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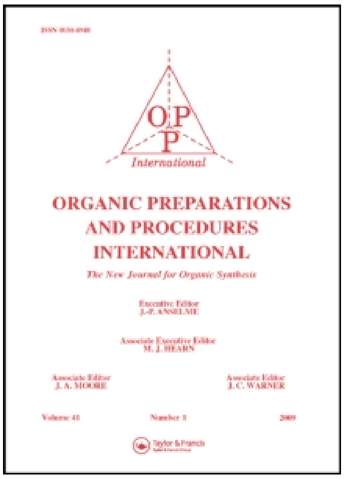

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# AN IMPROVED LARGE-SCALE PREPARATION OF 3,3',4,4'-TETRAAMINODIPHENYL ETHER

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# AN IMPROVED LARGE-SCALE PREPARATION OF 3,3',4,4'-TETRAAMINODIPHENYL ETHER

*Submitted by*
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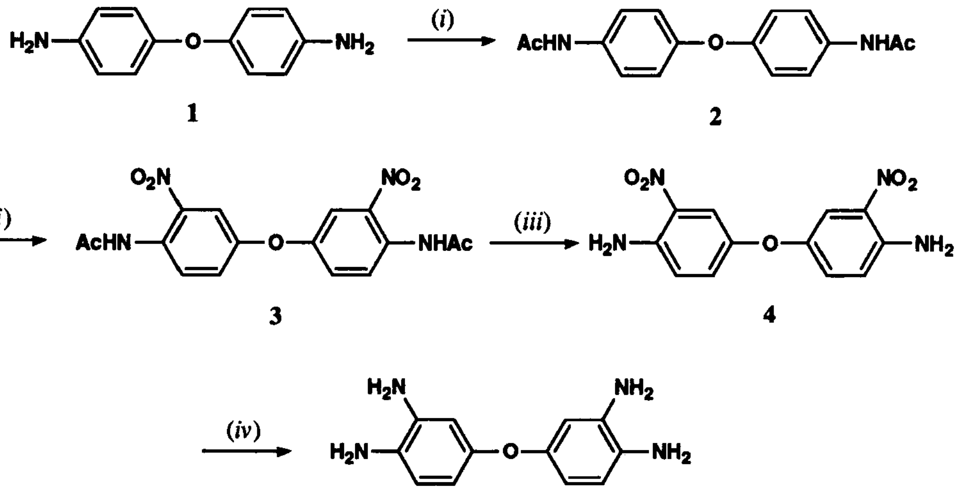
3,3',4,4'-Tetraaminodiphenyl ether (**5**), an intermediate of potential industrial importance,[1] has previously been prepared *via* a four-step procedure commencing from 4,4'-diaminodiphenyl ether.[1] However, few of its physical, chemical or spectroscopic properties have been reported. In connection with other work, we needed this compound in quantity. Hence, each step of the existing procedure was reinvestigated and optimized. This resulted in an improvement in the overall yield from 43% to 69%.

Thus, acylation of 4,4'-diaminodiphenyl ether (**1**) with $Ac_2O$/AcOH by a procedure in which the reaction time was longer than that previously reported gave 4,4'-diacetamidodiphenyl ether (**2**) in 91% yield (lit.[1] 77%). Nitration of **2** with fuming nitric acid in glacial acetic acid was optimized to afford the dinitro derivative **3** in 92% yield (lit.[1] 82%). Hydrolysis of **3** was carried out in refluxing dilute hydrochloric acid to give 4,4'-diamino-3,3'-dinitrodiphenyl ether (**4**) in a yield of 90% (lit.[1] 90%).



(*i*) $Ac_2O$, AcOH; (*ii*) Fuming $HNO_3$, AcOH; (*iii*) 6NHCl, Δ, 5 hrs;

(*iv*) $NH_2NH_2$/graphite, EtOH, Δ, 18 hrs.

In our hands, reduction of **4** under the conditions described in the literature[1] (Raney-Ni/$NH_2NH_2 \cdot H_2O$, ethanol/THF), left unchanged a substantial amount of starting material, even after extended periods of reflux; we were able to isolate only small quantities of pure **5**. Utilization of excess hydrazine monohydrate with Raney nickel (to assist the reaction to completeness) gave complex mixtures. Hydrazine monohydrate/graphite has been used successfully in reductions of polynitro compounds by Han *et al.*[2] This method with an extended ethanolic reflux accomplished the reduction cleanly and provided 3,3',4,4'-tetraaminodiphenyl ether (**5**) in 92% yield ( lit.[1] 76%). The structure of **5** was confirmed by $^1H$ and $^{13}C$ NMR, mass spectrometry and by elemental analysis.

