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Electron-Transfer Substitution Reactions: Stereochemistry[1]

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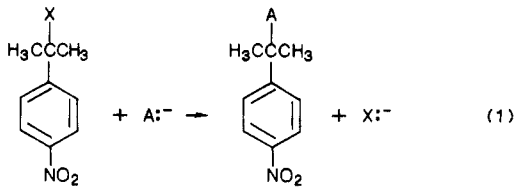
Substitution of the aliphatic nitro group of optically active 2-(*p*-nitrophenyl)-2-nitrobutane (II) by sodium azide, sodium thiophenoxide, sodium benzenesulfinate, and the lithium salt of 2-nitropropane invariably occurs with complete loss of optical activity. Furthermore, levorotatory II is racemized by sodium nitrite. These facts support the view that substitution reactions in *p*-nitrocumyl systems proceed via the electron-transfer chain mechanism of eq 2–5.

p-Nitrocumyl chloride (Ia) and α,*p*-dinitrocumene (Ib) react readily with a wide range of nucleophiles in the manner described by eq 1.[2] It has been proposed that

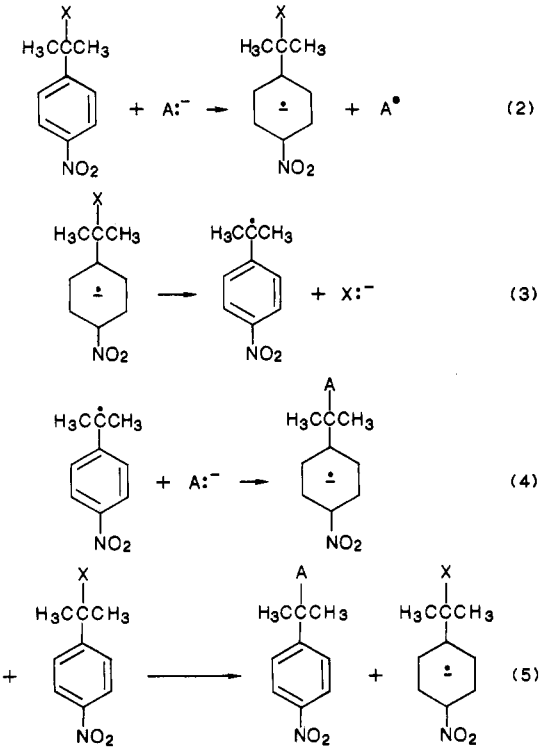


Ia: X = Cl
Ib: X = NO_2

these transformations proceed via the electron-transfer chain mechanism of eq 2–5 and a substantial body of evidence which supports this mechanism has been presented.[2]

The present paper is concerned with a distinctly different test of the proposed mechanism—a stereochemical test. It will be seen from eq 3 and 4 that free *p*-nitrocumyl radicals are invoked as intermediates. Such radicals would be expected to adopt, or rapidly to pass through, the planar configuration[3], and this leads to the prediction that optically active 2-(*p*-nitrophenyl)-2-nitrobutane (II), when treated with nucleophiles, will give substitution products that are racemic. It should be noted that Norris[3c] has proposed that *p*-nitrocumyl-type radicals are initially produced as pyramidal structures that then collapse to effectively planar radicals. This proposal, which rests on experiments involving only one compound, and only a single nucleophile, is inadequately documented and we find it less than compelling.

The synthesis of levorotatory II is outlined in Scheme I. Racemic II, readily available by the action of the lithium salt of 2-nitrobutane on *p*-dinitrobenzene,[4] is



converted to the nitro azide III by sodium azide; this reaction parallels the known reaction of α,*p*-dinitrocumene

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(1) This is paper 31 in the series "Substitution Reactions Which Proceed via Radical Anion Intermediates". For the preceding paper, see: Wade, P. A.; Morrison, H. A.; Kornblum, N. *J. Org. Chem.* **1987**, *52*, 3102. This paper is based on the Ph.D. dissertation of P. A. Wade, Purdue University, 1973.

(2) Kornblum, N.; Cheng, L.; Davies, T. M.; Earl, C. W.; Holy, N. L.; Kerber, R. C.; Kestner, M. M.; Manthey, J. W.; Musser, M. T.; Pinnick, H. W.; Snow, D. H.; Stuchal, F. W.; Swiger, R. T. *J. Org. Chem.* **1987**, *52*, 196.

