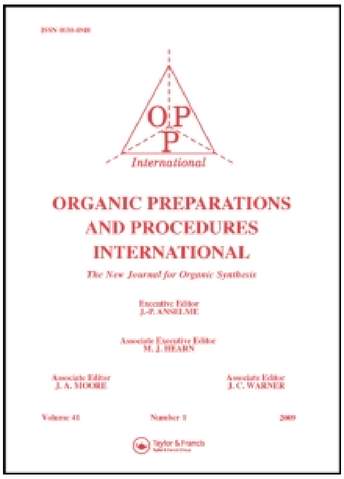

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SYNTHESIS OF 2,5- AND 2,6-DINITROFLUOROBENZENES AND RELATED HYDROQUINONES

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The solvent of the filtrate from the isolation of 1,1'-DNM was evaporated to afford a pale brown solid which was recrystallized from anhydrous methanol to yield 8.2 g (29%) of 1,2'-DNM as pale brown crystals, mp 139-140°C, *lit.*[5] 135-136°C. IR (KBr): 3050, 1690, 1620, 1500, 1470, 1350, 1280, 1230, 1190, 1160, 1110, 910, 870, 790 cm^{-1}. ^{1}H NMR: δ 7.48-7.66 (m, 5H), 7.83-7.85 (d, 1H), 7.90-7.97 (dm, 5H), 8.04-8.12 (m, 2H), 8.25 (s, 1H). MS (*m/z*): 282 (M$^+$, 100), 253 (M-C_2H_5, 24), 155 (M-$C_{10}H_8$, 78), 127 (155-CO, 90). λ_{max} (CH_3OH): 285.5 nm.
Anal. Calcd for $C_{21}H_{14}O$: C, 89.34; H, 5.00. Found: C, 89.43; H, 4.93

REFERENCES

1. S. Jha, A. Reiser, L. Sroubkova and R. Zahradnik, *Macromolecules*, **31**, 6549 (1998).
2. R. C. Larock and S. A. Hershberger, *J. Org. Chem.*, **45**, 3840 (1980).
3. C. S. Cho, T. Ohe and S. Uemura, *J. Organomet. Chem.*, **496**, 221 (1995).
4. L. Wu, Y. M. Qin, B. Huang, G. L. Zou, X. Y. Wei, Z. M Zong and Q. R. Chen, *Wuhan University J. Nat. Sci.*, **6**, 854 (2001); *Chem. Abstr.*, **136**, 325135t (2002).
5. S. V. Jovanovic, D. G. Morris, C. N. Pliva and J. C. Scaiano, *J. Photochem. Photobiol. A: Chem.*, **107**, 153 (1997).

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SYNTHESIS OF 2,5- AND 2,6-DINITROFLUOROBENZENES AND RELATED HYDROQUINONES

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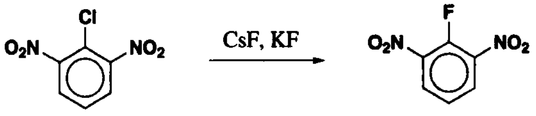
Two dinitrofluorobenzenes (**1** and **2**) and the commercially available 2,4-isomer were required in connection with a mechanistic study on the Elbs oxidation.[1] Although the 2,6-isomer (**1**) had been prepared previously using four different procedures,[2] all involving reaction of 2,6-dinitrochlorobenzene with a solid fluoride salt, the yields were difficult to reproduce. The difficulty seems to lie in the physical state of the fluoride salts as was nicely discussed by Smyth *et* *al.*[3] This paper describes a fifth modification which includes DMSO for rate acceleration, azeotropic drying, and a finely divided fluoride reagent made from a mixture of CsF and KF. The other isomer, 2,5-dinitrofluorobenzene (**2**), was unknown in spite of a report of it in the literature.[4] It has now been prepared by dimethyldioxirane oxidation of 2-amino-5-nitrofluorobenzene. It is worth noting that we tried a number of unsuccessful routes to this molecule including displacement of chloride by fluoride in 2,5-dinitrochlorobenzene, a Sandmeyer reaction on 2-fluoro-4-nitroaniline, treatment of 2-fluoro-4-nitroaniline with either peroxydisulfate in sulfuric acid or with trifluoroperoxyacetic acid, as well as some other dimethyldioxirane protocols. In addition, two related dinitrohydroquinones were also needed and were made by Elbs oxidations of the corresponding dinitrophenols. The Elbs oxidation is an easier and shorter procedure than previous syntheses of these hydroquinones particularly for the 2,5-isomer (five steps). The Elbs oxidation is a two-step synthesis involving reaction of the phenol under alkaline conditions with peroxydisulfate ion followed by acid-catalyzed hydrolysis of the sulfate ester to the hydroquinone. The simplicity of the Elbs procedure frequently overcomes its principal drawback of low yield.



