Preparation of Mononitropyrogallols and their Methyl Ethers, Acetates, and Benzenesulphonates

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Mononitration of pyrogallol 1,3- and 1,2-dibenzenesulphonate, gave 5-nitropyrogallol 1,3-dibenzenesulphonate 4-nitropyrogallol 1,2-dibenzenesulphonate and 4-nitropyrogallol 2,3-dibenzenesulphonate; these were separated and characterised. Mononitration of pyrogallol triacetate gave a mononitro-compound which was separated and characterised as the 4-nitropyrogallol 1,2-diacetate. From the above nitro-derivatives of 5-nitropyrogallol and 4-nitropyrogallol, a number of mono-, di-, and tri-methyl ethers, acetates, and benzenesulphonates were prepared.

THE preparation of mononitropyrogallols and their methyl ethers, acetates, and benzenesulphonates is described; the compounds have synthetic uses.

The action of nitric acid on pyrogallol 1,3-dibenzenesulphonate, in acetic acid solution gave two main products, a mononitro-compound and a quinone. The nitrating or oxidative influence of the nitric acid, depends mainly upon the density of the acid, the temperature of the reaction, and, to a lesser degree, upon the concentrations of the diester and nitric acid. Such a reaction can be controlled to give either a maximum yield of 30% quinone together with 20% nitrocompound or a 95% yield of nitro-compound. The quinone was identical with authentic 2,6-dibenzenesulphoxy-1,4-benzoquinone.¹ The mononitro-compound when reduced, with sodium dithionite solution, gave an aminophenol which could be oxidised ¹ to give the same 2,6-dibenzenesulphoxy-1,4-benzoquinone. Thus the aminophenol must be p-aminophenol; this characterised the mononitro-compound as the 5-nitropyrogallol 1,3-dibenzenesulphonate.

On mild nitration pyrogallol 1,2-dibenzenesulphonate gave two separable mononitro-compounds (A and B). The nitro-compound A (less soluble in acetic acid) when reduced by sodium dithionite solution gave an aminophenol which, when examined by the spot test method,² gave the characteristic pink colour of o-aminophenols. The nitro-compound B which was readily soluble in acetic acid gave an aminophenol which when examined by the spot method gave the characteristic blue spot of p-aminophenols. Thus the nitro-compound A was characterized as 4-nitropyrogallol 1,2-dibenzenesulphonate, while the nitro-compound B was characterised as the 4-nitropyrogallol 2,3-dibenzenesulphonate.

Ease of hydrolysis of the mononitro-diesters was in the order o > p - > m-hydroxy-groups. In a stepwise hydrolysis of the nitro-compounds, the m-ester groups were found to need considerably stronger conditions of reaction. Complete hydrolysis gave 5-nitropyrogallol and 4-nitropyrogallol respectively.

Methylation followed by partial or complete hydrolysis, or stepwise methylation and hydrolysis gave the methyl ethers of 4- and 5-nitropyrogallol.

Mononitration of pyrogallol triacetate gave a mixture from which unchanged product and one mononitrocompound were separated. Analysis showed that the mononitro-compound was a diacetate. Methylation with diazomethane gave a diester-monomethyl ether which can be completely hydrolysed by alkali, to give a mononitro-biphenol. This latter compound was identical with the previously prepared 4-nitropyrogallol 3-methyl ether. Thus the product of the nitration was characterised as the 4-nitropyrogallol 1,2-diacetate.

The 1,2-diacetate, when subjected to partial hydrolysis with 5% sodium acetate solution, gave a monoacetate. This product when methylated with diazomethane gave a dimethyl ether which could be hydrolysed to give 4-nitropyrogallol 1,3-dimethyl ether. Thus the monoacetate was characterised as the 4-nitropyrogallol 2-acetate and the dimethyl ether as the 4-nitropyrogallol 2-acetate 1,3-dimethyl ether.

