Nitration of Phenylacetaldehyde

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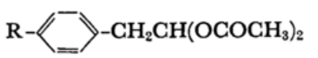
There has been only one report about the direct nitration of phenylacetaldehyde (I); in that experiment Forrer[1] used concentrated nitric acid as a nitrating agent, but failed to obtain *o*-nitrophenylacetaldehyde (II). II is one of most important materials for preparing indole[2] and *N*-hydroxyindole,[3] but it is not convenient to synthesize II from *o*-nitrocinnamamide[2] or 1-chloro-4-(*o*-nitrophenyl)-2-butene.[4] We attempted to obtain II by the direct nitration of I with fuming nitric acid in acetic anhydride. The conditions were similar to those in the *o*-nitration with acetylnitrate.[5] Contrary to our expectations, however, II could not thus be obtained. Four compounds were isolated instead; they were identified as phenylacetaldehyde-diacetate (III), *p*-nitrophenylacetaldehyde-diacetate (IV), bis-(α-acetoxy-β-phenylethyl)-ether (V), and bis-(α-acetoxy-β-*o*-nitrophenylethyl)-ether (VI).

To an acetic anhydride solution of I, an equivalent amount of fuming nitric acid was added slowly at 0°C. An ether solution of the reaction mixture afforded an insoluble solid. The fractional distillation of the ether solution under reduced pressure gave two main fractions. The thin-layer chromatography of the yellow distillate, with a lower boiling point, showed that it contained the known compound III[6,7] as a main component. The orange distillate, with a higher boiling point, partly solidified upon cooling or standing for several days. After recrystallization, two crystalline compounds were isolated. One of them was identified with an authentic compound, V.[6,7] The structure of the other crystal (mp 102°C) was established to be IV by elemental analyses, and by a study of the IR, UV and NMR spectra. The NMR spectrum contained two symmetrical doublets with the same relative area centered at τ 1.82 and τ 2.59. The methine triplet was centered at τ 3.08.

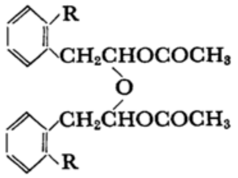
The solid which was insoluble in the ether solution from the reaction mixture was recrystallized four times from acetone to afford colorless crystals (mp 196°C). The NMR spectrum showed an extensively split doublet (2 H) centered at τ 1.88 (the proton *ortho* to the nitro group) and a complex multiplet (6 H) with the strongest peak at τ 2.80 (the remaining three aromatic protons). The methine triplet was centered at τ 3.88. These data, as well as the results of elemental analyses and the IR and UV spectra of the crystal, were consistent with the structure of VI.

From a consideration of the reaction products, III, IV, V and VI, it seems reasonable to assume that direct nitration with fuming nitric acid in acetic anhydride cannot give II, but it can give III, from which IV and V are formed, and V can change into VI.



III, R=H

IV, R=NO_2



V, R=H

VI, R=NO_2

Experimental

All boiling points and melting points are uncorrected.

Nitration of Phenylacetaldehyde. To 100 g of phenylacetaldehyde (I) in 200 m*l* of acetic anhydride in a 500 m*l*, three-necked flask equipped with a mechanical stirrer, 53 g of fuming nitric acid (d 1.50) were added, drop by drop, over a period of 6 hr at 0°C. The liquid mixture was then stirred for 6 hr, during which the ice in the bath melted and the solution warmed to room temperature. The mixture was poured onto ice and left to stand overnight. The oily product was separated by decantation from the aqueous acidic solution, and washed with a sodium carbonate solution and water. By extraction with ether, the oily product was separated into two parts; part A was an oily solid, only slightly soluble in ether, while part B was readily soluble in ether.

Bis-(α-acetoxy-β-*o*-nitrophenylethyl)-ether (VI). Part A, a crude oily solid (about 10 g), was recrystallized four times from acetone to give colorless leaflets of VI, mp 196°C. NMR spectrum in deuterochloroform: τ 1.88 (doublet, 2 H), τ 2.80 (multiplet, 6 H), τ 3.88 (triplet, 2 H), τ 6.95 (doublet, 4 H) and τ 8.13 (singlet, 6 H). ν^{KBr} 2920, 2850, 1440, 1435 and 1375 ($-CH_3$ and $-CH_2-$); 1740 (CO); 3070, 1605 and 1495 (aromatic); 1510 and 1350 (NO_2); 1245 and 1230 (C–O–C) cm^{-1}.