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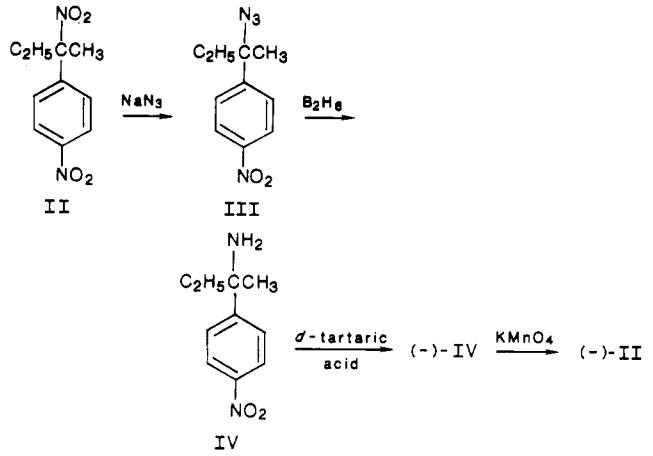
Scheme I



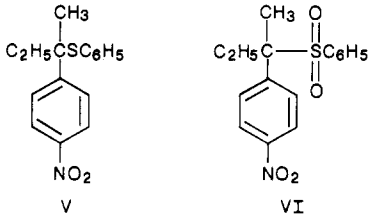
(Ib) with sodium azide[2] and occurs in equally good yield (94%). Diborane reduces azido groups[5] but does not readily reduce nitroaromatics; its use enables one to convert the nitro azide III into the nitro amine IV in 70% yield. Resolution of the nitro amine was achieved via its *d*-tartrate salt. Finally, oxidation of the optically active amine IV by potassium permanganate[6] gave the levorotatory dinitro compound II.

Stereochemistry

A solution of the optically active dinitro compound II in hexamethylphosphoramide (HMPA) suffers no loss of rotation after 3.5 h—a time longer than that employed in the following experiments. Furthermore, the dinitro compound is recovered in 98% yield with its optical activity intact.

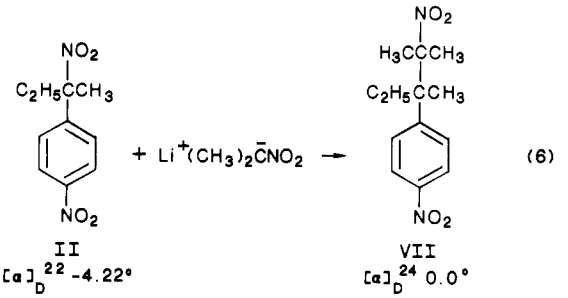
An HMPA solution of the levorotatory dinitro compound II, $[\alpha]^{22}_D$ −4.22°, on treatment with sodium azide gives optically inactive nitro azide III; this nitro azide, upon being reduced with diborane, yields the optically inactive nitro amine IV. Clearly, racemization occurs on replacing the aliphatic nitro group of II by azide.[7]

In dimethyl sulfoxide (Me_2SO) the reaction of sodium thiophenoxide with the optically active dinitro compound II is complete in 30 min. The pure nitro sulfide V, which is isolated in 85% yield, is optically inactive.



An HMPA solution of sodium benzenesulfinate and the levorotatory dinitro compound II after 70 min gives the sulfone VI in 95% yield. The sulfone exhibits zero optical rotation and melts at 137–137.5 °C, which is the melting point of the racemic sulfone.

The reaction of the lithium salt of 2-nitropropane with the levorotatory dinitro compound II in HMPA results in a 78% yield of the pure carbon alkylate VII (eq 6).



Compound VII is devoid of optical activity and melts at 94–95 °C—the melting point of racemic VII. Thus, here, as in all the other cases, substitution occurs with complete loss of optical activity.

Sodium nitrite is known to displace chloride ion from *p*-nitrocumyl chloride (Ia) via the electron-transfer chain mechanism of eq 2–5 to give α,*p*-dinitrocumene (Ib) in 91% yield.[2] This prompted the thought that, if the optically active dinitro compound II were treated with sodium nitrite, displacement of the aliphatic nitro group by nitrite ion via a chain sequence analogous to eq 2–5 might occur and, as a consequence, racemization of II would be observed. And, indeed, this is precisely what happens. Addition of sodium nitrite to an HMPA solution of the levorotatory dinitro compound II leads, at room temperature, to racemization. Thus, after 3.5 h the quantitatively recovered II, which is fully characterized and shown to be pure, has lost 25% of its optical activity. And, after 13.3 h the recovered II has lost 60% of its optical activity.[8]

The fact that substitution of the aliphatic nitro group of optically active 2-(*p*-nitrophenyl)-2-nitrobutane (II) invariably occurs with racemization constitutes significant evidence for the view that substitution reactions in *p*-nitrocumylic systems proceed via an electron-transfer chain mechanism in which free radicals are intermediates.

