Relative Energy Levels of the Two Transition States in the Nitration of Derivatives of 1,3,5-Trineopentylbenzene

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By competitive nitration, with nitric acid in nitromethane, of deuteriated and non-deuteriated materials at 0°C the following isotopic rate ratios $k_D/k_H$ were found: for 1,3,5-trineopentylbenzene $1.057 \pm 0.005$, for 2-methyl-1,3,5-trineopentylbenzene $0.999 \pm 0.009$, for 2,4-dimethyl-1,3,5-trineopentylbenzene $1.015 \pm 0.004$, for 2-bromo-1,3,5-trineopentylbenzene $1.041 \pm 0.004$, for 2,4-dibromo-1,3,5-trineopentylbenzene $0.872 \pm 0.010$, for 2-bromo-4-iodo-1,3,5-trineopentylbenzene $0.692 \pm 0.008$ and for 2,4-dibromomesitylene $1.017 \pm 0.006$.

The most likely explanation of the above results seems to be the two-step reaction mechanism generally accepted for nitration. For less hindered compounds the second transition state is at a considerably lower energy level than the first, and only when steric crowding becomes very strong does it surpass the latter.

Appreciable kinetic hydrogen isotope effects in aromatic nitration have been found with derivatives of 1,3,5-tri-tert-butylbenzene and with anthracene. To explain these effects, it was assumed that the steric requirements of the reactions were such that the second step was rate-determining.

It was considered of interest to study the nitration of derivatives of 1,3,5-trineopentylbenzene in order to see whether the steric requirements are large enough to cause kinetic isotope effects owing to a rate-determining second reaction step. In this paper the results of these investigations are reported.

The substrates chosen were 1,3,5-trineopentylbenzene (TNB), 2-methyl-1,3,5-trineopentylbenzene (MeTNB), 2,4-dimethyl-1,3,5-trineopentylbenzene (Me₂TNB), 2-bromo-1,3,5-trineopentylbenzene (BrTNB), 2,4-dibromo-1,3,5-trineopentylbenzene (Br₂TNB), 2-bromo-4-iodo-1,3,5-trineopentylbenzene (BrI₂TNB) and 2,4-dibromomesitylene (Br₂M). The latter compound was included to make possible a comparison between Br₂TNB and a compound having substituents with approximately the same electronic effects as Br₂TNB, but with different steric requirements.

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EXPERIMENTAL

The NMR spectra were recorded on a Varian A 60 spectrometer. About 10 % by weight solutions in carbon tetrachloride were used at a temperature of 35°C. The chemical shifts are reported in ppm downfield from tetramethylsilane as internal standard.

The IR spectra were recorded on a Beckman IR 9 spectrophotometer, with potassium bromide pellets. The absorption maxima are reported in cm⁻¹ and the intensities are indicated as weak (w), medium (m), strong (s) or very strong (vs).

All deuterium analyses were carried out on an AEI MS 902 mass spectrometer, using the direct inlet system. The following conditions were used: inlet temperature 0°C, ion chamber temperature 100°C, electron energy 70 eV, accelerating voltage 8 kV and emission 100 μA. The isotopic compositions were determined by measuring the intensities for the parent peaks of the deuteriated and non-deuteriated molecules. It was checked that loss of hydrogen giving rise to disturbing peaks did not occur. The ratio between the masses of interest was calculated and set on the instrument. One of the peaks was tuned in and, simply by switching, the other one could be tuned in with a very short time lag. This was done in order to avoid errors due to a decrease in intensity caused by evaporation of the sample. The intensities were measured at the collector galvanometer. At least 30 measurements were made, and the median value of the composition was finally calculated. The correction for the natural abundance of isotopes was made by repeating the measurements with non-deuteriated material. The standard deviation was found to be 0.1 mol %. The accuracy of the determinations was checked by measuring the isotopic content of weighed mixtures of TNB and TNB-d₄. The isotopic compositions determined by mass spectrometry agreed with the calculated ones within 1 mol %.

