The Nitration of a-Phenyl-o-toluic Acid

By Dean E. Welch

The nitration of α -phenyl-o-toluic acid with fuming (90%) nitric acid gives α -2,4-dinitrophenyl-5-nitro-o-toluic acid as the major product. Optimum conditions for the preparation, and experiments leading to the structural assignment, are described.

TREATMENT of α -phenyl-o-toluic acid (I) with fuming nitric acid at room temperature has been reported ¹ to give a mixture of mono- and di-nitro-acids from which the dinitro-acid (II) was isolated. Subsequent oxidation gave the dinitro-o-benzoylbenzoic acid (III). In our hands this procedure repeatedly produced a trinitroderivative as the major product to which we assign structure (IV). Some mono- and di-nitro-acids were probably formed, but these were not isolated. The reason for the difference is not clear, but it is possible that the earlier workers' nitric acid was not as concentrated as the 90% specified. This could explain the formation of a dinitro-acid as the major product. We here describe our brief study of the nitration of (I).

The addition of *a*-phenyl-o-toluic acid in small portions to a large excess of fuming nitric acid maintained at room temperature gave a yellow solution, which after 26 hr. was quenched in water, giving trinitro-α-phenyl-otoluic acid (IV) in 60-70% yield. The amide was prepared in 78% yield. The same acid was obtained under a variety of conditions. Rapid mixing of (I) with excess of fuming nitric acid caused an exothermic reaction $(80-90^{\circ})$ which subsided after a few minutes; the acid (IV) was obtained in *ca*. 50% yield after 26 hr. at room temperature. Heating of the nitration mixture at 85° for 4 hr. gave (IV) in 40% yield. The addition of (I) in small portions to the nitric acid at -15° gave a 60% yield of (IV) after the mixture had been allowed to stand for 28 hr. at that temperature. Maximum yields (80-85%) of (IV) were obtained by the addition of (I) in small portions to an excess of fuming nitric acid at room temperature, followed by heating at $35-40^{\circ}$ for 24 hr. Several unsuccessful attempts were made to

prepare a tetranitro-derivative by heating the reaction mixture at $100-150^{\circ}$ in a Paar pressure apparatus.

Oxidation of (IV) with dilute permanganate gave trinitro-*o*-benzoylbenzoic acid (V). Several attempts to carry out a Baeyer–Villiger oxidation on (V) were



unsuccessful. Treatment of (V) with hydroxylamine gave the oxime anhydride (VI). Similar oxime anhydrides had been prepared from other *o*-benzoylbenzoic acids.² When (VI) was heated with concentrated sulphuric acid, 4-nitrophthalic acid and 2,4-dinitroaniline were produced, thereby confirming structure (IV) for

¹ O. R. Quayle and E. E. Reid, J. Amer. Chem. Soc., 1925, **47**, 2357.

² J. Meisenheimer and H. Meis, Ber., 1924, 57, 289.

the trinitro-acid. The conventional structure proof for substituted *o*-benzoylbenzoic acids is their cyclisation to substituted anthraquinones of known structure. The Beckmann rearrangement was chosen because no trinitroanthraquinones have been reported, and because cyclisation would not distinguish between some of the possible trinitro-*o*-benzoylbenzoic acids.

EXPERIMENTAL

Melting points were determined with a Mel-Temp heated block, and are corrected. Infrared spectra were determined in potassium bromide discs with a Beckman IR4 recording spectrometer. Thin-layer chromatography was performed by the ascending technique on glass plates coated with Mallinckrodt 2847 Silicic Acid, A.R., activated at 100° . Zones were located by spraying with an aqueous solution of titanium trichloride (5%), dimethylaminocinnamaldehyde (0·10%), and acetic acid (50%). The n.m.r. spectrum was determined in deuterated dimethyl sulphoxide at 60Mc. with a Varian A-60 spectrometer; chemical shifts are downfield from tetramethylsilane.

 α -Phenyl-o-toluic Acid (I)³—Catalytic reduction of obenzoylbenzoic acid (Matheson, Coleman, and Bell) in glacial acetic acid gave (I) in 90—95% yield, m. p. 111—112° (lit.,³ 111—113°). The reduction was carried out in a Paar pressure apparatus with a palladium-charcoal catalyst at 70° and 80 lb./sq. in. of hydrogen.

