Nitration of 2,6-Xylenyl Acetate with Nitronium Tetrafluoroborate in Acetic Anhydride

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Nitration of phenols is limited by their susceptibility to oxidation. Usually, they are protected as esters or ethers during the reaction. A convenient protecting group is esters, but this is easily hydrolyzed on nitration. We attempted to nitrate 2, 6-xylenyl acetate (1) in acetic anhydride and found that a strong nitrating agent, nitronium tetrafluoroborate,¹⁾ is useful in spite of a decrease in genuine activity. The synthesis of 3,5-dinitro-2,6-xylenyl acetate (2) under these conditions is described. When 2,6-xylenyl acetate (1) was nitrated with cupric nitrate in acetic anhydride²⁾ at 60°C, 3-nitro-2,6-xylenyl acetate (3) was obtained in 86.2% yield and no additional dinitro compound was obtained at higher temperatures. When the acetate (1) was treated with nitronium tetrafluoroborate in acetic anhydride, 3,5-dinitro-2,6-xylenyl acetate (2), mp 154°C, was obtained in 83.3% yield. The mononitro acetate (3) also gave the dinitro acetate (2) on treatment similar to that described above. In sulfolane,¹⁾ the mononitro acetate (3) gave 3,4,5-trinitro-2,6-xylenol (4), mp 151°C, in a 2.5% yield and in nitromethane,¹⁾ 3,4-dinitro-2,6-xylenol* (5) in *ca.* a 2.5% yield. The structure of the dinitro acetate (2) was determined by its NMR spectrum. The methyl and the aromatic proton signals appeared as singlets at 2.44 and 8.44 ppm, respectively. These facts are further evidence for a symmetric structure as in 2. Moreover, the dinitro acetate (2) was converted to 2,4-dimethylphloroglucin triacetate^{3b)} (7), mp 124.5°C. Thus, nitration with nitronium tetrafluoroborate in acetic anhydride was found to be regioselective and to be stronger than that with cupric nitrate. The difference in activity between the two reagents can be explained by the fact that the former reacts directly,¹⁾ while the cupric nitrate reacts indirectly.⁴⁾ As additional examples of this reaction, phenyl acetate (8) and anisol (9) were nitrated under these conditions with respective yields of *p*-nitrophenyl acetate^{3c)} (10) (60.1% yield) and 2,4-dinitroanisole^{3d)} (11) (42.3% yield).

* 3,4-Dinitro-2,6-xylenol (5) was identified as the acetate (6), mp 102°C.

During the reaction in the absence of acetic anhydride, however, the acetoxyl group was hydrolyzed and the nitro group entered para to the hydroxyl group. On treatment with a mixed acid, the acetate (1) gave 4-nitro-2,6-xylenol^{3e)} (12) as a trace. Under these conditions, the yields were low.

EXPERIMENTAL

Melting points were uncorrected. IR spectra were recorded on a Hitachi EPI G-2 spectrometer. NMR were measured with a Hitachi R-24 (60 MHz) spectrometer in ppm with tetramethyl silane as the internal standard. MS spectra were measured with a JEOL JMS-01SG-2 spectrometer. The reaction was usually carried out as described in the references. The reaction conditions and yields were tabulated below. Physical data (mp, IR and NMR) of the products were also listed. Nitration with nitronium tetrafluoroborate in acetic anhydride was carried out as follows.

3,5-Dinitro-2,6-xylenyl acetate (2)

Nitronium tetrafluoroborate (32.4 g, 243.61 mmoles) was added to an acetic anhydride (20 ml) solution of 2,6-xylenyl acetate (1) (10 g, 60.9 mmoles) at 30~60°C (below at 70°C) with ice cooling. The reaction was exothermic, and a rise in temperature decreased the yield. After the addition of the reagent, the reaction mixture was stirred for 30 min at room temperature, then the whole was poured into ice water. After stirring the mixture for an hour, crystals were collected, which were washed with water and dried under reduced pressure. Dinitro acetate (2) was obtained on recrystallization with ether in 83% yield (12.9 g, 50.8 mmoles), mp 154°C (needle). IR $\nu_{\text{max}}^{\text{NaCl}}$ cm⁻¹: 1770 (OCOCH₃), 1605, 1599 (phenyl), 1530, 1345~50 (NO₂). NMR (CDCl₃) δ : 2.41 (6H, s, CH₃), 2.44 (3H, s, OAc), 8.43 (1H, s, C₄-H). MS *m/e*: 245 (M⁺), 195 (M⁺-OAc), 91, 65. Polymorphism of 2 was observed, mp 102°C (cubic). Mono acetate (3) (5.0 g, 23.92 mmoles) also gave the dinitro acetate (2) (2.0 g, 7.87 mmoles, 32.9% yield) on treatment with the reagent (4.2 g, 31.58-mmoles) in acetic anhydride (5 ml) and sulfolane (12ml).

