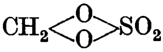
CCXL.—*Cyclic Esters of Sulphuric Acid. Part I. The Reactions of Methylene Sulphate.*

By WILSON BAKER.

THE methods available for the methylenation of aromatic *o*-dihydroxy-compounds to the methylenedioxy-compounds are unsatisfactory. The reaction has invariably been carried out by the action of dihalogenomethanes on the alkali salts of catechol and derivatives. The so-called methylene sulphate is here shown to be a satisfactory agent for the methylenation of *o*-dihydric phenols, monohydric phenols, alcohols, and glycols.

Methylene sulphate, to which the formula  $CH_2<\substack{O\\O}>SO_2$ has been ascribed, was first prepared by Delépine (*Compt. rend.*, 1899, **129**, 831; *Bull. Soc. chim.*, 1899, **21**, 1055) by the action of paraformaldehyde on fuming sulphuric acid. He described it as a colourless crystalline solid, m. p. about 155° (decomp.), which was hydrolysed to formaldehyde and sulphuric acid by heating with water or aqueous alkaline solutions and gave acetals of formaldehyde, $CH_2(OR)_2$, when heated with alcohols. Methylene sulphate figures incidentally in certain patents for the preparation of aromatic hydroxy-aldehydes (Eng. Pats. 160765, 157850, 161679, 164715), and Delaby (*Bull. Soc. chim.*, 1926, **39**, 1612) has prepared the methylene ether of thymol, $(C_{10}H_{13}O)_2CH_2$, by the interaction of sodium thymoxide and methylene sulphate in acetone solution. This author refers to a thesis by Darrigarde (Paris, 1912) in which certain methylene ethers are prepared by means of methylene sulphate, but the work has apparently not been published.

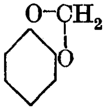
Methylene sulphate has now been prepared by a modification of the methods described by Delépine and Delaby in a yield of over 60%. It is completely stable, can be kept indefinitely, and can be used in much the same way as methyl sulphate. The reactions of this compound may be summarised as follows.

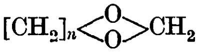
Reaction with o-*Dihydric Phenols.*—Catechol reacts readily with methylene sulphate in 50% acetone solution in presence of sodium hydroxide to give catechol methylene ether (methylenedioxybenzene) (I), which thus becomes a readily accessible substance. Protocatechuic aldehyde in dilute alcoholic solution similarly gives piperonal, but the yield in this case is not so satisfactory. It was not found possible to effect the methylenation of protocatechuic acid.

Reaction with Monohydric Phenols.—Monohydric phenols react with methylene sulphate under specific conditions to give ethers of the type $PhO{\cdot}CH_2{\cdot}OPh$. The methylene ethers of phenol, *o*-, *m*-, and *p*-cresols, and *o*-, *m*-, and *p*-nitrophenols are prepared by heating with methylene sulphate and anhydrous potassium carbonate in benzene. The methylene ethers of guaiacol, and *p*-methoxyphenol are best prepared by the action of methylene sulphate and sodium hydroxide in dilute acetone. The methylene ethers of phenol and the cresols have previously been prepared from the sodium phenoxides and dihalogenomethanes (Henry, *Ann. Chim. Phys.*, 1883, **30**, 269; Arnhold, *Annalen*, 1887, **240**, 201; Bently, Haworth, and Perkin, J., 1896, **69**, 166; Bischoff and Fröhlich, *Ber.*, 1907, **40**, 2789). *p*-Acetamidophenol yields its methylene ether when warmed with methylene sulphate in dilute sodium hydroxide solution. Hydrolysis of the acetyl groups by boiling with dilute alcoholic sodium hydroxide yields *di-*p*-aminophenyl methylene ether*, $NH_2{\cdot}C_6H_4{\cdot}O{\cdot}CH_2{\cdot}O{\cdot}C_6H_4{\cdot}NH_2$; acid hydrolysis causes partial demethylenation.

Reaction with Alcohols.—This yields acetals, $CH_2(OR)_2$ (Delépine, *loc. cit.*).

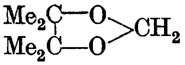
(I.)





$[CH_2]_n{<}\begin{matrix}O\\O\end{matrix}{>}CH_2$

(II.)



$\begin{matrix}Me_2C—O\\ |\\ Me_2C—O\end{matrix}{>}CH_2$

(III.)

Reaction with Glycols.—Ethylene and trimethylene glycols, when distilled with water and methylene sulphate, readily yield the volatile methylene ethers (II; $n = 2$ and 3), and pinacol yields (III). Compounds (II) are totally miscible with water, but (III), which has a strong camphoraceous odour, is only very sparingly soluble.