Experimental Section

The DMF, Me_2SO, and HMPA were purified as described earlier.[2] Sodium nitrite (Baker Reagent) was dried for 5 h at 80 °C under reduced pressure. Boron trifluoride etherate was distilled from calcium hydride at reduced pressure. *p*-Dinitrobenzene (Fluka) was sublimed, mp 172.5–173 °C. *d*-Tartaric acid (Eastman White Label) was recrystallized from absolute ethanol–hexane and then dried under reduced pressure for 18 h, mp 170–171 °C. Sodium benzenesulfinate (Matheson, Coleman & Bell) was recrystallized from ethanol and dried at 120 °C for 4 h under reduced pressure. 2-Methoxyethyl ether (peroxide free!) was distilled from CaH_2 and then redistilled at reduced pressure from $LiAlH_4$. THF was distilled from LAH and was stored under N_2.

Preparation of 2-(*p*-Nitrophenyl)-2-butyl Azide (III). A solution containing sodium azide[2] (26.1 g, 0.40 mol) in Me_2SO (1 L) was placed in a three-neck flask fitted with a bypass addition

(3) (a) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill, Inc.: New York, 1962, (b) Kaplan, L. In *Free Radicals*; Kochi, J., Ed.; Wiley: New York, 1973, Vol. II. (c) Norris, R. K.; Smyth-King, R. J. *J. Chem. Soc., Chem. Commun.* **1981**, 79; *Tetrahedron* **1982**, *38*, 1051; *Aust. J. Chem.* **1983**, *36*, 88–89.

(4) Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.

(5) Fowler, F. W.; Hassner, A.; Levy, L. A. *J. Am. Chem. Soc.* **1967**, *89*, 2077.

(6) Kornblum, N.; Clutter, R. J.; Jones, W. J. *J. Am. Chem. Soc.* **1956**, *78*, 4003; *Org. Synth.* **1963**, *43*, 87.

(7) If no racemization had occurred in the conversion of II to IV the nitro amine IV would have had $[\alpha]^{24}_D$ −7.96°. It seems appropriate to ascribe the racemization to the first step, i.e., II → III.

(8) It might be thought that the nitrite ions liberated when optically active II reacts with nucleophiles racemize it, and that thereby reactions employing azide, thiophenoxide, benzenesulfinate, and 2-nitropropane anions produce racemic products. This possibility is excluded on two grounds. Racemization of optically active II by sodium nitrite is much slower than the reactions of these nucleophiles with (−)-II. And, secondly, when the reaction of the levorotatory dinitro compound II with sodium azide is carried out only halfway to completion, the nitro azide III (50% yield) is again devoid of optical activity; however the recovered dinitro compound II (44% recovery) has lost none of its optical activity. Thus, it is apparent that dinitro compound II is not racemized prior to substitution.

funnel containing racemic II (44.9 g, 0.20 mol). The azide solution was thoroughly deoxygenated by passing a fast stream of nitrogen through it for 4 h while stirring. The reaction set-up was evacuated and argon was introduced. Compound II was added from the addition funnel and the resulting yellow solution was stirred for 4 days under a "light bank".[9] The reaction mixture was poured into 2400 mL of ice water layered with 500 mL of benzene and, after separating the layers, the aqueous phase was further extracted with two 600-mL portions of benzene. The combined benzene layers were washed repeatedly with water, dried (K_2CO_3), and concentrated under reduced pressure. The resulting 42.9 g of yellow oil was dissolved in hexane–benzene (7:3) and chromatographed on acid-washed alumina to give 41.1 g (94% yield) of pure nitro azide III: this pale yellow-green oil has n^{20}_D 1.5547; IR (neat) 4.77 (N_3), 6.61, 7.49 (NO_2) μm; NMR (CCl_4) δ 8.2 (d, 2 H), 7.6 (d, 2 H), 1.95 (q, 2 H), 1.7 (s, 3 H), 0.8 (t, 3 H). For analysis a small sample of the nitro azide III was short-path distilled under reduced pressure. Anal. Calcd for $C_{10}H_{12}N_4O_2$: C, 54.54; H, 5.49; N, 25.44; M_r, 220. Found: C, 54.31; H, 5.40; N, 25.61; M_r, 221.

Preparation of 2-(*p*-Nitrophenyl)-2-butylamine (IV). An all-glass diborane reduction apparatus[10] consisting of separate generator and reaction flasks was employed. The generator flask was charged with boron trifluoride etherate (187.5 g, 1.25 mol) and 2-methoxyethyl ether (150 mL) under nitrogen; diethyl ether was distilled off by brief warming on a steam bath. The reaction flask was attached and was charged with nitro azide III (30.5 g, 0.14 mol) and THF (250 mL); it was then immersed in an ice bath. To the generator flask was added dropwise over 1 h approximately two-thirds of a solution containing $NaBH_4$ (23.9 g, 0.63 mol) in 2-methoxyethyl ether (600 mL). The generator flask was gradually warmed to 70 °C over 30 min while maintaining a slow flow of nitrogen from the generator flask through the cold (0–5 °C) solution in the reaction flask. The reaction flask was warmed (46 ±1 °C) in a constant-temperature bath for 3 days. At that time more diborane was generated as before by adding the remaining one-third of the borohydride solution to the generator flask. The reaction flask was then warmed at 46 °C for an additional 3 days.