EXPERIMENTAL

Nitration of Pyrogallol 1,3-Dibenzenesulphonate.3-Nitric acid (d 1.4; 4 ml.) was added dropwise, at room temperature, to a stirred solution of pyrogallol 1,3-dibenzenesulphonate (20.3 g.) in acetic acid (200 ml.). After 2 hr. the stirred mixture was cooled; the precipitate was collected, washed with cold acetic acid and water, and dried to give 5-nitropyrogallol 1,3-dibenzenesulphonate (17.5 g., 77%). Dilution of the mother liquors gave more product to a total yield of 96%. Crystallisation of the product from methanol gave prisms m.p. 161-162° (Found: N, 3.0; S, 14.1. C18H13- NO_9S_2 requires N, 3.1; S, 14.2%). Acetylation yielded the acetate, m.p. 125-126° (from methanol), while benzenesulphonylation with benzenesulphonyl chloride in pyridine gave the tribenzenesulphonate, m.p. 151-152° (from xylene) (Found: N, 2.2; S, 16.2. C₂₄H₁₇NO₁₁S₃ requires N, 2.4; S, 16.3%). Methylation with diazomethane or with dimethyl sulphate yielded the 2-methyl ether, m.p. 135-136° (prisms from benzene) (Found: N, 2.8; S, 13.9. $C_{19}H_{15}NO_9S_2$ requires N, 3.0; S, 13.8%).

Partial Hydrolysis of 5-Nitropyrogallol 1,3-Dibenzenesulphonate .--- Potassium hydroxide solution (20%; 67 ml.) was added, at 50°, to a stirred solution of 5-nitropyrogallol 1,3-dibenzenesulphonate (18 g.) in methanol (400 ml.). The mixture was stirred, at this temperature to give yellow needles of phenolic salt; these were converted into a sandy precipitate which then redissolved. After 5 min. at 55°, the deep red solution was cooled to room temperature, diluted with water (to 2 l.), acidified with hydrochloric acid, and kept cool. Next day the precipitated

⁸ E. Sakellarios, I. Kampouris, and J. Sakellarios, Ber., 1961, 94, 2544.

E. Kampouris, J. Chem. Soc. (C), 1968, 2125.
 F. Feigl, 'Spot Tests in Organic Analysis,' Elsevier, London, 1966, pp. 515, 517.

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J. Chem. Soc. (C), 1971

crystalline product was filtered off, washed with water, and dried to give the 1-benzenesulphonate (10.8 g., 87%), m.p. 199-200° (dec.) (from xylene) (Found: N, 4.4; S, 10.2. C₁₂H₉NO₇S requires N, 4.5; S, 10.3%). Acetylation with acetic anhydride in pyridine gave incomplete acetylation, while acetylation at 80-90° in the presence of a drop of conc. sulphuric acid yielded 1-benzenesulphonate 2,3-diacetate, m.p. $126-127^{\circ}$ (from benzene) (Found: N, 3·3; S, 8·3. $C_{16}H_{13}NO_9S$ requires N, 3·5; S, 8·1%). Methylation with diazomethane gave 1-benzenesulphonate 2,3-dimethyl ether, m.p. 100-101° (flakes from methanol) (Found: N, 3.9; S, 9.5. C14H13NO7S requires N, 4.1; S, 9.5%).

5-Nitropyrogallol 1-Benzenesulphonate 2-Methyl Ether .---The product was obtained by partial hydrolysis of the 1.3-dibenzenesulphonate (9.3 g.) in methanol (100 ml.), by potassium hydroxide solution (20%; 11.2 ml) at room temperature; yield 5.2 g. (80%), m.p. 162-163° (from benzene) (Found: N, 4.1; S, 10.0. C13H11NO7S requires N, 4.3; S, 9.8%). Acetylation gave 1-benzenesulphonate 3-acetate 2-methyl ether, m.p. 71° (from methanol) (Found: N, 3.8; S, 8.9. C₁₅H₁₃NO₈S requires N, 3.8; S, 8.7%). Methylation with diazomethane yielded the 1-benzenesulphonate 2,3-dimethyl ether, m.p. 100-101° (from methanol) also prepared by methylation of the 1-benzenesulphonate.