Reaction with Saligenin.—A case of the methylenation of a phenolic alcohol is afforded by saligenin (*o*-hydroxybenzyl alcohol). This substance reacts with methylene sulphate in a dilute aqueous (or, better, aqueous acetone) solution of sodium hydroxide, or with potassium carbonate in benzene to give 1 : 3-*benzdioxin* (IV).* A derivative of 1 : 3-benzdioxin appears to have been first made by Borsche and Berkhout (*Annalen*, 1903, **330**, 91), who prepared the 6-nitro-derivative (5-nitrosaligenin methylene ether) by acting upon *p*-nitrophenol with formaldehyde in presence of sulphuric acid. Highly halogenated derivatives of homologues have been prepared in the same manner by Chattaway and co-workers by the action of halogen derivatives of acetaldehyde on *p*-substituted phenols (J., 1926, 2720; 1927, 685, 2013; 1928, 1088, 2913, 3241). A second

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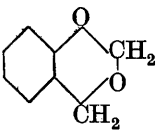
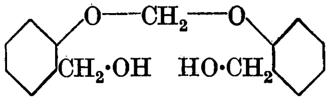
* (Note added in proof) The author's attention has been directed to a paper by Chattaway and Calvet y Prats (*Anal. Fís. Quím.*, 1928, **26**, 417) in which they describe the preparation of 1 : 3-benzdioxin (b. p. 211–212°/758 mm.) from 6-nitro-1 : 3-benzdioxin (Borsche and Berkhout, *loc. cit.*).

non-phenolic product can be isolated from the interaction of saligenin and methylene sulphate, and has proved to be *di-*(o-*hydroxymethylphenoxy*)*methane* (V).

(IV.)





(V.)

The constitution of methylene sulphate will be considered in a later communication, but it may be stated that evidence is available to show that it does not possess the simple formula $CH_2{<}\substack{O\\O}{>}SO_2$ as has previously been supposed.

EXPERIMENTAL.

Methylene Sulphate (compare Delépine and Delaby, *locc. cit.*).—To stirred molten fuming sulphuric acid containing 50% of sulphur trioxide (500 g.), finely powdered paraformaldehyde (100 g.) is added, the temperature being kept between 60° and 70° (2 hours). After 12 hours the pasty product is drained on a sintered glass filter and, air having been sucked through it for a short time, dropped in portions into a stirred mixture of water and ice. The methylene sulphate is collected, washed with cold water till almost neutral, and dried in the air and finally in a vacuum over calcium chloride; it now consists of small colourless crystals (228 g.), m. p. 155° (partial decomp.; rapidly heated : much lower when slowly heated). Washing the product with alcohol and ether as recommended by Delépine is only necessary for purposes of analysis [Found : C, 11·0; H, 1·9; S, as H_2SO_4 by hydrolysis with water for 1 hour on the water-bath, 29·2. Calc. for $(CH_2SO_4)_n$: C, 10·9; H, 1·8; S, 29·1%]. Methylene sulphate in small quantities may be crystallised from acetone, paracetaldehyde, methylal, glycol methylene ether, and dioxan; the hot solutions are not very stable.

Catechol Methylene Ether.—The methylenation of catechol in benzene containing potassium carbonate, or of its disodium salt in acetone, gave very poor results.

To a mixture of catechol (80 g.) in acetone (300 c.c.) and sodium hydroxide (80 g.) in water (300 c.c.), air being excluded by a current of coal gas, methylene sulphate (80 g.) was added in portions with vigorous stirring, so that the temperature kept at about 45°. After 1 hour's stirring, water was added, acetone and catechol methylene ether were distilled in steam, and the latter was extracted with ether; it was obtained as a colourless oil (22 g.), b. p. 170—175°, mainly at 173—174°/756 mm.

Piperonal.—Protocatechuic aldehyde (1·4 g.) in alcohol (10 c.c.) was treated with potassium hydroxide (4·9 g.) in water (10 c.c.) and methylene sulphate (4·4 g.), and warmed till a vigorous reaction set in. After further heating on the water-bath for 5 minutes, cooling, and dilution with water, crude piperonal (0·15 g.) was extracted with ether; m. p. 37° after crystallisation from ligroin.