The reaction mixture was cooled in an ice bath and cautiously added to 100 g of ice. Then 100 mL of cold 12 N hydrochloric acid was carefully added and the resulting mixture was heated on a steam bath for 20 min, diluted with 1500 mL of water, and filtered to remove a white solid. The aqueous filtrate was then extracted with three 50-mL portions of benzene and the combined benzene solutions were dried (K_2CO_3) and then concentrated in vacuo. In this way 4.5 g of the impure starting azide III was obtained.

The above aqueous filtrate was layered with 100 mL of benzene and made basic by the addition of cold 50% aqueous NaOH. The layers were separated and the aqueous phase was twice extracted with 100-mL portions of benzene. The combined benzene layers were washed with three 50-mL portions of water, dried (K_2CO_3), and concentrated under reduced pressure to give 22.9-g (0.12 mol, 84% yield) of nitro amine IV as a yellow oil. By VPC and NMR this material was nearly pure and was suitable for resolution (vide infra).

When the crude IV was allowed to stand it slowly crystallized. After 2 days, these crystals were washed with several portions of hexane and dried in vacuo to give 16.21 g of IV. The hexane extracts were combined, concentrated, and distilled under reduced pressure (bp 103–107 °C at 0.25 Torr) to give an additional 2.17 g of pure IV. Both batches of IV were combined to give 18.38 g (70% yield) of pure 2-(*p*-nitrophenyl)-2-butylamine (IV): mp 40–41 °C; IR (melt) 2.93 (NH_2), 6.61, 7.48 (NO_2) μm; NMR (CCl_4) δ 8.1 (d, 2 H), 7.6 (d, 2 H), 1.75 (q, 2 H), 1.45 (s, 3 H), 1.35 (varies with concentration) (br s, 2 H), 0.75 (t, 3 H). For analysis a small sample of nitro amine IV was short-path distilled under reduced pressure. Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.27; N, 14.42; M_r, 194. Found: C, 61.95; H, 7.45; N, 14.52; M_r, 196.

Resolution of 2-(*p*-Nitrophenyl)-2-butylamine (IV). To a hot (70 °C) solution containing 38.1 g (0.254 mol) of *d*-tartaric acid in 600 mL of water was added 44.99 g (0.231 mol) of crude nitro amine IV (vide supra). The mixture was heated on a steam bath until a clear solution was attained. The solution when treated with Darco, filtered, and allowed to cool to room temperature precipitated white crystals. These crystals were collected, recrystallized three times from water, and dried in vacuo to give 11.99 g (0.0349 mol) of acid *d*-tartrate salts. Anal. Calcd for $C_{14}H_{20}N_2O_8$: C, 48.83; H, 5.86; N, 8.14. Found: C, 48.76; H, 5.85; N, 8.05.

The entire 11.99 g of salts was treated with 100 mL of 5% aqueous NaOH. The resulting mixture was extracted with three 20-mL portions of benzene and the combined extracts were washed with 20 mL of 5% aqueous NaOH followed by two 20-mL portions of water. This benzene solution was dried (K_2CO_3) and then the solvent was removed under reduced pressure to give 6.74 g (0.0347 mol) of pure (VPC and NMR) levorotatory 2-(*p*-nitrophenyl)-2-butylamine (IV): mp 40–56 °C; α −1.17° (1 dm); $[\alpha]^{26}_D$ −7.96° (*c* 14.7, ethanol).

Preparation of Levorotatory 2-(*p*-Nitrophenyl)-2-nitrobutane (II). To a solution of 1.9941 g (10 mmol) of the levorotatory nitro amine IV, $[\alpha]^{26.4}_D$ −4.79° (*c* 14.4, ethanol) in 80 mL of distilled acetone were added 20 mL of distilled water and 1.50 g of magnesium sulfate (dried powder). Using a mechanical stirrer, vigorous stirring was instituted and maintained during the entire course of the oxidation. The reaction flask was cooled in an ice bath for 15 min and then over a period of 1 h, 9.3614 g (59.2 mmol) of potassium permanganate was added in small portions. A water bath maintained at 15 °C was then exchanged for the ice bath and the reaction mixture was stirred for 6 days at 15 °C after which the water bath was removed and stirring continued an additional day at room temperature. The reaction mixture was then cooled in an ice bath and treated with 20 mL of benzene followed by 60 mL of 15% aqueous sodium bisulfite. The resulting mixture was filtered to remove manganese dioxide and to the filtrate was added 10 mL of 6 N hydrochloric acid. The benzene phase was then separated and the aqueous layer extracted with two 20-mL portions of benzene. The combined extracts were washed twice with 30-mL portions of 5% aqueous HCl and twice with 30-mL portions of water, dried (K_2CO_3), and concentrated under reduced pressure to give 0.9731 g of a yellow oil that by NMR and VPC was a mixture of three compounds. This mixture, when chromatographed on an acid-washed alumina column gave three compounds. The first (eluted by benzene–hexane 1:1) was an oil that by VPC and NMR was pure II. On seeding this oil with racemic II, crystals of levorotatory 2-(*p*-nitrophenyl)-2-nitrobutane (II) formed: 1.085 g (49% yield); mp 38–44 °C; α −0.38° (1 dm); $[\alpha]^{26.3}_D$ −2.70° (*c* 14.1, benzene). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.40; N, 12.49. Found: C, 53.45; H, 5.32; N, 12.25.