2,4-Dimethylphloroglucin triacetate^{3b)} (7)

2,4-Dimethylphloroglucin^{3a)} (6) was obtained in the manner as described in the references.⁵⁾ 3,5-Dinitro-2,6-xylenyl acetate (2) (5 g) was reduced with zinc metal (24 g) and conc hydrochloric acid (22.4 ml), then hydrolyzed at pH 3 in CO₂ gas on refluxing for 24 hr. Oily unstable 2,4-dimethylphloroglucin^{3a)} (2.0g) was obtained on purification with silica gel column (20g) (benzene and ethyl acetate; 10:1, eluate) in 66% yield. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3520, 3470 (OH), 1630, 1610 (phenyl) NMR (Pyr- d₆) δ : 2.67 (6H, s, CH₃), 6.66 (1H, s, C₄-H), 8.64 (s, OH). Acetylation of this product gave

a triacetate (7) quantitatively, mp 124.5°C.^{3b)} IR $\nu_{\max}^{\text{nujol}}$ cm⁻¹: 1760, 1220 (OAc), 1620, 1600 (phenyl). NMR (CDCl₃) δ : 1.92 (6H, s, CH₃), 2.25 (6H, s, OAc), 2.30 (3H, s, OAc), 6.83 (1H, s, C₄-H). Found: C, 59.81; H, 5.87. Calcd. for C₁₄H₁₆O₆: C, 59.99; H, 5.75.

(3H, s, CH₃), 2.30 (3H, s, OAc), 7.86 (1H, s, C₆-H). MS m/e : 254 (M⁺), 195 (M⁺-OAc), 165 (195-NO), 91.

4-Nitro-2,6-xyleneol^{3e)} (12)

mp 170°C (decomp.). IR $\nu_{\max}^{\text{nujol}}$ cm⁻¹: 3470 (OH), 1595 (phenyl), 1510, 1340 (NO₂). NMR (CDCl₃+

Starting material (g)	Product (g)	Reagent (g)	Solvent (ml)	Yield %	Reaction temperature °C
1 (5.0)	3 (5.5)	A (20)	a (80)	86.3	60
1 (10)	2 (12.9)	B (32.4)	a (20)	83	30~60
3 (5.0)	2 (2.0)	B (4.2)	a(5)+b(12)	32.9	30~60
3 (1.0)	4 (0.03)	B (1.5)	b (5)	2.5 ^{1b)}	30~60 ^{1e)}
3 (1.0)	5 ^{a)}	B (1.5)	c (5)	2.5 ^{2b)}	30~60
8 (1.0)	10 (0.8)	B (4.5)	a (6)+b (8)	60	30~60
9 (5.0)	11 (3.7)	B (20)	a (20)	42.3	30~60
1 (5.0)	12 (0.02)	C	—	3.8 ^{3b)}	60 ^{2e)}

A, cupric nitrate; B, nitronium tetrafluoroborate; C, mixed acid (nitric acid: sulfuric acid=6.8 g: 35.9 g); a, acetic anhydride; b, sulfolane; c, nitromethane. ^{a)} The crude oil (590 mg) of 5 showed no absorption between 1750~1800 cm⁻¹ in its IR spectrum. ^{1b)} Purified on a silica gel column (7 g) (benzene elution, 100 ml). ^{2b)} The yield was obtained as an acetate (6) which was purified from the crude acetate. ^{3b)} The crude oil (0.56 g) was purified on a silica gel column (7 g) (benzene+ether, 10: 1, elution, 100 ml). ^{1e)} After the addition of the reagent, the reaction mixture was stirred overnight, then heated at 100°C for 30 min. ^{2e)} For 30 min.

3-Nitro-2,6-xyleneol acetate (3)

IR $\nu_{\max}^{\text{nujol}}$ cm⁻¹: 1770 (OAc), 1615, 1599 (phenyl), 1525, 1355 (NO₂). NMR (CDCl₃) δ : 2.19, 2.30 (3H, s, CH₃), 2.33 (3H, s, OAc), 7.14 (1H, d, $J=9$, C₅-H), 7.70 (1H, d, $J=9$, C₄-H). MS m/e : 209 (M⁺), 164 (M⁺-C₂H₅O), 150 (M⁺-C₂H₃O), 122, 91, 65.

Pyr-d₅) δ : 2.35 (6H, s, CH₃), 7.92 (2H, s, C₃ & C₅-H), 9.24 (OH). MS m/e : 167 (M⁺), 150 (M⁺-OH), 137 (M⁺-NO), 121 (M⁺-NO₂), 91, 77, 65.

p-Nitrophenyl acetate^{3e)} (10)

mp 82°C. This was identified with an authentic sample by IR spectrum.

3,4,5-Trinitro-2,6-xyleneol (4)

mp 151°C. IR $\nu_{\max}^{\text{nujol}}$ cm⁻¹: 3480 (OH), 1540, 1350 (NO₂). NMR (CDCl₃+Pyr-d₅) δ : 2.09 (s, CH₃), 7.27 (OH). MS m/e : 275 (M⁺), 240 (M⁺-OH), 210 (240-NO), 198, 168, 164 (210-NO₂).

2,4-Dinitroanisole^{3d)} (11)

mp 94°C. IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 1610 (phenyl), 1535, 1355 (NO₂). NMR (CDCl₃): 4.90 (3H, s, OCH₃), 7.28 (1H, d, $J=9.5$, C₆-H), 8.46 (1H, dd, $J=9.5$ & 3, C₅-H), 8.70 (1H, d, $J=3$, C₃-H). MS m/e : 198 (M⁺), 180, 168 (M⁺-NO), 152 (M⁺-NO₂), 151, 138, 107, 105, 77.

3,4-Dinitro-2,6-xyleneol acetate (6)

mp 102°C. IR $\nu_{\max}^{\text{nujol}}$ cm⁻¹: 1770 (OAc), 1540, 1345 (NO₂), 1585 (phenyl). NMR (CDCl₃) δ : 2.06, 2.15

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