Methylene Ethers of Phenol, o-, m-, *and* p-*Cresols.*—The methylenation in aqueous alkaline solutions gave unsatisfactory results. To the phenolic compound (21·6 g.) in benzene (100 c.c.) were added, with shaking, potassium carbonate (40 g.) and methylene sulphate (12·1 g.). The mixture was rapidly heated and shaken till the evolution of carbon dioxide almost ceased, then heated on the water-bath for 1 hour, and water added. In the case of diphenyl methylene ether the benzene layer was separated, shaken with aqueous sodium hydroxide solution, then with water, dried, and distilled, leaving a colourless oil (8 g.), b. p. 293—295°. This was best distilled under diminished pressure, b. p. 187—188°/42 mm., and solidified to a crystalline mass, m. p. 16°. Di-*m*- and -*p*-tolyl methylene ethers were isolated by distilling the benzene in steam, cooling the residue in ice after addition of sodium hydroxide, and collecting the solid product. Di-*m*-tolyl methylene ether (4·5 g.) had b. p. 187—188°/19 mm. and m. p. 44°; di-*p*-tolyl methylene ether (5·2 g.), b. p. 191—192°/18 mm. and m. p. 40°. Di-*o*-tolyl methylene ether was isolated by extraction with ether, shaking the extracts with aqueous sodium hydroxide, and drying and distilling them; b. p. 178—179°/16 mm., m. p. 30°.

*Di-*m*-nitrophenyl Methylene Ether.*—A mixture of *m*-nitrophenol (13·9 g.) in benzene (100 c.c.), potassium carbonate (20 g.), and methylene sulphate (6·1 g.) was heated on the water-bath with frequent shaking for 2 hours. After addition of water and distillation of the benzene, the solid product was collected, washed with aqueous sodium hydroxide, then with water, dried (2·4 g.), and crystallised from alcohol (charcoal); long needles were collected from the warm solution and recrystallised from alcohol; m. p. 112° (Found: N, 9·7. $C_{13}H_{10}O_6N_2$ requires N, 9·7%).

*Di-*p*-nitrophenyl methylene ether*, prepared in the same way as the preceding compound (yield, 0·7 g.) and crystallised twice from alcohol (charcoal), was obtained in faintly pink, prismatic needles, m. p. 147° (Found: N, 9·5%).

*Di-*o*-nitrophenyl methylene ether*, similarly prepared (but 1·5 times the quantity of methylene sulphate being used) (yield, 1 g.) and crystallised, formed pale yellow, branching crystals, m. p. 129° (Found: N, 9·9%). It was slowly hydrolysed by hot dilute aqueous-alcoholic sodium hydroxide.

Guaiacol Methylene Ether.—Methylene sulphate (25 g.) was added in portions to a stirred mixture of guaiacol (25 g.), acetone (100 c.c.), and sodium hydroxide (25 g.) in water (100 c.c.) at 50°. The whole was kept for an hour at 50°, water added, the acetone distilled off, and the oily product, which solidified, washed with dilute sodium hydroxide solution, then with water, and crystallised twice from alcohol (charcoal). The ether separated in thin leaf-shaped plates (2·7 g.), m. p. 83° (Found : C, 69·3 ; H, 6·1. Calc. for $C_{15}H_{16}O_4$: C, 69·2 ; H, 6·6%). It formed a cherry-red solution in concentrated sulphuric acid. Marfori (*Jahresber. Chem.*, 1890, 1197) gives m. p. 83—84°, and Bouveault (*Bull. Soc. chim.*, 1897, **17**, 950), m. p. 79°.

Di-p-*methoxyphenyl Methylene Ether.*—This was prepared from *p*-methoxyphenol as in the preceding case, but further equal amounts of methylene sulphate and alkali were added after an hour. The alkali-washed product, crystallised twice from alcohol, formed flat cigar-shaped crystals (8 g.), m. p. 54° (Found : C, 69·2 ; H, 6·2. $C_{15}H_{16}O_4$ requires C, 69·2 ; H, 6·1%).

A similar experiment with resorcinol monomethyl ether gave a thick, pale yellow oil, b. p. 119—121°/16 mm. It could not be obtained crystalline, and analysis showed it to be impure (Found : C, 70·0 ; H, 6·6%). It is probable that some nuclear condensation may take place in this case.

Di-p-*acetamidophenyl Methylene Ether.*—*p*-Acetamidophenol (15 g.) (Hewitt and Ratcliffe, J., 1912, **101**, 1766 ; Woroshzow, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 787), alcohol (50.c.c.), sodium hydroxide (16 g.) in water (50 c.c.), and methylene sulphate (22 g.) were stirred at 30—35° for 3 hours, the temperature was then raised to 50° for 1 hour, the solution diluted with water (200 c.c.), and the product collected, washed, and dried (1·3 g.). The *methylene ether* separated from methyl alcohol in colourless needles, m. p. 191—192° (Found : C, 65·0 ; H, 6·1 ; N, 8·5. $C_{17}H_{18}O_4N_2$ requires C, 65·0 ; H, 5·8 ; N, 8·9%).