The second compound (eluted with benzene) was *p*-nitroacetophenone: 0.13 g (7% yield); it was identified by NMR and IR; mp 76.5–78.5 °C; the mp when mixed with authentic *p*-nitroacetophenone (mp 78–80 °C) was 77.5–79 °C.

The third compound (eluted with ether) was 2-(*p*-nitrophenyl)-2-butanol:[12] 0.32 g (17% yield); α +0.02 ± 0.02° (1 dm); $[\alpha]^{22.7}_D$ 0° (*c* 15.0, CCl_4); n^{20}_D 1.5532; IR (film) 2.75–3 (OH), 6.60, 7.47 (NO_2) μm; NMR (CCl_4) δ 8.1 (d, 2 H), 7.6 (d, 2 H), 2.2 (varies with concentration (s, 1 H), 1.8 (q, 2 H), 1.55 (s, 3 H), 0.8 (t, 3 H). Anal. $C_{10}H_{13}NO_3$: for $C_{10}H_{13}NO_3$: C, 61.52; H, 6.71; N, 7.18; M_r, 195. Found: C, 61.71; H, 6.61; N, 7.06; M_r, 201.

In a separate experiment, nitro amine IV, $[\alpha]^{26}_D$ −7.96 (*c* 14.7, ethanol) was oxidized to pure (VPC, NMR, and IR) dinitro compound II which, with seeding, only partially solidified at room temperature: α −0.67° (1 dm); $[\alpha]^{22}_D$ −4.22° (*c* 15.9, benzene). Anal. Calcd for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.40. Found: C, 53.81; H, 5.47.

(9) This "light bank" consisted of four 20-W fluorescent tubes arranged in a square configuration 17 cm on edge.

(10) Zweifel, G.; Brown, H. C. *Org. React. (N.Y.)* **1963**, *13*, 1.

(11) (a) Kornblum, N.; Carlson, S. C.; Widmer, J.; Fifolt, M. J.; Newton, B. N.; Smith, R. G. *J. Org. Chem.* **1978**, *43*, 1397. (b) Wade, P. A. Ph.D. dissertation, Purdue University, 1973, p 32.

(12) Permanganate oxidation of tertiary carbinamines provides a general method for the synthesis of tertiary nitroparaffins in excellent yields;[6] the only recorded failure involves triphenylmethylamine which gives triphenylcarbinol as the sole product. Product distribution in the permanganate oxidation of nitro amine IV is temperature-dependent. Above 15 °C larger amounts of 2-(*p*-nitrophenyl)-2-butanol are formed at the expense of dinitro compound II (the amount of *p*-nitroacetophenone formed remains constant).

Reactions of Levorotatory 2-(*p*-Nitrophenyl)-2-nitrobutane (II). (A) With Sodium Azide. (a) Stereochemistry after 50% Reaction. A deoxygenated solution was prepared[11] containing 0.39 g (6.0 mmol) of sodium azide[2] and 0.673 g (3.01 mmol) of dinitro compound II ($[\alpha]^{22}_D$ −4.22) in 30 mL of HMPA. This solution was stirred in room light for 25 min and was then worked up by being poured into 300 mL of H_2O layered with 125 mL of benzene. After separating, the aqueous phase was further extracted with two 75-mL portions of ether. The combined organic extracts were washed with five 200-mL portions of H_2O and then dried ($MgSO_4$) and concentrated under reduced pressure. The crude product (0.663 g; α −0.40° (2 dm); $[\alpha]^{23}_D$ −1.69° (*c* 11.9, benzene)) was chromatographed on an acid-washed alumina column. Elution by a 30% benzene–70% hexane solution gave, after concentration, 0.331 g (50% yield) of pure (VPC, NMR, IR) nitro azide III: α 0.00 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.0° (*c* 14.3, benzene).

Further elution of the column with benzene gave, after concentration, 0.296 g (44% recovery) of pure (VPC, NMR, IR) II as an oil: α −1.34 ± 0.02° (2 dm); $[\alpha]^{24}_D$ −4.22° (*c* 15.9, benzene).

