

The Nitration and Hydroxylation of Phenetole, Phenyl *n*-Propyl Ether, and Acetophenone by Pernitrous Acid.

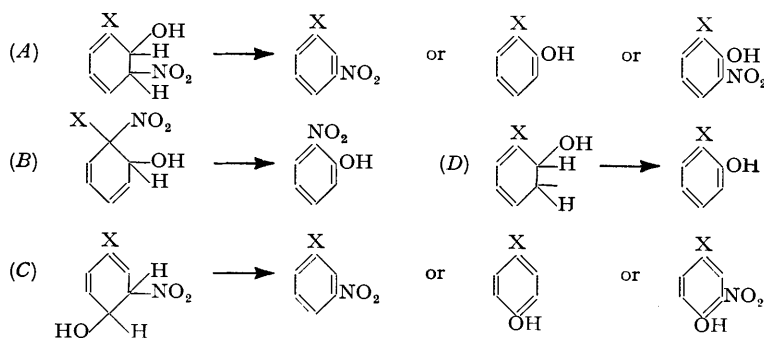
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Reaction of pernitrous acid (cf. Halfpenny and Robinson, *J.*, 1952, 928, 939) with the compounds mentioned in the title leads to nitration and hydroxylation, the nature of the side-chain influencing the susceptibility of the nucleus and the nature of the products. The hydroxy- and mononitro-derivatives conform to the scheme previously advanced, but dinitro-compounds are formed to a considerable extent from the two ethers.

HALFPENNY and ROBINSON (*J.*, 1952, 928, 939) reported the use of pernitrous acid as a nitrating and hydroxylating agent for anisole. We now describe its reactions with phenetole, phenyl *n*-propyl ether, and acetophenone. Halfpenny and Robinson (*loc. cit.*) considered the main products to arise by homolytic fission of pernitrous acid: $\text{HO}\cdot\text{O}\cdot\text{NO} \rightarrow \text{HO} + \text{NO}_2$. The hydroxyl radical then enters the nucleus, preferentially in the *ortho*- or *para*-position to form an aryl radical. This reacts with nitrogen dioxide to give an unstable molecular species which breaks down with the elimination of water, nitrous acid, or hydrogen. The expected products from a monosubstituted benzene are then as in (A)–(C).

It was also pointed out that purely hydroxylated products can result from a more direct process (D) in which there is no intervention of nitrogen dioxide.



Our results are tabulated below, along with those already reported for anisole, the yields being those from the same weight (2000 g.) of each starting material.

Starting material,	$\text{R}\cdot\text{C}_6\text{H}_3(\text{NO}_2)\cdot\text{OH}$		$\text{R}\cdot\text{C}_6\text{H}_2(\text{NO}_2)_2\cdot\text{OH}$	$\text{o}\cdot\text{R}\cdot\text{C}_6\text{H}_4\cdot\text{OH}$	Other products
	4 : 2 : 1- (g.)	6 : 2 : 1- (g.)			
PhR					
Ph·OMe	7.6	0.4	—	—	{ Ph·OH (29.6 g.) o-NO ₂ ·C ₆ H ₄ ·OH (7.9 g.)
Ph·OEt	—	8.25	2.6	8.55	
Ph·OPr	—	—	2.0	—	
Ph·COMe	—	3.65	—	2.5	{ m-NO ₂ ·C ₆ H ₄ ·COMe (15.6 g.) Ph·CO ₂ H (0.08 g.)

When the side-chain is longer than methoxyl it is not replaced by hydroxyl. There is a slight conversion of acetyl into carboxyl, by either substitution of the methyl by an hydroxyl group or oxidation: apart from this, the attack is restricted to the benzene nucleus. With increasing molecular weight, compounds 4 : 2 : 1- $\text{R}\cdot\text{C}_6\text{H}_3(\text{NO}_2)\cdot\text{OH}$ are replaced, in the cases of phenetole and acetophenone, by derivatives of the 6 : 2 : 1-type. Apparently this does not happen with phenyl *n*-propyl ether; here the only compound identified was 2 : 4-dinitro-6-propoxyphenol, corresponding to the dinitro-derivative

obtained as minor product from phenetole. Dinitration increases concurrently with the length of the side-chain. The high yield of *m*-nitroacetophenone is a notable feature.

In light of the views previously advanced, *o*-R·C₆H₄·OH arise from reaction (A) or (D), 6 : 2 : 1-R·C₆H₃(NO₂)·OH from reaction (A), and *m*-nitroacetophenone from reaction (C). Where there is simple hydroxylation, it is found, as predicted, in the *ortho*-position with respect to the original substituent; where there is both hydroxylation and nitration the former occurs in the *ortho*- and the latter in the *meta*-position. The two dinitro-compounds produced are identical in form, but that they spring from further nitration of mononitro-compounds is doubtful since we have not been able to find evidence of the presence of 2-nitro-6-propoxyphenol. The nature of the dinitro-compounds lends support to our opinion that the reactions involved are not ionic.

Diphenyl ether gave so little evidence of attack by pernitrous acid as to discourage an attempt to work up the products. This result is in line with the marked effect of the mass of the aliphatic side-chain.

EXPERIMENTAL

The aromatic compound (100 g.) was agitated with 5% hydrogen peroxide solution (100 c.c.), 3*N*-hydrochloric acid (5 c.c.), and water (250 c.c.), and 5% sodium nitrite solution (150 c.c.) was added during about 30 min. at room temperature (slightly higher for acetophenone). Only the organic liquid layer was examined.