The mass spectra (MS) for identification were recorded on the same AEI MS 902 spectrometer, using the same conditions as for the deuterium analyses. The intensities of the peaks are reported in parentheses as percentages of the base peak, and only the most abundant peaks are reported together with the parent peaks and the isotope peaks corresponding to them.

The gas chromatographic (GLC) determinations were performed on a Perkin-Elmer F11 gas chromatograph, fitted with a hot wire detector. The outer diameter of the column used was 1/8 inch and the length 2 m. The stationary phase was 3 % of SE-30 silicon gum rubber on Gaschrom Q 100—120 mesh and the flow rate of helium was 20 ml/min. The areas of the peaks were determined with a Perkin-Elmer D2 integrator. In order to check the reliability of the gas chromatographic determinations, calibration mixtures were made up in every case. The gas chromatograph gave ratios of peak areas equal to the molar ratios in each case. For these determinations, the standard deviation was found to be 0.5 mol %.

The melting points (m.p.) were determined on a Koehler micro hot stage.

For adsorption chromatography either Merck neutral 0.05—0.2 mm silica gel with activity 2—3 or Fluka type 507 C neutral aluminium oxide with activity 1 was used.

The anhydrous silver perchlorate used was stored over phosphorus pentoxide. The deuteriated sulphuric acid used was CIBA 96—98 %, density 1.86 g/cm³, > 99 % deuterium. The deuterium oxide used was CIBA 99.75 %, deuterium. The deuteriostiboronic acid used was prepared according to a method described by Márton. The 90 % nitric acid used was prepared by mixing proper amounts of 100 % nitric acid and 65 % nitric acid, both of analytical grade. Fisher's certified nitromethane with a specified water content of 0.01 % was used. All other chemicals were of reagent grade and were used without further purification.

All substances were analyzed with GLC and the amounts of impurities never exceeded 0.5 %, as could be estimated from GLC peak heights.

1,3,5-Trineopentylbenzene (TNB) was prepared as described by Martinson and Márton. The 2-Methyl-1,3,5-trineopentylbenzene (MeTNB) was prepared by a two-step procedure. TNB was chloromethylated and the product, 2-chloromethyl-1,3,5-trineopentylbenzene (CICH₂TNB), was reduced with lithium tetrahydridoaluminate. MeTNB was originally prepared by Dr. Per Martinson in this way.

TNB (8.64 g, 30 mmol), 11.2 ml (12.1 g, 150 mmol) of chloromethyl methyl ether, 0.35 ml (0.78 g, 3 mmol) of tin(IV) chloride and 3.4 ml (5.1 g, 30 mmol) of silicon tetrachloride were added to 50 ml of carbon disulphide. The mixture was stirred at room temperature and the reaction was followed by GLC. After 9 days, the reaction mixture

was poured into ice water and filtered. The organic phase of the filtrate was separated off, and the water phase was extracted with carbon disulphide. The combined organic phases were washed with water until neutral and dried with magnesium sulphate. After evaporation of the solvent, the CICH$_2$TNB was recrystallized from nitromethane. The yield was 8.6 g (55 %). M.p. 65.5 – 67°C.

NMR: 6.81 (singlet, 2 H, aromatic), 4.82 (singlet, 2 H, CH$_2$Cl), 2.70 (singlet, 4 H, CH$_4$), 2.43 (singlet, 2 H, CH$_3$), 0.95 (singlet, 18 H, C(CH$_3$)$_3$), 0.92 (singlet, 9 H, C(CH$_3$)$_3$). IR: 2960vs, 2865s, 1608m, 1580w, 1481s, 1468m, 1429g, 1395m, 1364s, 1331w, 1280w, 1258m, 1235s, 1200m, 1157w, 1122w, 914w, 882m, 840w, 767m, 692s, 654m, 542m. MS: 41(55), 43(25), 57(100), 61(36), 71(18), 120(15), 132(25), 133(11), 134(15), 168(18), 173(13), 187(13), 188(30), 189(13), 224(16), 244(23), 245(18), 336(5.2), 337(0.87), 338(1.15).