A duplicate reaction gave identical results.

(b) Stereochemistry after Complete Reaction. A deoxygenated solution was prepared containing 0.39 g (6.0 mmol) of sodium azide and 0.667 g (2.98 mmol) of the dinitro compound II ($[\alpha]^{22}_D$ −4.22°) in 30 mL of HMPA. The solution was stirred in room light for 2 h and was then worked up as in (a) to give 0.658 g (99% yield) of pure (VPC, NMR, IR) 2-(*p*-nitrophenyl)-2-butyl azide (III): α 0.00 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.0° (*c* 11.8, benzene). This nitro azide III (0.645 g, 2.93 mmol) was reduced to the nitro amine IV with 7.0 mL of 3 M diborane in THF solution. After 5 days at 45 °C, the resulting solution was worked up as described above for the preparation of IV. A yellow oil that was pure nitro amine IV, except for a trace of impurities (VPC and NMR), was obtained: 0.378 g (67% yield); α 0.00 ± 0.03° (1 dm); $[\alpha]^{23}_D$ 0° (*c* 15.2, ethanol). This oil solidified on seeding with racemic IV to give, after hexane washing, white crystals of pure (VPC, NMR, IR) IV: mp 40–41 °C; α 0.00 ± 0.02° (1 dm); $[\alpha]^{24}_D$ 0.0° (*c* 14.8, ethanol).

(B) With Sodium Thiophenoxide. (a) Isolation. A deoxygenated solution[11] was prepared that contained 0.78 g (6.0 mmol) of sodium thiophenoxide[4] and 0.648 g (2.89 mmol) of the racemic dinitro compound II dissolved in 30 mL of Me_2SO. After 45 min, the blackish yellow solution was poured into 300 mL of H_2O and 125 mL of benzene in a separatory funnel. The aqueous phase was isolated and extracted twice with 75-mL portions of ether. The combined organic extracts were washed with three 150-mL portions of H_2O, dried ($MgSO_4$), and concentrated to a pale greenish yellow oil (0.885 g) which, when chromatographed on a silica gel column and eluted with benzene–hexane (3:7), gave 0.007 g of diphenyl disulfide: white crystals mp and mp of a mixture with an authentic sample 57.5–59 °C.

Further elution with benzene gave 0.824 g (99% yield) of 2-(*p*-nitrophenyl)-2-butyl phenyl sulfide (V) as an oil: IR (film) 6.60, 7.48 (NO_2) μm; NMR (CCl_4) δ 8.1 (d, 2 H), 7.4 (d, 2 H), 6.95–7.3 (m, 5 H), 1.8–2.4 (m, 2 H), 1.6 (s, 3 H), 0.85 (t, 3 H). Anal. Calcd for $C_{16}H_{17}NO_2S$: C, 66.88; H, 5.96, N, 4.88; S, 11.14. Found: C, 66.96; H, 6.06; N, 4.85; S, 10.94.

(b) Stereochemistry. A deoxygenated solution[11] was prepared that contained 0.26 g (2.0 mmol) of sodium thiophenoxide[4] and 0.223 g (1.00 mmol) of dinitro compound II ($[\alpha]^{26}_D$ −4.22°) in 10 mL of Me_2SO. The solution was stirred in room light for 30 min and was then worked up to give an oil: 0.289 g; α −0.01 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.00° (*c* 12.9, benzene).

This crude oil was chromatographed on silica gel to give 0.003 g of diphenyl disulfide, mp 57.5–59 °C, and 0.249 g (85% yield) of pure (VPC, NMR, IR) nitro sulfide V: α −0.01 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.0° (*c* 11.3, benzene).

A duplicate experiment gave similar results.

(C) With Sodium Benzenesulfinate. (a) Isolation. A deoxygenated solution[11] was prepared that consisted of 0.34 g (2.0 mmol) of sodium benzenesulfinate and 0.223 g (1.00 mmol) of the racemic dinitro compound II dissolved in 20 mL of HMPA. This solution, which was deep yellow, was stirred for 2 h in the light bank[13] and was then worked up to give 0.323 g (100% yield) of 2-(*p*-nitrophenyl)-2-butyl phenyl sulfone (VI) as a pale yellow solid: mp 134.5–137.5 °C. A portion of this sulfone was recrystallized three times from CCl_4: white crystals, mp 137.2–137.5 °C; IR (KBr pellet) 6.60, 7.48 (NO_2) μm: NMR ($CDCl_3$) δ 8.2 (d, 2 H), 7.5 (d) on 7.45 (s) [total 7 H], 1.95–3.0 (m, 2 H), 1.8 (s, 3 H), 0.8 (t, 3 H). Anal. Calcd for $C_{16}H_{17}NO_4S$: C, 60.18; H, 5.37; N, 4.39; S, 10.02; M_r, 319. Found: C, 60.21; H, 5.61; N, 4.37; S, 10.10; M_r, 322.