5-Nitropyrogallol.—Potassium hydroxide solution (20%; 22.5 ml.) was added, at 60°, to a shaken solution of 5-nitropyrogallol 1-benzenesulphonate (3.1 g.) in methanol (30 ml.). The temperature was then raised to 65°; the mixture was kept for 15 min. after which it was cooled to room temperature, diluted with water to 250 ml., acidified with hydrochloric acid, and kept cooled for 12 hr. Any unhydrolysed ester which precipitated was filtered off and the filtrate was extracted with ether; the ether was evaporated off and the residue was dried in vacuo to give 5-nitropyrogallol (1.4 g., 82%). Crystallisation from water gave yellow needles of the monohydrate, while crystallisation from xylene yielded yellow needles of the anhydrous product, m.p. 198-200° (decomp.) (lit., 194-196°; 4 203-204°; 5 205° 6). Acetylation gave 5-nitropyrogallol triacetate, m.p. 133-134° (from methanol) (Found: C, 48.6; H, 3.6; N, 4.8. C12H11NO8 requires C, 48.5; H, 3.7; N, 4.7%). Methylation with diazomethane gave impure product while methylation with dimethyl sulphate yielded 5-nitropyrogallol trimethyl ether, m.p. 98-99° (from methanol) (lit., 99°;7 100° 8).

5-Nitropyrogallol 2-Methyl Ether .--- The methyl ether was obtained by a similar hydrolysis in 90% yield, from 5-nitropyrogallol 1,3-dibenzenesulphonate 2-methyl ether and from 5-nitropyrogallol 1-benzenesulphonate 2-methyl ether. The product crystallised from xylene as needles m.p. 183-184° (Found: C, 45.2; H, 4.0; N, 7.5. C7H7-NO₅ requires C, 45·4; H, 3·8; N, 7·6%). Acetylation gave the diacetate, m.p. 96-97° (from methanol), while methylation with dimethyl sulphate yielded the trimethyl ether, m.p. 98---99°.

5-Nitropyrogallol 1,2-Dimethyl Ether.--The dimethyl ether was obtained by hydrolysis of 5-nitropyrogallol 1-benzenesulphonate 2,3-dimethyl ether, at room temperature, in 95% yield. Crystallisation of the product

 ⁴ M. Köhn and S. Grün, Monatsh., 1925, 46, 83.
 ⁵ T. Gardner, E. Wenis, and J. Lee, J. Org. Chem., 1950, 15, 841.

from benzene gave yellow needles or prisms, m.p. 115-116° (Found: C, 48.3; H, 4.4; N, 7.1. $C_8H_9NO_5$ requires C, 48.2; H, 4.6; N, 7.0%). The product of Pollak and Goldstein,9 m.p. 112-114°, which it was suggested was the 1,2- or 1,3-dimethyl ether of 5-nitropyrogallol must have been impure 1,2-dimethyl ether. Acetylation gave the acetate, m.p. 85° (from methanol), while methylation with dimethyl sulphate yielded the trimethyl ether, m.p. 98-99°.

Nitration of Pyrogallol 1,2-Dibenzenesulphonate.³-Nitric acid ($d \mathbf{1.4}$; 4 ml.) was added dropwise to a water-cooled solution of pyrogallol 1,2-dibenzenesulphonate (20.3 g.) in acetic acid (100 ml.). The mixture was stirred for 1 hr., after a crystalline product had started to precipitate. Next day the precipitated product was filtered off, washed with cold acetic acid and with water, and dried to give 4-nitropyrogallol 1,2-dibenzesulphonate (11 g., 49%), m.p. 143-144° (yellow prisms from benzene) (Found: N, 3.2; S, 14.4. $C_{18}H_{13}NO_9S_2$ requires N, 3.1; S, 14.2%). Acetylation gave the acetate, m.p. 154° (from benzene), benzenesulphonylation with benzenesulphonyl while chloride in pyridine, yielded the tribenzenesulphonate, m.p. 175-176° (from acetic acid) (Found: N, 2.2; S, 16.4. C24H17NO11S3 requires N, 2.4; S, 16.3%). Methylation with diazomethane produced the 3-methyl ether, m.p. 117-118° (from methanol) (Found: N, 2.9; S, 13.7. C₁₉H₁₅NO₉S₂ requires N, 3.0; S, 13.8%).

