyl)naphthalene was slow (cf. Part I) and the yield was therefore not materially improved by dropwise addition of chloromethylnaphthalene. The Sommelet reaction is the best method of preparation of this aldehyde.

For the preparation of No. 6, the corresponding amine ("Marfanil") was used in most runs because of its availability. It has been ascertained in several cases that the use of an amine hydrochloride, with 1 mol. of hexamine and 1 mol. of formaldehyde, is equivalent to the use of the corresponding hexaminium salt. The low yield in this case is probably due to side-reactions between the sulphonamide group and formaldehyde since amorphous by-products were formed.

Whilst one electron-attracting group reduces the yield of the Sommelet reaction, two apparently inhibit it completely (No. 5). Introduction of an additional hydroxy-group, which accelerates the hexaminium salt formation enormously, has little effect on step (iii). Indeed, in its effect a hydroxy-group is not different from an acetoxy-group, as is shown by comparison of Nos. 8*a* and 8*b*. In the latter the acetyl group has been lost presumably during the acid hydrolysis following the reaction.

The relative position of the substituents is important, however, as is shown by a comparison of Nos. 7 and 8. When the hydroxy-group is in an *o*-position to the prospective aldehyde group, not only the yield but also the reaction rate is reduced. Thus in glacial acetic acid, in the concentration given in the table, the best yield (70%) of No. 7 was obtained after 0·25 hour; on boiling for one hour the yield fell to 51%. In the same concentration, the yield of No. 8 after 0·25, 1, and 2 hours was 45, 57, and 36%, respectively. This effect is even more noticeable in the case of Nos. 11*a* and 11*b* where the same aldehyde was obtained in a lower yield from the isomer having a group *ortho* to the chloromethyl group.

The same effect is responsible for the low yield of 2-methoxy-5-acetylbenzaldehyde (No. 12). This aldehyde, the toxic principle of the leaves of *Encelia farinosa*, was synthetised by Gray and Bonner (*J. Amer. Chem. Soc.*, 1948, **70**, 1249) from *p*-methoxyacetophenone in four steps, using Stephen's aldehyde synthesis. Though the Sommelet reaction is unsatisfactory in this case, it still gives a much better overall yield from *p*-methoxyacetophenone than Gray and Bonner's method.

The Sommelet reaction is not applicable to phenolic compounds unless the activity of the ring is reduced by electron-attracting substituents (Nos. 7, 8, 11), otherwise condensation with formaldehyde occurs. One chlorine does not reduce the activity sufficiently, since No. 9 was obtained in poor yield and with such a low m. p. that purification was not practicable; it was identified only as the semicarbazone. When the benzene ring was substituted with two chlorine atoms (No. 10) yields were again satisfactory.

Dialdehydes.—The preparation of dialdehydes by the Sommelet reaction has not been described previously. A double Sommelet reaction on a bishalogenomethyl compound is feasible but because one aldehyde group acts as an electron-attracting substituent in the formation of the other, and because the incidence of side-reactions is also doubled, the yields are not particularly good. That formation of the second aldehyde group is slower is indicated in the preparation of terephthalaldehyde by the isolation of a by-product which appears to be a polymeric Schiff's base of *p*-aminomethylbenzaldehyde.

While this work was in progress, a paper was read by Wood, Tung, Perry, and Gibson to the September, 1949 (Atlantic City), meeting of the American Chemical Society. In this paper, which is available to us in abstract only, they report the preparation of eleven bishexaminium salts of which six yielded dialdehydes. While waiting for the publication of their results we have suspended the work on dialdehydes. Their general conclusions agree with ours: *o*-dialdehydes were not obtained (cf. No. 14), and others only if at least one position adjacent to each aldehyde group was unsubstituted (cf. Part II, *loc. cit.*).

No. 15, 2 : 5-dimethoxyterephthalaldehyde, is remarkable for its intense yellow colour and strong fluorescence. The reason for its colour is similar to that for 2 : 5-dihydroxyterephthalic acid and its esters which were extensively studied by Hantzsch (*Ber.*, 1915, **48**, 797; 1917, **50**, 1213). The colour would nowadays be explained by resonance.