Trinitro-a-phenyl-o-toluic Acid (IV) --- Well-stirred fuming nitric acid (200 g., 133 ml., 2.86 moles; Mallinckrodt 2713, 90%) was maintained at 25° with an ice-bath while (I) (24.0 g., 0.113 mole) was added in small portions during 1 hr. The resulting yellow solution was stirred at room temperature (27°) for 26 hr. and then poured on to crushed ice (ca. 400 ml.). After the suspension had been in a refrigerator overnight, the solid was broken up and collected on a suction filter. The residue was washed with water and dried, to give a yellow solid (26.0 g., 67%), m. p. 190-198°. This reaction was repeated several times with similar results. Recrystallisation from acctic acid-water gave a pale yellow solid (23.5 g., 60%), m. p. 205—206°, $\nu_{\rm max.}$ 3500m, 3100m, 2980w, 1710s, 1610s, 1580w, 1538s, 1485w, 1415m, 1350s, 1305w, 1250s, 1142w, 1128m, 1065m, 920m, 860w, 833m, 808w, 740m cm.⁻¹ (Found: C, 48.5; H, 2.6; N, 11.9%; Equiv., 346.00. C₁₄H₉N₃O₈ requires C, 48.5; H, 2.6; N. $12\cdot1\%$; Equiv., $347\cdot24$); n.m.r.: singlet at δ 4.88 (2H, ArCH₂Ar), quartet at δ 7.52 (2H, substituted phenyl, $J_o = 12$, $J_m = 9$ c./sec.), complex absorption at $\delta 8.30$ —8.55(2H, substituted phenyl), quartet at δ 8.73 (2H, substituted phenyl, $J_o = 6$, $J_m = 2.5$ c./sec.). The carboxyl hydrogen was not resolved.

Rapid mixing of (I) $(12 \cdot 0 \text{ g.}, 0.0565 \text{ mole})$ and fuming nitric acid (100 g., 1.43 moles) caused an exothermic reaction $(80-90^{\circ})$. After the mixture had been at room temperature for 26 hr., it was quenched in crushed ice (300 ml.), to give (IV) (44 and 53%). When the mixture was heated at 85° for 4 hr. after the exothermic reaction, the yield of (IV) was 40%. Addition of (I) in small portions to the nitric acid at -15° gave (IV) in 60% yield after 28 hr. at that temperature.

The best procedure for the preparation of (IV) was the following. The acid (I) (96.0 g., 0.452 mole) was added in small portions to fuming nitric acid (800 g., 11.44 moles) maintained at 20-25°, and the yellow solution was heated

at 35—40° for 24 hr. After a few hours a solid started to precipitate and continued to form during the reaction. The suspension was then filtered on a sintered-glass Buchner funnel. The residue was washed with water and dried, to give pure (IV) which usually represented *ca*. one-third of the total yield. The filtrate was quenched in crushed ice (1 1.) and worked up as described previously. The total yield of (IV) was 77—85% in five runs, and in each case it was compared (m. p., mixed m. p., infrared) with that from the original reaction.

α-2,4-Dinitrophenyl-5-nitro-o-toluamide.—A solution of (IV) (34·7 g., 0·10 mole) in freshly distilled thionyl chloride (300 ml.) was heated under reflux for 4 hr. The excess thionyl chloride was vacuum-distilled and the residue was dissolved in anhydrous benzene (250 ml.). The benzene solution was maintained at 20—30° with external cooling and purged with anhydrous ammonia for 45 min. The mixture was then filtered and the residue washed with water (1 l.). This gave a pale yellow solid (32·0 g., 93%), m. p. 193—196°. Recrystallisation from ethyl alcohol (several Darco treatments) gave colourless needles (27·0 g., 78%), m. p. 199—200°, ν_{max}. 3475s, 3105w, 1680s, 1610s, 1580vw, 1540s, 1420w, 1350s, 1145w, 1125w, 1068w, 915w, 838w, 805w, 740m cm.⁻¹ (Found: C, 48·45; H, 3·0; N, 15·95. C₁₄H₁₀N₄O₇ requires C, 48·6; H, 2·9; N, 16·2%).

Trinitro-o-benzoylbenzoic Acid (V) .--- A suspension of (IV) (34.7 g., 0.10 mole) in water (200 ml.) was heated to ca. 65° and treated dropwise during 2 hr. with reagent grade potassium permanganate (35.0 g., 0.22 mole) in water (300 ml.). The exothermic-reaction mixture was maintained below 80° with external cooling during the addition, and then heated at 80° for $2\frac{1}{2}$ hr., cooled, and filtered. The dark red filtrate was added dropwise to well-stirred 10 % hydrochloric acid (2 l.). The suspension was stored in a refrigerator overnight and then the chunky solid was broken up and filtered off. The residue was washed with water and dried, to give yellow solid (28.0 g., 77%), m. p. 216-218°. Recrystallisation from acetic acid-water gave 22.0 g. (61%), m. p. 226—227.5°, ν_{max} 3475s, 3125m, 1722s (shoulder at 1710), 1610m, 1545s, 1490vw, 1425w, 1355s, 1315w, 1275s, 1245m, 1145w, 1130w, 1075w, 948m, 920m, 897m, 860m, 838m, 808w, 745m cm.⁻¹ (Found: C, 46.65; H, 2.0; N, 11.5%; Equiv., 361.00. C₁₄H₇N₃O₉ requires C, 46.6; H, 1.95; N, 11.65%; Equiv., 361.22).