The acetic acid mother liquors were diluted with water (to 1 l.), and then cooled. The solid product was pulverised, washed with water, and dried to give 4-nitropyrogallol 2,3-dibenzenesulphonate (10.5 g., 46%), m.p. 163-164° (from benzene or xylene, bright yellow prisms containing solvent, slowly disintegrated in air) (Found: N, 3.0; S, 14.1. $C_{18}H_{13}NO_{9}S_{2}$ requires N, 3.1; S, 14.2%). Acetylation gave the acetate, m.p. 132-133° (from acetic acid), while benzenesulphonylation yielded the tribenzenesulphonate, m.p. 175-176° (also prepared by benzenesulphonylation of the 1,2-dibenzenesulphonate). Methylation with diazomethane gave the 1-methyl ether, m.p. 150-151° (from acetic acid) (Found: N, 3.1; S, 14.0. C₁₉H₁₅NO₉S₂ requires N, 3.0; S, 13.8%).

Partial Hydrolysis of 4-Nitropyrogallol 1,2- and 2,3-Dibenzenesulphonate.-Potassium hydroxide solution (20%; 8.5 ml.) was added to a stirred dispersion of powdered 4-nitropyrogallol 1,2-dibenzenesulphonate (or to a solution of 4-nitropyrogallol 2,3-dibenzenesulphonate) (4.5 g.) in methanol (45 ml.). The mixture was stirred at room temperature for 10 min. after the diester had disappeared; the solution was diluted with water (to 500 ml.) and acidified with hydrochloric acid. The precipitated product was filtered off, washed with water and dried to give 4-nitropyrogallol 2-benzenesulphonate (2.8 g., 90%), m.p. 168-169° (from benzene) (Found: N, 4.4; S, 10.5. C12H9NO7S requires N, 4.5; S, 10.3%). Acetylation yielded the 1,3-diacetate, m.p. 108-109° (prisms from methanol) (Found: N, 3.6; S, 7.9. C₁₆H₁₃NO₉S requires N. 3.5; S, 8.1%). Methylation with dimethyl sulphate gave the 1,3-dimethyl ether, m.p. 134-135° (needles from methanol) (Found: N, 4.0; S, 9.5. C₁₄H₁₃NO₇S requires N, 4.1; S, 9.5%).

- ⁷ V. Harding, J. Chem. Soc., 1914, 105, 2790.
 ⁸ W. Will, Ber., 1888, 21, 602.
- J. Pollak and E. Goldstein, Annalen, 1907, 351, 168.

⁶ A. Barth, Monatsh., 1879, 1, 882.

4-Nitropyrogallol 2-Benzenesulphonate 3-Methyl Ether.— The monoester-monoether was obtained by partial hydrolysis of powdered 4-nitropyrogallol, 1,2-dibenzenesulphonate 3-methyl ether, in the form of the monohydrate; it had m.p. 92—94° (from dilute methanolic solution by dilution with water) (Found: H_2O , 5·5. $C_{13}H_{11}NO_7S, H_2O$ requires H_2O , 5·2%). Anhydrous material crystallised from benzene in prisms had m.p. 137—138° (Found: N, 4·4; S, 9·6. $C_{13}H_{11}NO_7S$ requires N, 4·3; S, 9·8%). Acetylation gave the acetate, m.p. 79—80° (from methanol), while methylation with diazomethane yielded the 1,3-dimethyl ether, m.p. 134—135°; it was identical with the product obtained on methylation of 4-nitropyrogallol 2-benzenesulphonate.