(b) Stereochemistry. A deoxygenated solution[11] was prepared that contained 0.34 g (2.0 mmol) of sodium benzenesulfinate and 0.224 g (1.00 mmol) of dinitro compound II ($[\alpha]^{22}_D$ −4.22°) in 20 mL of HMPA. This solution was stirred for 70 min in the light bank[13] and was then worked up to give 0.312 g of a yellow solid: mp 134.5–137.5 °C; α 0.00 ± 0.03° (1 dm); $[\alpha]^{24}_D$ 0° (*c* 14.3, benzene). This crude product was chromatographed on an acid-washed alumina column. Elution with benzene gave 0.008 g (4% recovery) of VPC-pure dinitro compound II as an oil. Continued elution with ether gave 0.301 g (95% yield) of pure (VPC, NMR, IR) sulfone VI: white crystals, mp 137–137.5 °C; racemic sulfone VI has mp 137–137.5 °C; α −0.01 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.0° (*c* 13.8, benzene).

A duplicate experiment gave similar results.

(D) With the Lithium Salt of 2-Nitropropane. (a) Isolation. A deoxygenated solution[11] was prepared that contained 1.44 g (15.0 mmol) of the lithium salt of 2-nitropropane[2] and 0.676 g (3.01 mmol) of racemic II in 30 mL of HMPA. The deep red solution was stirred in the light bank[13] for 3 h. Workup gave 0.745 g of a pale yellow solid: mp 86–92 °C. This solid was chromatographed on a acid-washed alumina column. Elution with benzene gave 0.654 g (82% yield) of the carbon alkylate (VII), a white solid: mp 94–95 °C. A portion of the alkylate was recrystallized from CCl_4 and then sublimed: mp 96.5–97.5 °C; IR (KBr pellet) 6.65, 7.48 (NO_2) μm; NMR ($CDCl_3$) δ 8.2 (d, 2 H), 7.45 (d, 2 H), 1.7–2.6 (m, 2 H), overlapping at 1.5–1.55 (s, 3 H, and s, 6 H), 0.7 (t, 3 H). Anal. Calcd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N, 10.52; M_r, 266. Found: C, 58.66; H, 7.07; N, 10.39; M_r, 273.

Further elution of the column with methanol gave 0.036 g (6% yield) of yellow, but otherwise pure (VPC, NMR, IR) 2-(*p*-nitrophenyl)-2-butanol[2,12] (vide supra).

(b) Stereochemistry. A deoxygenated solution[11] that contained 0.48 g (5.0 mmol) of the lithium salt of 2-nitropropane and 0.226 g (1.01 mmol) of dinitro compound II ($[\alpha]^{22}_D$ −4.22°) in 10 mL of HMPA was prepared. This solution was stirred in the light bank[13] for 3.5 h and was then worked up to give 0.256 g of a yellow solid: mp 87–92 °C; α +0.01 ± 0.02° (1 dm); $[\alpha]^{24}_D$ 0.0° (*c* 12.0, benzene).

This crude product was chromatographed on an acid-washed alumina column. Elution with benzene gave 0.210 g (78% yield) of pure (NMR, IR) carbon alkylate VII: mp 94–95 °C; racemic VII has mp 94–95 °C; α −0.012 ± 0.02° (2 dm); $[\alpha]^{24}_D$ 0.0° (*c* 9.8, benzene). Further elution of the column with methanol gave 0.012 g (6% yield) of yellow, but otherwise pure (VPC) 2-(*p*-nitrophenyl)-2-butanol.[2,12]

A duplicate experiment gave similar results.

Sodium Nitrite Induced Racemization of Levorotatory 2-(*p*-Nitrophenyl)-2-nitrobutane (II). A deoxygenated solution[11] was prepared containing 0.14 g (2.0 mmol) of sodium nitrite and 0.227 g (1.01 mmol) of II, $[\alpha]^{24}_D$ −2.60° (*c* 13.5, benzene), in 10 mL of HMPA. This solution was stirred for 3.5 h in room light and then worked up to give 0.229 g (100% recovery) of pure (VPC, NMR, IR) dinitro compound II as an oil: α −0.24° (1 dm); $[\alpha]^{26}_D$ −1.92° (*c* 13.5, benzene).

Two deoxygenated solutions each containing 0.14 g (2.0 mmol) of sodium nitrite and 0.23 g (1.0 mmol) of dinitro compound II, $[\alpha]^{22}_D$ −4.22° (*c* 15.9, benzene), in 10 mL of HMPA were prepared. These solutions were stirred for 13.3 h and then worked up separately to give 0.23 g (100% recovery) each of pure (VPC, IR, NMR) II: α −0.28°; α −0.29 ± 0.02° (1 dm); $[\alpha]^{24}_D$ −1.8° (*c* 15.8, benzene).