Phenetole.—After the addition of the nitrite, the organic layer appeared bright orange, the aqueous layer paler. Organic material from 20 experiments was extracted with 8% aqueous sodium hydroxide. This dark red solution was shaken several times with ether to remove unchanged phenetole, then acidified (becoming yellow) and extracted with ether and finally ethyl acetate. The two extracts, after drying (Na₂SO₄) and removal of solvents, left a brown viscous liquid (21.0 g.) from which crystals separated (2.4 g.). These recrystallised from alcohol as yellow needles, m. p. 155° (Found: C, 42.65; H, 3.85; N, 11.8. Calc. for C₈H₈O₆N₂: C, 42.1; H, 3.5; N, 12.3%). De-ethylation with hydrobromic acid in glacial acetic acid gave pale yellow crystals, m. p. 164°, suggesting that the original compound was 6-ethoxy-2 : 4-dinitrophenol (Reverdin and Fürstenberg, *J. pr. Chem.*, 1913, **88**, 327).

The remaining liquid gave a yellow oil, b. p. 65—70°/3 mm., and an orange solid, b. p. 120—130°/3 mm. A further 0.2 g. of the 6-ethoxy-2 : 4-dinitrophenol was extracted from the brown residue.

The orange solid (8.25 g.), recrystallised from aqueous alcohol, gave orange needles, m. p. 79° (Found: C, 51.95; H, 5.15; N, 7.5. Calc. for C₈H₈O₄N: C, 52.25; H, 4.9; N, 7.65%). De-ethylation as above gave yellow needles, m. p. 82°, identified as 3-nitrocatechol by a mixed m. p. (82—84°) with the authentic compound (m. p. 86°) (Foglesong and Newell, *J. Amer. Chem. Soc.*, 1930, **52**, 834), the red-purple colour with sodium hydroxide solution (Weselsky and Benedikt, *Monatsh.*, 1882, **3**, 386), and the green colour with ferric chloride solution (catechol derivative). This evidence suggests that the original compound is probably 6-ethoxy-2-nitrophenol. It is appreciably volatile in steam.

The yellow oil (8.55 g.) was shown to be principally 2-ethoxyphenol by de-ethylation to almost colourless crystals (from hydrochloric acid) shown to be catechol by a mixed m. p. determination, the green colour with ferric chloride solution, and formation of the dibenzoyl derivative, m. p. 85°.

Phenyl n-Propyl Ether.—After the addition of nitrite the organic layer appeared lemon-yellow, the aqueous layer much paler. The organic material from 20 experiments, worked up as above, gave, by acidification of the alkaline extract, a light brown precipitate (1.9 g.). Recrystallisation from alcohol yielded yellow crystals, m. p. 88° (Found: C, 45.5; H, 4.65; N, 13.4. Calc. for C₉H₁₀O₆N₂: C, 44.6; H, 4.1; N, 11.6%). Attempts to depropylate the substance were unsuccessful, but it gave absorption curves, in both the ultra-violet and the visible range, which were so similar to those of the 6-ethoxy-2 : 4-dinitrophenol as to leave little doubt that it was 2 : 4-dinitro-6-propoxyphenol. The remaining aqueous solution was extracted and the products were distilled as above, to give a yellow oil (0.4 g.), b. p. 60—65°/5 mm., and a viscous orange liquid (1.0 g.), b. p. 130°/5 mm. A further 0.1 g. of the solid, m. p. 88°, was obtained from the residue. Attempts at depropylation of both fractions failed and the compounds have not been identified. Absorption spectra did not however indicate that either contained 2-nitro-6-propoxyphenol.

Acetophenone.—To prevent solidification the reaction was carried out at 20—25°. On

addition of the sodium nitrite the organic layer became dark amber and the aqueous layer lemon-yellow. The organic material from twenty experiments was worked up as above, giving from the extractions, a brown oil (7.7 g.). Steam-distillation produced a pale yellow distillate which was extracted with ether. After drying (Na_2SO_4) and removal of the ether, distillation under reduced pressure gave a pale brown oil (2.5 g.), and sublimation of the residue yielded an almost colourless solid (0.08 g.) and left a trace of tar. The oil was identified as *o*-hydroxyacetophenone by its semicarbazone, m. p. 210° , and its oxime, m. p. 116° . The solid, after recrystallisation from hot water, melted at 121° and was proved to be benzoic acid by the ferric chloride test, and a mixed melting point determination.

The residue from the steam-distillation was extracted with ether, and the solution dried (Na_2SO_4). Removal of the solvent left a brown, viscous liquid (4.1 g.) which, on distillation at 4 mm., gave a pale yellow solid (3.65 g.), m. p. 90° after recrystallisation from dilute aqueous acetic acid. It was, probably, 2-hydroxy-3-nitroacetophenone. Unfortunately we have been unable to prepare the oxime, the only derivative mentioned in the literature. This was made (Lindemann and Romanoff, *J. pr. Chem.*, 1929, **122**, 214) by nitrating the oxime of *o*-hydroxyacetophenone and the ketone was obtained from it. We have made the 2:4-dinitrophenylhydrazone, m. p. 242° , but neither it nor the corresponding amino-compound appears in the literature. Our ketone is, however, like that of Lindemann and Romanoff in m. p. and ready solubility in cold benzene, acetic acid, and hot water.

The acetophenone, after removal of the phenols, washing with water, and drying (Na_2SO_4), was evaporated under reduced pressure, to leave a brown solid (16.2 g.). Distilled at 3 mm. pressure, this gave a pale yellow solid (15.6 g.) which, after crystallisation from alcohol, was almost colourless and had m. p. 81° . It was shown to be *m*-nitroacetophenone by means of its oxime, m. p. 130° , and phenylhydrazone, m. p. 128° .

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