4-Nitropyrogallol 2-Benzenesulphonate 1-Methyl Ether. —This compound was obtained by partial hydrolysis of 4-nitropyrogallol 2,3-dibenzenesulphonate 1-methyl ether, m.p. 155—156° (from acetic acid) (Found: N, 4·2; S, 9·6. $C_{13}H_{11}NO_7S$ requires N, 4·3; S, 9·8%). Acetylation with acetic anhydride and a drop of conc. sulphuric acid at 80—85°, failed to give the diacetate. Methylation with diazomethane yielded the 1,3-dimethyl ether, m.p. 134—135°, identified with the same product obtained by other ways.

4-Nitropyrogallol.—Complete hydrolysis of 4-nitropyrogallol 1,2- or 2,3-dibenzenesulphonate or 4-nitropyrogallol 2-benzenesulphonate in methanol, at 50°, with potassium hydroxide solution, gave 4-nitropyrogallol (80%), m.p. 161—162° (from benzene) (lit.,¹⁰ 162°). Acetylation gave the triacetate, m.p. 85—86° (from methanol) (lit.,¹⁰ 85°). Methylation with diazomethane or dimethyl sulphate failed to give the completely methylated product.

4-Nitropyrogallol 1-Methyl Ether.—Hydrolysis of 4-nitropyrogallol 2-benzenesulphonate 1-methyl ether (1.6 g.) in methanol (20 ml.) by potassium hydroxide solution (20%; 11.5 ml.), at 60°, gave 4-nitropyrogallol 1-methyl ether (85%), m.p. 122—123° (from benzene) (Found: C, 45.5; H, 3.6; N, 7.8. $C_7H_7NO_5$ requires C, 45.4; H, 3.8; N, 7.6%). Acetylation gave the diacetate, m.p. 117—118° (from benzene–light petroleum 1:1 v/v), while methylation yielded the trimethyl ether, m.p. 44—45° (from dilute methanol) (lit., 44°; ¹⁰ 44—45° ¹¹).

4-Nitropyrogallol 3-Methyl Ether.—The monoether was obtained (yield 80%) by complete hydrolysis of 4-nitropyrogallol 1,2-dibenzenesulphonate 3-methyl ether and 4-nitropyrogallol 2-benzenesulphonate 3-methyl ether, in the form of monohydrate, m.p. 97—99° (Found: H₂O, 9·1. C₇H₇NO₅,H₂O requires H₂O, 8·8%). Anhydrous material crystallised from xylene as needles, m.p. 123— 124°(Found: C, 45·2; H, 3·7; N, 7·6. C₇H₇NO₅ requires C, 45·4; H, 3·8; N, 7·6%). Acetylation gave the 1,2-diacetate, m.p. 92—93° (from methanol) (Found: C, 49·2; H, 3·9; N, 5·1. C₁₁H₁₁NO₇ requires C, 49·0; H, 4·1; N, 5·2%). Methylation with diazomethane yielded impure product.

4-Nitropyrogallol 1,3-Dimethyl Ether.—The diether was obtained in 90% yield, by hydrolysis of 4-nitropyrogallol 2-benzenesulphonate 1,3-dimethyl ether, in the form of the dihydrate, m.p. 67—68° (Found: H_2O , 15.5. $C_8H_9NO_{5,-}2H_2O$ requires H_2O , 15.3%) (lit., 67—68°,¹² 67—69° ¹¹). Anhydrous material crystallised from benzene as yellow