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[1] C. Forrer, *Ber.*, **17**, 982 (1884).

[2] R. A. Weerman, *Ann.*, **401**, 1 (1913).

[3] M. Mousseron-Canet and J. P. Boca, *Bull. Soc. Chim. France*, **1967**, 1296.

[4] W. E. Noland and J. H. Sellstedt, *J. Org. Chem.*, **31**, 345 (1966).

[5] A. Pictet and E. Khotinsky, *Ber.*, **40**, 1163 (1907).

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[7] E. Spath, *Monatsh. Chem.*, **36**, 29 (1915).

λ_{max}^{EtOH} (log ε) 270 (3.97) mμ. $\lambda_{max}^{0.1N\ NaOH-EtOH}$ (log ε) 263 (4.09) and 470 (4.64) mμ.

Found: C, 55.91; H, 4.66; N, 6.17%; mol wt (Rast), 448. Calcd for $C_{20}H_{20}O_9N_2$: C, 55.55; H, 4.66; N, 6.48%; mol wt, 432.38.

Phenylacetaldehyde-diacetate (III). Part B was concentrated on a rotary evaporator, and then the residue was, under reduced pressure, distilled into three fractions, together with 30—50 g of a tarry residue. Fraction 1, 5 g of a yellow liquid, bp 50—125°C/2.5 mmHg; fraction 2, 26 g of a yellow liquid, bp 125°C/2.5 mmHg, and fraction 3, 27 g of an orange liquid, bp 125—175°C/2.5 mmHg. Most of the fraction 1 consisted of the starting material, I. Fraction 3 was redistilled to give two main fractions; fraction a, 17 g of a yellow liquid, bp 126°C/2.5 mmHg, and fraction b, 6 g of an orange liquid, bp 165—178°C/2.5 mmHg. Fraction 2 and fraction a were combined and redistilled to give a faint yellow liquid of III (35 g), bp 126°C/2.5 mmHg (lit. 146—148°C/10 mmHg[6,7]). NMR spectrum in carbon tetrachloride: τ 2.82 (multiplet, 5 H), τ 3.18 (triplet, 1 H), τ 6.98 (doublet, 2 H) and τ 8.04 (singlet, 6 H). ν 2950, 2850, 1455, 1435 and 1375 ($-CH_3$ and $-CH_2-$); 1760 (CO); 3050, 1605 and 1495 (aromatic); 1240 and 1200 (C–O–C) cm^{-1}. λ_{max}^{EtOH} 253 and 259 mμ. $\lambda_{max}^{0.1N\ NaOH-EtOH}$ 250 and 297 mμ.

***p*-Nitrophenylacetaldehyde-diacetate (IV).** Fraction b was partly solidified in the flask by cooling or standing for several days. Recrystallization several times from methanol afforded prisms of IV (3 g), mp 102°C. NMR spectrum in deuterochloroform: τ 1.82 and τ 2.59 (two symmetrical doublets with the same relative area, 4 H), τ 3.08 (triplet, 1 H), τ 6.78 (doublet, 2 H) and τ 7.92 (singlet, 6 H). ν^{KBr} 2950, 2850, 1440, 1430 and 1378 ($-CH_3$ and $-CH_2-$); 1750 (CO); 3080, 1608 and 1490 (aromatic); 1512 and 1350 (NO_2); 1240 and 1200 (C–O–C) cm^{-1}. λ_{max}^{EtOH} (log ε) 268 (4.02) mμ. $\lambda_{max}^{0.1N\ NaOH-EtOH}$ (log ε) 270 (4.03) and 471 (4.39) mμ.

Found: C, 54.18; H, 4.98; N, 5.10%. Calcd for $C_{12}H_{13}O_6N$: C, 53.93; H, 4.90; N, 5.24%.

Bis-(α-acetoxy-β-phenylethyl)-ether (V). The mother liquid of the recrystallization of IV was concentrated to give crude crystals, from which 0.05 g of V was obtained by recrystallization from ethanol, mp 126—127°C. The melting point was identical with that of an authentic sample.[7] ν^{KBr} 2930, 2850, 1455, 1435 and 1380 ($-CH_3$ and $-CH_2-$); 1740 (CO); 3050, 1605 and 1495 (aromatic); 1255 and 1240 (C–O–C) cm^{-1}. λ_{max}^{EtOH} 260 mμ. $\lambda_{max}^{0.1N\ NaOH-EtOH}$ 297 mμ.