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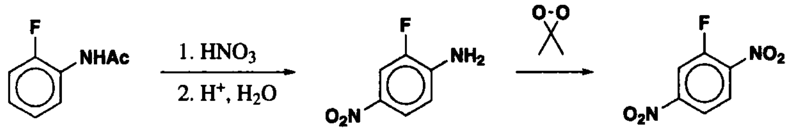

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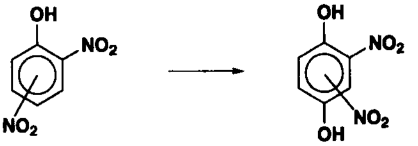

3

a) 5-NO_2 b) 6-NO_2

EXPERIMENTAL SECTION

NMR spectra were obtained at 600MHz (Bruker). IR spectra were recorded on a Nicolet FT instrument. Melting points were determined on a MelTemp apparatus. Chemicals were obtained from Aldrich or Lancaster.

2,6-Dinitrofluorobenzene (1).- A 1:1 mixture of KF and CsF (prepared by reaction of Cs_2CO_3 and KHF_2) was dissolved in methanol and dried as described by Smyth *et al*;[3] a final drying was carried out at 150°C in an oven overnight. Then, 1 g. of this powder, 0.6 mL of redistilled DMSO, and 2 mL of toluene (distilled from CaH_2) were heated in a distillation apparatus until about 1 mL of the toluene had been distilled. The mixture was cooled to RT and 0.5 g (2.5 mmol) of 2,6-dinitrochlorobenzene (Lancaster, freed of some insoluble impurities by dissolution in about 3 mL of benzene, filtration and evaporation of the solvent) was added. This mixture was refluxed for 45 min. TLC, performed as described,[2c] showed disappearance of the chloro compound and formation of the product ($R_{f\text{-}Cl}$ = 0.55, $R_{f\text{-}F}$ = 0.35). Some of the dinitrophenol was also found (R_f = 0). The mixture was cooled and then partitioned between cold water and ether. The combined ethereal extracts were washed with water, dried ($MgSO_4$) and evaporated to a colorless oil. Addition of pentane to this oil led to crystallization of **1**, mp 58-59°C, *lit.*[2] ca. 60°C, 0.30-0.35 g (65-75%). IR (thin film, melt): 3095, 3052, 1613, 1597, 1538, 1526, 1465, 1347, 1310, 1088, 916, 850, 823, 740, 714, 589 cm^{-1}. The ^{1}H NMR spectrum agreed with the literature data.[2d]

2,5-Dinitrofluorobenzene (2).- 2-Fluoroacetanilide (Lancaster) was nitrated using nitric acid alone exactly as described by Wepster and Verkade[5] to yield 4-nitro-2-fluoroacetanilide, mp 205-207°C. Hydrolysis of 2.0 g (10 mmol) of this material by reflux in a mixture of 6 mL conc. HCl and 10 mL ethanol for 6 hr. yielded 1.4 g (89%) of 2-fluoro-4-nitroaniline, mp 133-134°C, *lit.*[5] 134-134.5°C. Oxidation of this compound, 1 g (6.4 mmol) with dimethyldioxirane by the hexane-water-acetone procedure of Makosza *et al.*[6] followed by extraction with methylene chloride and drying, gave the desired product which was freed of starting material by crystallization from hexane to give 0.5 g (42%) of small yellow needles, mp. 74-75°C.

Anal. Calcd for $C_6H_3FN_2O_4$: C, 38.72; H, 1.62; N, 15.05. Found: C, 38.98; H, 1.70; N, 14.78

^{1}H NMR (DMSO-d_6): δ 8.53, dd, H-6 ($J_{F,6}$ = 10.7 Hz, $J_{4,6}$ = 2.4 Hz) δ 8.42, dd, H-3 ($J_{3,4}$ = 9.0 Hz, $J_{F,3}$ = 7.6 Hz) δ 8.26, ddd, H-4 ($J_{3,4}$ = 9.0Hz, $J_{4,6}$ = 2.3Hz, $J_{F,4}$ = 1.3 Hz). ^{13}C (DMSO-d_6). δ 154.3, C-1 (J_{CF} = 265Hz); 150.7, C-2 (J_{CF} = 8.3 Hz); 140.7, C-5 (J_{CF} = 7.5Hz.); 127.7, C-4; 120.2, C-3, (J_{CF} = 3.9Hz); 114.6, C-6 (J_{CF} = 26Hz). IR (Thin film, melt): 3117, 3092, 3061,1627, 1601, 1555, 1481, 1427, 1347, 1313, 1253, 1145, 1104, 1072, 946, 890, 841, 811, 732 cm^{-1}.