Di-p-*aminophenyl Methylene Ether.*—The preceding diacetyl derivative (0·85 g.) was refluxed for 4 hours with alcohol (25 c.c.) and 20% aqueous potassium hydroxide (25 c.c.), the solution diluted with water, and the alcohol distilled off; on cooling, the oily drops obtained solidified. The product was washed, dried, and recrystallised from benzene, forming colourless compact prisms, m. p. 103° (Found : N, 12·1. $C_{13}H_{14}O_2N_2$ requires N, 12·2%). *Di*-p-*aminophenyl methylene ether* yields a very sparingly soluble sulphate, and is readily tetrazotised and coupled.

Ethylene Glycol Methylene Ether (II, $n = 2$).—Ethylene glycol (15·5 g.), water (100 c.c.), and methylene sulphate (27·5 g.) were gently agitated and the reaction was started by heating. When boiling ceased, the liquid was distilled, the distillate saturated with potassium carbonate, and the upper layer separated, dried over calcium chloride, and redistilled over sodium; b. p. 76°/752 mm. (yield, 7·5 g.). Henry (*Compt. rend.*, 1895, **120**, 107) and Delépine (*ibid.*, 1900, **131**, 745) give b. p. 78°; Verley (*Bull. Soc. chim.*, 1899, **21**, 275) gives b. p. 74·5°.

Trimethylene glycol methylene ether (II, $n = 3$) was obtained from crude trimethylene glycol (7·6 g.), water (100 c.c.), and methylene sulphate (11 g.) as in the preceding case. The yield of dried redistilled product from two such experiments was 7·5 g.; b. p. 105°/754 mm. (compare Henry, *Bull. Acad. roy. Belg.*, 1902, 460; Clarke, J., 1912, **101**, 1803).

Pinacol Methylene Ether (III).—This was prepared from pinacol (13 g.), water (100 c.c.), and methylene sulphate (11 g.) as in the two preceding experiments (yield, 10·3 g.). Redistilled over sodium, it had b. p. 125°/752 mm. and readily solidified to very soft, ice-like, branching crystals, m. p. 12°. (Found: C, 64·2; H, 10·6. $C_7H_{14}O_2$ requires C, 64·5; H, 10·8%).

1 : 3-*Benzdioxin* (IV).—A mixture of saligenin (3·1 g.) (Hart and Hirschfelder, *J. Amer. Chem. Soc.*, 1920, **42**, 2679), sodium hydroxide (5 g.) in water (20 c.c.), acetone (10 c.c.), and methylene sulphate (5·5 g.) was heated and agitated under reflux, the vigorous reaction being controlled by occasional cooling. The mixture was finally heated for a few minutes on the water-bath, water (75 c.c.) added, and the whole distilled till the distillate became clear. Ether extracted from the distillate a colourless oil (1·0—1·1 g.). After two distillations under diminished pressure, 1 : 3-*benzdioxin* was obtained as a colourless, highly refracting oil, b. p. 101°/20 mm., 208—209°/749 mm., which solidified in a freezing mixture; m. p. 12·5° (Found: C, 70·9; H, 6·1. $C_8H_8O_2$ requires C, 70·6; H, 5·9%). The isolation may be effected by seeding the original distillate at 0°, and collecting the solid. The substance is oxidised by cold alkaline potassium permanganate, the methylene group in position 4 probably being converted into a carbonyl group (compare Borsche and Berkhout, *loc. cit.*).

*Di-(*o*-hydroxymethylphenoxy)methane* (V).—A mixture of saligenin (3·1 g.), sodium hydroxide (4 g.) in water (50 c.c.), and methylene sulphate (5·5 g.) was stirred at 40° for 4 hours, the temperature being finally raised to 50°. After addition of water and distillation of a trace of 1 : 3-benzdioxin, the residual solution was extracted with ether, the extracts were shaken with aqueous sodium hydroxide and dried, and the ether removed, leaving a colourless crystalline residue (0·2 g.), which separated from benzene–ligroin in boat-shaped plates, m. p. 118° (Found: C, 69·0; H, 6·2; *M*, in camphor, 256.

$C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%; *M*, 260). *Di*-(o-*hydroxymethylphenoxy*)*methane* separates in needles from hot water, in which it is sparingly soluble. Its aqueous alkaline suspension is readily oxidised by cold aqueous potassium permanganate.

The author wishes to record his thanks to Miss E. S. Hutton for help with the experiments on the methylenation of saligenin.

THE DYSON PERRINS LABORATORY,
OXFORD.

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