The Trinitro-oxime Anhydride (VI).—A mixture of (V) (5.0 g., 0.0139 mole), hydroxylamine hydrochloride (4.5 g., 0.0648 mole), and barium carbonate (6.0 g., 0.030 mole) in ethyl alcohol (75 ml.) was heated under reflux for 7 hr., filtered hot, and the residue washed with hot alcohol. The filtrate was concentrated under a vacuum, to give an orange solid (8.0 g.), m. p. 80—100°, which was washed with water and recrystallised several times from alcohol (Darco treatment), to give light brown crystals (3.2 g., 64%), m. p. 211—212°, v_{max} . 3100m, 1760s, 1615m, 1600m, 1545s, 1533s, 1420w, 1348s, 1310vw, 1250m, 1238m, 1138w, 1090s, 1045m, 980w, 925s, 910s, 860m, 838m, 795m, 750m, 700m cm.⁻¹ (Found: C, 46.65; H, 1.9; N, 15.45. C₁₄H₆N₄O₈ requires C, 46.95; H, 1.7; N, 15.65%).

Rearrangement of (VI).—A solution of (VI) (1.5 g., 0.0042 mole) in concentrated sulphuric acid (6.0 g.) was heated at 100° for 1 hr. The dark brown mixture was poured on to crushed ice (100 ml.), left for 2 hr., filtered, and the residue washed with water and dried, to give a light brown solid

³ E. C. Horning and D. B. Reisner, J. Amer. Chem. Soc., 1949, 71, 1036.

Thin-layer chromatography of the acidic, aqueous filtrate showed that it contained 4-nitrophthalic acid and a small amount of 2,4-dinitroaniline. No other isomers were detected. Identification was by comparison of the $R_{\rm F}$ with the zone obtained from an authentic sample solution and a mixture of the unknown and the authentic solution. The 2,4-dinitroaniline zone was purple, the 3-nitrophthalic acid zone was pink, and the 4-nitrophthalic acid zone was red. A 95:5 benzene-ethyl alcohol eluent gave $R_{\rm F}$ 0.40 for 2,4-dinitroaniline and 0.00 for 3- or 4-nitrophthalic acid. A 10:25:30:35 diethyl ether-methanol-ammonium hydroxide-ethyl alcohol eluent gave $R_{\rm F}$ 0.55 for 3-nitrophthalic acid, 0.70 for 4-nitrophthalic acid, and gave a clean separation of an authentic mixture of the two acids. The 2,4-dinitroaniline moved with the solvent front $(R_{\rm F} > 0.95).$

Thin-layer chromatography of the yellow ether extract showed that it contained 2,4-dinitroaniline and a trace of 4-nitrophthalic acid. The ether was then removed under a vacuum. The solid residue was dissolved in benzene and chromatographed over silica in a 20×300 mm. column using a 95:5 benzene-ethyl alcohol eluent. The eluent was monitored by thin-layer chromatography. The eluent fractions (15 ml.) were combined and concentrated under a vacuum, to give 2,4-dinitroaniline (0.34 g., 0.0018 mole) as a yellow, crystalline residue, m. p. 175—178° (lit.,4 175—177°). A mixed m. p. with authentic (Eastman Organic Chemicals) 2,4-dinitroaniline was not depressed, and their infrared spectra were identical.

The acidic, aqueous filtrate was neutralised with ammonium hydrogen carbonate and then concentrated to dryness under a vacuum. The residue was extracted with ether and the ether extracts were combined and acidified with a few drops of 10% hydrochloric acid, dried (MgSO₄), and filtered, and the filtrate was evaporated to dryness under a vacuum. The residue was chromatographed over silica in the same column as described previously, first using a 95:5 benzene-ethyl alcohol eluent to elute 2,4-dinitroaniline, followed with methyl alcohol to elute 4-nitrophthalic acid. The eluent fractions (10 ml.) were followed by thinlayer chromatography. Combination and concentration to dryness of the benzene-ethyl alcohol eluents gave only a trace of 2,4-dinitroaniline. The methanol eluents were combined and concentrated to dryness under a vacuum, to give 4-nitrophthalic acid (0.36 g., 0.0017 mole) as a crystalline residue, m. p. 161-163° (lit.,⁵ 163-164°). A mixed m. p. with authentic 4-nitrophthalic acid (Eastman Organic Chemicals) was not depressed, and their infrared spectra were superimposable.

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- ⁴ Org. Synth., Coll. Vol. II, p. 221.
- ⁵ Org. Synth., Coll. Vol. II, p. 457.