Optical Stability of Levorotatory 2-(*p*-Nitrophenyl)-2-nitrobutane (II). A deoxygenated solution containing 0.242 g (0.99 mmol) of II ($[\alpha]^{26}_D$ −2.7°) in 11 mL of HMPA was stirred

(13) This "light bank", in contrast to the one described in ref 9, consisted of two 20-W fluorescent tubes mounted horizontally 9 cm apart.

in room light for 3.5 h and then worked up to give 0.238 g (98% recovery) of pure (VPC, NMR) dinitro compound II: α −0.35 ± 0.02° (1 dm); $[\alpha]^{26.2}_D$ −2.5° (*c* 14.3, benzene).

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Starburst Polyether Dendrimers

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The synthesis of two starburst polyether dendrimers, by a protection–deprotection scheme, is described. A bicyclic ortho ester or a dioxane is used to temporarily mask three or two hydroxyl groups, respectively. Dendrimer type I was synthesized with a pentaerythritol core and a hydroxymethyl bicyclic orthoformate as the dendrimer synthon, while in dendrimer type II, 1,1,1-tris(hydroxymethyl)ethane and a (hydroxymethyl)dioxane were used. Dendrimer type I is the most compact starburst molecule synthesized to date. No spacer groups or excess reagent are needed in the synthesis, even though all reactions occur at neopentyl positions. In just three generations, 108 functionalities are present in the exterior layer. The size of these molecules calculated from CPK models is in excellent agreement with the data obtained from size-exclusion chromatography.

The successful synthesis and characterization of starburst dendrimers have allowed precision control of space at the molecular level as a function of size, shape, and disposition of desired organic moieties.

Preliminary accounts of the synthesis and concept of the starburst topology are described in earlier papers.[1-3] More recently, considerable theoretical[4,5] and synthetic interest has evolved, wherein Newkome and co-workers have synthesized similar molecules, which they refer to as "cascade molecules".[6,7]

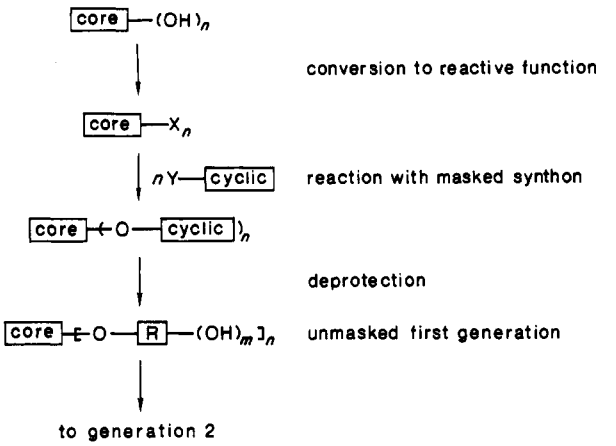
Starburst dendrimers are constructed from various initiator cores, upon which concentric, branched layers (generations) are built up that follow geometric progressions. The final exterior layer allows introduction of a variety of terminal moieties that reside on the surface of the dendrimer. The shape of the core, as well as its multiplicity (N_c) and that of the repeating unit (N_r), determines the general shape and ultimately the size of the dendrimer. The number of functionalities in each generation can be calculated by using the following formula:

$$\text{number of terminal units} = N_c(N_r)^G$$

in which G = number of generations.

Previously, the synthesis of starburst polyamidoamine dendrimers with a core multiplicity $N_c = 3$ and repeating unit multiplicity $N_r = 2$ has been reported.[1] In this study, we describe the synthesis of highly branched starburst polyether dendrimers, whose core is pentaerythritol (PE, $N_c = 4$) and the repeating unit is a pentaerythritol ether ($N_r = 3$). A two-dimensional representation of the two first generations of these two cases is shown in Figure 1, parts A and B, respectively. In addition, an account is given of efforts to synthesize starburst polyethers derived from a tris(hydroxymethyl)ethane core (THE, $N_c = 3$) with a repeating unit with a multiplicity $N_r = 2$.

Scheme I[a,b]



[a] Route A: X = electrophile; Y = nucleophile. Route B: X = nucleophile; Y = electrophile. [b] $n = N_c$, $m = N_r$.

Dendrimer Synthon Strategy. The synthesis of polyamidoamine dendrimers was based upon two consecutive reactions to build each generation in which the second reaction reintroduced the functional group on which the first reaction could take place. Exhaustive Michael addition of an amine with excess methyl acrylate was followed by exhaustive amidation of the resulting ester with an excess of diamine. The branching junctures were built-in so that the number of functionalities increased in each generation. This scheme led to rather loosely spaced dendrimers in that about five-carbon chains were present

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