We were unable to prepare diphenyl-2 : 2′-dialdehyde by the Sommelet reaction. The reason for this failure is not clear but it may be the same as in the case of *o*-dialdehydes, *i.e.*, interaction of the adjacent functions. We hope to investigate this problem later.

Recently Hass and Bender (*J. Amer. Chem. Soc.*, 1949, **71**, 1767) described another method for the preparation of aldehydes from halogenomethyl compounds: the reaction with the sodium salt of 2-nitropropane. To compare the value of this method with the Sommelet reaction in the case of polysubstituted aldehydes it was tried for the preparation of Nos. 10, 11, and 12, but without success.

EXPERIMENTAL.

(M. p.s are corrected.)

Preparation of Aldehydes.—The hexaminium salts, or the halogenomethyl compounds and hexamine, in the amounts given in Table I, were boiled under reflux for the time indicated. Concentrated hydrochloric acid (350 c.c. for each mole of hexamine or hexaminium salt) was then added and boiling continued for another 5 minutes. If this acid treatment was omitted the aldehydes were sometimes contaminated by Schiff's bases. The reaction mixture was diluted with water and allowed to cool; the aldehydes crystallised out. Where a significant amount remained in solution it was recovered by solvent extraction as indicated in the table. It was not found necessary to purify any of the aldehydes by conversion into their bisulphite compounds.

Preparation of Hexaminium Salts.—The chloromethyl compound (0·1 mole) and hexamine (15·5 g.) were boiled under reflux in chloroform (100 c.c.), and the quaternary salt filtered off after the solution had cooled. Times of boiling and yields are given for the salts prepared from the following chloromethyl compounds: 1-chloromethylnaphthalene, 1 hour, 96%; 2 : 4-dinitrobenzyl chloride,* 5 hours, 74%; 3-nitro-4-hydroxybenzyl chloride, 1 hour, 96%, yellow, m. p. 174°; 3-nitro-6-hydroxybenzyl chloride,* 1 hour, 95%, yellow, m. p. 193° (decomp.); 3-nitro-6-acetoxybenzyl chloride, 7 hours, 70%, yellow, m. p. 191—193° (decomp.); 3-chloro-4-hydroxybenzyl chloride, 2 hours, 105%, m. p. 140—141° (this compound contained chloroform which could not be removed without decomposition); 3 : 5-dichloro-2-hydroxybenzyl chloride, 3 hours, 93%, m. p. 174—178° (decomp.); 5-chloromethylsalicylaldehyde,* 3½ hours, 90%, yellow, m. p. 178—182° (decomp.); 4-hydroxy-3-chloromethylbenzaldehyde, 3 hours, 94%, m. p. 184—185° (decomp.); 2-methoxy-5-acetylbenzyl chloride, 2 hours, 93%, m. p. 182° (decomp.). The salt marked by * were described by Jacobs and Heidelberger (*loc. cit.*) but without giving yields.

p-Sulphamylbenzylhexaminium chloride was prepared in alcohol according to Angyal and Jenkin (*loc. cit.*).

Since the nitrobenzylhexaminium chlorides are somewhat souble in chloroform the yields were improved by removing, after 4 hours' boiling, half of the chloroform by distillation and adding an equal volume of acetone. Yields obtained thus from the nitrobenzyl chlorides were: *o*-, 89*; *m*-, 89*; *p*-, 91%.* Mayer and English (*loc. cit.*) reported 61% and 68% for the *o*- and *p*-derivative, respectively.

Since the bishexaminium salts decompose on being heated, they were prepared by adding the bishalogenomethyl compounds (0·1 mole) to a solution of hexamine (30 g.) in chloroform (330 c.c.) and leaving its solution at room temperature for two days. The salts were thus obtained from *p*-xylylene dichloride, 90%, m. p. 160—170° (decomp.); from *o*-xylylene dibromide, 71%; and from 2 : 5-dimethoxy-*p*-xylylene dichloride, 99%, m. p. 195—197° (decomp.).

The chloroform solutions of the two nitrohydroxybenzyl chlorides gave precipitates immediately on being mixed with a cold solution of hexamine in chloroform. These yellow precipitates were at first believed to be phenolic salts until it was found that they contained the chlorine in ionic form and were identical with the salts formed on boiling the reactants for an hour. All the other chloromethyl compounds having a hydroxy-group gave immediate precipitates with hexamine, some of which changed in appearance on being boiled; but it was not ascertained whether they were phenolic or quaternary salts. The activating effect of the hydroxy-group is eliminated by acetylation since 3-nitro-6-acetoxybenzyl chloride reacts only slowly with hexamine.