In conclusion, the methodology described herein represents a reliable, inexpensive and efficient procedure for the large scale (100 g batches in each step) preparation of 3,3',4,4'- tetraaminodiphenyl ether.

## EXPERIMENTAL SECTION

Melting points were determined on a Bristoline hot-stage microscope and are uncorrected. $^1H$ NMR spectra were recorded on a Varian VXR-300 spectrometer with TMS as an internal reference. $^{13}C$ NMR spectra were recorded at 75 MHz on the same instrument using the solvent peak ($CDCl_3$, δ 77.0 ppm; DMSO-$d_6$, δ 39.50 ppm) as reference. Microanalyses were carried out using a Carlo Erba 1106 elemental analyser. Mass spectrometry was carried out on a Finnegan Mat 95.

**4,4'-Diacetamidodiphenyl Ether (2).**- Acetic anhydride (100 mL) was added dropwise to an ice-cooled solution of 4,4'-diaminodiphenyl ether (100 g, 0.5 mol) in glacial acetic acid (500 mL). During the addition of the final 20 mL, large amounts of precipitate formed. The reaction mixture was allowed to stand at room temperature overnight followed by dilution with water (1000 mL). The solid product was collected, washed with water (3 x 500 mL) and dried to afford 129 g of pale-white crystals (91%), mp. 229-230°, lit.[1] mp. 222°. $^1H$ NMR (DMSO-$d_6$): δ 9.94 (s, 2H), 7.58 (d, J = 8.8Hz, 4H), 6.94 (d, J = 8.8Hz, 4H), 2.04 (s, 6H). $^{13}C$ NMR: δ 23.9, 118.6, 120.6, 134.9, 152.3, 168.0.

**4,4'-Diacetamido-3,3'-dinitrodiphenyl Ether (3).**- Fuming nitric acid (170 mL, d 1.5) was added dropwise to an ice-cooled solution of **2** (100 g, 0.352 mol) in glacial acetic acid (520 mL) over 30-40 min. Large amounts of precipitate formed after the addition was complete. The reaction mixture was allowed to stand at room temperature for an additional 2 hrs and poured onto crushed ice. The solid product was collected, washed with water (3 x 600 mL) and dried to yield 122 g of a yellow solid (92%), mp. 209-211°, lit.[1] mp. 212°. $^1H$ NMR (DMSO-$d_6$): δ 10.26 (s, 2H), 7.70-7.59 (m, 4H), 7.50-7.43 (m, 2H), 2.06 (s, 6H). $^{13}C$ NMR: δ 23.2, 114.9, 124.3, 127.3, 127.4, 143.3, 152.3, 168.5.

**4,4'-Diamino-3,3'-dinitrodiphenyl Ether (4).**- A suspension of **3** (100 g, 0.267 mol) in hydrochloric acid (6 N, 1600 mL) was refluxed with vigorous stirring for 8 hrs. The reaction mixture was cooled and neutralized with aqueous ammonia (30%). The solid product which formed was collected, washed with water (3 x 600 mL) and dried to afford 70 g of a light-brown solid (90%), mp. 171-173°, lit.[1] mp. 176°. $^1H$ NMR (DMSO-$d_6$): δ 7.49 (d, J = 2.2Hz, 2H), 7.44 (s, 4H), 7.30 (dd, $J_1$ = 9.1 and $J_2$ = 2.2Hz, 2H), 7.11 (d, J = 9.1Hz, 2H). $^{13}C$ NMR: δ 112.7, 121.1, 128.8, 129.1, 143.3, 145.7.

**3,3',4,4'-Tetraaminodiphenyl Ether (5).**- A mixture of **4** (100 g, 0.345 mol), hydrazine monohydrate (98%) (150 mL, 3.09 mol), graphite (250 g) and ethanol (1000 mL) was refluxed for 18 hrs. The solid catalyst was removed through a pad of Celite and the filtrate evaporated under reduced pressure to a viscous brown oil which was triturated with methanol to afford 73 g of a light-yellow solid (92%), mp. 141-143°. $^1$H NMR (DMSO-$d_6$): δ 6.42 (d, J = 8.3Hz, 2H), 6.15 (d, J = 2.6Hz, 2H), 5.98 (dd, $J_1$ = 8.3 and $J_2$ = 2.6Hz, 2H), 4.52 (s, br, 4H), 4.12 (s, br, 4H). $^{13}$C NMR: δ 105.1, 106.6, 114.9, 129.9, 136.4, 150.1.

*Anal.* Calcd for $C_{12}H_{14}N_4O$: C, 62.59; H, 6.13; N, 24.33. Found: C, 62.52; H, 6.17; N, 24.05

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