2,5-Dinitrohydroquinone (3a).- A solution of 2,5-dinitrophenol (Aldrich, 0.136 g, 0.74 mmol) and potassium peroxydisulfate (0.54 g, 2 mmol) in 15 mL aqueous 0.33 *M* NaOH was prepared by stirring at 40°C. The solution was kept at 42°C for 18 hr. Glacial acetic acid was added to the cooled reaction mixture to bring the pH to about 3. A precipitate (0.021 g) of starting material was removed by filtration. Extraction with 10 mL ether gave an additional 0.01 g of starting material for a total recovery of 0.031 g. Conc. HCl (1 mL) was added to the extracted solution which was then heated at reflux for 30 min. Cooling gave brown crystals of **3a** (0.041 g, 28% or 36% based on recovered starting material) mp 207-209°C, *lit.*[7], 201-203°C. ^{1}H NMR (DMSO-d_6): δ 7.55 (s). The DMSO was wet so that the hydroxyl protons appeared only in the water resonance. IR (Nujol): 3313, 3078, 1568, 1441, 1306, 1229, 1083, 892, 875, 806, 768 cm^{-1}. Another route to this compound *via* 2,5-dinitro-1,4-dimethoxybenzene failed because of difficulty in the demethylation step.

2,6-Dinitrohydroquinone (3b).- A suspension of 2,6-dinitrophenol[8,9] (2.3 g, 12.5 mmol) in 200 mL of an aqueous solution of 4.5 g (42 mmol) sodium carbonate and sodium peroxydisulfate (3.5 g, 14.7 mmol) was stirred for two days at RT. An additional 3.5 g (14.7 mmol) of sodium peroxydisulfate was added. The homogeneous solution that formed was allowed to stand for another five days at RT. Paper electrophoresis at pH 7 (1400 V) showed two components moving with velocities of 1.1 and 2.0 relative to picrate ion corresponding to starting material and 2,6-dinitrohydroquinone monosulfate. The solution was cooled on ice and then acidified with 15 mL glacial acetic acid to about pH 3.3. Unreacted starting material was extracted with ether. The sulfate ester of 2,6-dinitrohydroquinone was hydrolyzed to 2,6-dinitrohydroquinone by boiling for 30 min following the addition of 15 mL conc. HCl to the reaction mixture. Upon cooling, the product crystallized as brown needles of the hydrate, mp 93-95°C, *lit.*[10] 93-94°C. Drying at 110°C gave tan needles of the anhydrous material quantitatively (mp 134-135°C, *lit.*[10] 137°C) with an IR spectrum identical to that of a commercial sample (Aldrich Rare Chemicals). Additional anhydrous material was obtained by extraction of the mother liquors with ether. The total yield was 0.67 g (35%). IR (anhydrous, Nujol): 1595, 1548, 1536, 1488, 1331, 1249, 1142, 982, 922, 877, 804, 765 , 736 cm^{-1}.

REFERENCES

1. E. C. Behrman, S. Chen and E. J. Behrman, *Tetrahedron Lett.*,**43**, 3221 (2002).

2. a) N. N. Voroshtsov, V. A. Sokolenko and G. G. Yakobson, *Izv. Sib. Otd. Akad.Nauk SSSR*, 87 (**1962**). C.A., **59**, 1507a (1963). b) R. E. Parker and T. O. Read, *J. Chem. Soc.*, 3149 (**1962**). c) J. F. K. Wilshire, *Australian J. Chem.*, **20**, 2809 (1967). d) R. Goumont, N. Faucher, G. Moutiers, M. Tordeux, and C. Wakselman, *Synthesis,* 691 (**1997**).

3. T. P. Smyth, A. Carey and B. K. Hodnett, *Tetrahedron,* **51**, 6363 (1995).

4. V. Krchnák, L. Szabo and J. Vágner, *Tetrahedron Lett.,* **41**, 2835 (2000).

5. B. M. Wepster and P. E. Verkade, *Recl. Trav. Chim. Pays-Bas,* **68**, 77 (1949).

6. T. Lemek, M. Makosza and J. Golinski, *Tetrahedron,* **57**, 4753 (2001).

7. E. M. Kampouris, *J. Chem. Soc. (C),* 1235 (**1967**).

8. M. A. Phillips, *Chem. Ind* ., 714 (**1952**).

9. L. Benda and A. Bertheim, *Ber.*, **44**, 3445 (1911).

10. R. Nietzki, *Ber.*, **11**, 469 (1878); *Ann.*, **215**, 125 (1882). B. Reichert and W. Turkewitsch, *Archiv. Pharm. (Weinheim)*, **270**, 397 (1938).