Comparative Reaction Rates.—(a) *Step* (i). Solutions of hexamine (1·4 g.) in chloroform (13 c.c.), warmed to 55°, were added to 0·01 mole each of benzyl, *p*-chlorobenzyl, and *p*-nitrobenzyl chlorides. After 30 minutes at 55°, ice-cold nitric acid (50 c.c.; 6%) was added with shaking, and the aqueous layer was separated and aliquots titrated for ionic chloride. Yields of salt were: benzyl, 31·5; *p*-chlorobenzyl, 30; *p*-nitrobenzyl, 10%.

(b) *Step* (iii). Solutions of hexamine (1·4 g.), amine hydrochloride (0·01 mole; benzyl- 1·44, *p*-chlorobenzyl-1·78, *p*-nitrobenzyl- 1·89 g.), and formaldehyde (0·1 c.c.; 40%) in 50% acetic acid (10 c.c.) were kept at 75° for 1 hour, then a mixture of hydrochloric acid (10 c.c.) and water (20 c.c.) was added. Benzaldehyde was removed by steam-distillation, oxidised by alkaline hydrogen peroxide, and weighed as benzoic acid. *p*-Chlorobenzaldehyde was extracted by ether, and *p*-nitrobenzaldehyde by benzene, and the extracts were washed with sodium carbonate solution and evaporated to dryness. Yields were: benzaldehyde, 18; *p*-chlorobenzaldehyde, 21; and *p*-nitrobenzaldehyde, 19%.

When benzylamine hydrochloride reacted under the same conditions in 80% ethanol, the yield was only 6%. Ethanol of lower concentration did not suffice to give a homogeneous solution. Comparison with the other two amines could not be made because, even from 80% ethanol, the Schiff's bases separated.

Reaction of Benzaldehyde with Hexamine in Acetic Acid.—Benzaldehyde (20 g.), hexamine (23 g.), and glacial acetic acid (70 c.c.) were refluxed for 1 hour, the temperature of the mixture being 140°. Addition of dilute hydrochloric acid and steam-distillation gave 6·3 g. of benzaldehyde. Steam-distillation was continued until all formaldehyde was removed. A heavy oil (6 g.) settled out from which no pure compound could be isolated. The supernatant liquid was concentrated, made alkaline with sodium hydroxide, and extracted with ether; evaporation of the solvent left 7·2 g. of amines. Distillation of these gave a fraction (2·0 g.), b. p. 76—82°/20 mm., a small amount of higher boiling material, and much undistillable residue. The distilled amines were treated with toluene-*p*-sulphonyl chloride and gave toluene-*p*-sulphonbenzylamide, m. p. 114°, and toluene-*p*-sulphonbenzylmethylamide, m. p. 94°, both identified by mixed m. p.s.

The By-products of the Sommelet Reactions.—The mother-liquor from the preparation of *p*-nitrobenzaldehyde (No. 2, Table I) was freed from formaldehyde by steam-distillation. Sodium hydroxide solution (150 c.c.; 5%) was added and the bases extracted with ether. Evaporation of the solvent yielded an oil (2·3 g.) which was treated with toluene-*p*-sulphonyl chloride (3 g.) in pyridine (27 c.c.). The sulphonamides were separated by treatment with hot sodium hydroxide solution (220 c.c.; 8%) and gave, after crystallisation from aqueous alcohol, toluene-*p*-sulphon-*N*-*p*-nitrobenzylamide (0·8 g.; m. p. 120°) and toluene-*p*-sulphon-*N*-*p*-nitrobenzyl-*N*-methylamide (3·2 g.; m. p. 127·5°) (Angyal, Morris, Rassack, Waterer, and Wilson, *J.*, 1949, 2722).

The By-product of the Preparation of Terephthalaldehyde.—The mother-liquor of No. 13 was freed from formaldehyde by steam-distillation and made alkaline with sodium hydroxide. A cream solid was precipitated which was insoluble in all solvents, soluble in acids, and on being heated charred without melting. With phenylhydrazine it gave a yellow precipitate.