 A. Einhorn, J. Cobliner, and H. Pfeiffer, Ber., 1904, 37, 100.
 F. Benington, R. Morin, and L. Clark, jun., J. Org. Chem., 1958, 23, 19. prisms, m.p. $84-85^{\circ}$ (Found: C, $48\cdot3$; H, $4\cdot4$; N, $6\cdot8$. C₈H₉NO₅ requires C, $48\cdot2$; H, $4\cdot6$; N, $6\cdot9\%$). Acetylation gave the 2-acetate, m.p. $93-94^{\circ}$ (from methanol) (lit., $92-93^{\circ}$; ¹² $94-95^{\circ}$ ¹¹). Methylation with diazomethane yielded the trimethyl ether, m.p. $44-45^{\circ}$ (also prepared and by methylation of 4-nitropyrogallol 1-methyl ether).

Nitration of Pyrogallol Triacetate.-Powdered pyrogallol triacetate (150 g.) was added in portions, at 5°, to stirred nitric acid $(d \ 1.4; \ 1 \ 1.)$. Soon after the complete addition the triester dissolved and the solution was stirred, at 5° , for 10 hr. The solution was then poured into water (4 l.)-crushed ice (2 kg.). The precipitated product was filtered off, washed with dilute hydrochloric acid (0.05N) and water and then dried in vacuo. The dried product was boiled with benzene (300 ml.) and the mixture was kept at 40° for 1 hr., the undissolved product, being pyrogallol triacetate, was filtered off and washed with benzene; the trates were evaporated under reduced pressure to a volume of ca. 150 ml. The precipitated pyrogallol triacetate was filtered off and washed with a little benzene; the filtrates were evaporated to give 4-nitropyrogallol 1,2-diacetate (22 g.), m.p. 106-107° (from benzene) (Found: C, 46.8; H, 3.6; N, 5.4. C₁₀H₉NO₇ requires C, 47.0; H, 3.5; N, 5.5%). Acetylation gave 4-nitropyrogallol triacetate identified, by mixed m.p., with the product of acetylation of 4-nitropyrogallol. Methylation with diazomethane yielded the 3-methyl ether which was identical with the product from the acetylation of 4-nitropyrogallol 3-methyl ether. Complete hydrolysis of the diacetate monomethyl ether, yielded 4-nitropyrogallol 3-methyl ether which was benzenesulphonylated, with benzenesulphonyl chloride in pyridine, to give 4-nitropyrogallol 1,2-dibenzenesulphonate 3-methyl ether; this was identical with the product obtained by methylation of 4-nitropyrogallol 1,2-dibenzenesulphonate.

Partial Hydrolysis of 4-Nitropyrogallol 1,2-Diacetate.-Powdered 4-nitropyrogallol 1,2-diacetate (10 g.) was added in portions to a stirred solution of sodium acetate (5%); 500 ml.), at room temperature. After the disappearance of the diester the mixture was stirred for a further 30 min. and was then acidified with hydrochloric acid. The precipitate was filtered off, washed with acidified water. and then dried in vacuo to give 4-nitropyrogallol 2-acetate (4.3 g., 50%), m.p. 169-170° (from benzene) (Found: C. 44.8; H, 3.5; N, 6.4. C₈H₇NO₆ requires C, 45.0; H, 3.3; N, 6.6%). Extraction with ether of the mother liquors gave a mixture (3.5 g.) consisting of partially and completely hydrolysed product. This mixture can be separated, with considerable losses, by fractional dilution in hot water, the monoester being less soluble than the 4-nitropyrogallol. Acetylation gave the 4-nitropyrogallol triacetate which was identical with authentic material. Methylation yielded 4-nitropyrogallol 2-acetate 1,3-dimethyl which was identical with the product obtained by acetylation of 4-nitropyrogallol 1,3-dimethyl ether. Alkaline hydrolysis of the monoacetate diether gave 4-nitropyrogallol 1,3-dimethyl ether which was identical with the product obtained by hydrolysis of 4-nitropyrogallol 2-benzenesulphonate 1,3-dimethyl ether.

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¹² K. Brand and H. Collischon, J. prakt. Chem., 1921, 2, 103, 345.