3-*Nitro*-4-*hydroxybenzyl Chloride.*—Hydrogen chloride was passed into a well-stirred mixture of *o*-nitrophenol (100 g.), formaldehyde (167 c.c.; 40%), concentrated hydrochloric acid (760 c.c.), and concentrated sulphuric acid (10 c.c.) at 90—100° for 6 hours. After cooling, the mixture was extracted with benzene (250 c.c.), and the extract dried [Na_2SO_4] and evaporated under reduced pressure until crystallisation started. Addition of anhydrous ethanol (150 c.c.) and cooling gave the crude product, m. p. 68—69° (75 g., 56%). After crystallisation from benzene (50 c.c.) with the addition of light petroleum (250 c.c.) yellow needles were obtained (48 g.), m. p. 72—74°. D.R.P. 132,475 (Friedländer, **6**, p. 142) reported m. p. 75°.

5-*Chloromethylsalicylaldehyde.*—Hydrogen chloride was passed into a well-stirred mixture of salicylaldehyde (30 g.), formaldehyde (18·5 c.c.; 40%), and concentrated hydrochloric acid (255 c.c.), kept at 15—20° by external cooling, for 3 hours. The precipitated white solid was filtered off and dissolved in ether (250 c.c.), and the solution dried (Na_2SO_4). Evaporation *in vacuo* of most of the solvent gave two successive solid fractions (14 g. each); these were combined and quickly dissolved in hot light petroleum (500 c.c.; b. p. 40—70°) which left some oil. On cooling, the product (15 g.) was obtained in colourless needles, m. p. 85—86°. D.R.P. 114,194 (Friedländer, **6**, p. 139) reported m. p. 88°. By concentration of the mother-liquor another 5 g. were obtained which yielded 3 g. on recrystallisation (total yield 43%). Heating should be avoided at all stages of this preparation since it causes reddening of the product.

4-*Hydroxy*-3-*chloromethylbenzaldehyde.*—Hydrogen chloride was passed into a well-stirred mixture of *p*-hydroxybenzaldehyde (25 g.), formaldehyde (16 c.c.; 40%), and concentrated hydrochloric acid (180 c.c.) for 3 hours. The temperature rose to 40°, and a blood red solution was obtained which started to deposit a solid after 2 hours. Cooling, filtration, and crystallisation from chloroform (400 c.c.) gave the crude product, m. p. 129—131° (18·9 g.; 48%). It was crystallised from acetone (25 c.c.)–chloroform (50 c.c.) giving a solid (12·3 g.), m. p. 135—136°. For analysis, the *aldehyde* was crystallised from chloroform; it formed colourless needles, m. p. 138° (Found: Cl, 20·9. $C_8H_7O_2Cl$ requires Cl, 20·8%).

2-*Methoxy*-5-*acetylbenzyl Chloride.*—Hydrogen chloride was passed into a well-stirred mixture of *p*-methoxyacetophenone (37 g.), formaldehyde (23 g.; 40%), and concentrated hydrochloric acid (150 c.c.) at 45° for 4 hours. The colour of the mixture changed to dark red and after 3 hours a red solid began to separate. Cooling and filtration gave the crude product (40 g.), m. p. 112—114°, which was crystallised from benzene (160 c.c.)–light petroleum (60 c.c.) yielding a solid (28 g., 69%), m. p. 115—117°. For analysis, the *chloride* was recrystallised from benzene and then melted at 118° (Found: C, 61·35; H, 5·9. $C_{10}H_{11}O_2Cl$ requires C, 60·5; H, 5·6%).

2 : 5-*Dimethoxyterephthalaldehyde.*—This *compound* sublimes *in vacuo* to give a powder, m. p. 207°, of intense yellow colour (Found: C, 61·35; H, 5·3. $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·2%). Its solutions in water or alcohol are yellow with a vivid fluorescence which disappears on the addition of strong acids or alkalis. The *dioxime*, m. p. 246—246·5°, is pale yellow (Found: N, 12·2. $C_{10}H_{12}O_4N_2$ requires 12·5%).

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[*Received, February 9th*, 1950.]