CICH$_2$TNB was reduced in the following way. In a nitrogen atmosphere, 0.5 g (13 mmol) of lithium tetrahydridoaluminate was slurried in 30 ml of tetrahydrofuran. CICH$_2$TNB (2.1 g, 6.2 mmol) in 15 ml of tetrahydrofuran was added and the mixture refluxed for 4 h. After the mixture was cooled in ice water, 0.5 ml of water, 0.5 ml of 10 % by weight sodium hydroxide in water, and 1.5 ml of water were added in that order. The mixture was filtered and the precipitate washed with tetrahydrofuran. The solvent was evaporated from the liquid phase and the residue was dissolved in diethyl ether. The solution was washed with water and dried with magnesium sulphate. After evaporation of the solvent, the product was decolorized by adsorption chromatography (aluminium oxide, hexane) and recrystallized from nitromethane. The yield was 1.4 g (75 %), m.p. 44 – 47°C.

NMR: 6.73 (singlet, 2 H, aromatic), 2.58 (singlet, 4 H, CH$_2$), 2.40 (singlet, 2 H, CH$_3$), 2.23 (singlet, 3 H, CH$_3$), 0.92 (singlet, 27 H, C(CH$_3$)$_3$). IR: 2955vs, 2908s, 2865s, 1610w, 1578w, 1480s, 1466s, 1394m, 1364s, 1320w, 1282w, 1238s, 1200m, 1161w, 1064w, 1025w, 923w, 911w, 828m, 767m, 750m, 646w, 624w, 550w. MS: 41(23), 43(18), 57(78), 71(15), 133(19), 134(52), 189(50), 190(56), 245(100), 246(59), 287(19), 302(36.1), 303(8.9), 304(1.0).

2,4-Dimethyl-1,3,5-trineopentylbenzene (Me$_2$TNB) was prepared by chloromethylation of MeTNB and subsequent reduction of the product by lithium tetrahydridoaluminate.

Me$\text{ TNB (6.6 g, 22 mmol)}$ was dissolved in 30 ml of carbon disulphide and 8.2 ml (8.9 g 110 mmol) of chloromethyl methyl ether, 0.26 ml (0.37 g, 2.2 mmol) of tin(IV) chloride, and 2.5 ml (3.7 g, 22 mmol) of silicon tetrachloride were added. The mixture was kept at 50°C and the reaction was followed by GLC. The reaction was fairly slow and after 4 days, 1.04 ml (2.3 g, 8.8 mmol) of tin(IV) chloride and 8.2 ml (8.9 g, 110 mmol) of chloromethyl methyl ether were added. The reaction mixture was kept at the same temperature for additional 4 days and it was then poured into 100 ml of water and filtered. The organic layer was separated off and the water layer extracted with water until neutral and dried with magnesium sulphate. After evaporation of the solvent, the product weighed 7 g and it was used in the next step without further purification.

The reaction was performed in the same way as described for CICH$_2$TNB. The raw product amounted to 5.1 g. Discoloration was effected by adsorption chromatography (aluminium oxide, hexane), and after several recrystallizations from nitromethane, 2.7 g (39 % from Me$_2$TNB) of pure Me$_2$TNB was obtained. M.p. 73 – 75°C.

NMR: 6.75 (singlet, 1 H, aromatic), 2.79 (singlet, 2 H, CH$_2$), 2.57 (singlet, 4 H, CH$_3$), 2.26 (singlet, 6 H, CH$_3$), 0.93 (singlet, 27 H, C(CH$_3$)$_3$). IR: 2950vs, 2860s, 1480s, 1391m, 1362s, 1234m, 1200m, 1155w, 1062w, 1025w, 915w, 889w. MS: 41(25), 43(17), 57(47), 147(12), 203(21), 204(100), 259(90), 260(31), 301(7), 316(25.0), 317(6.5), 318(1.0).

2-Bromo-1,3,5-trineopentylbenzene (Br$\text{ TNB}$) was synthesized according to a modification of a method described by Márton and Martinson.

TNB (1.9 g, 6.6 mmol) was dissolved in 35 ml of N,N-dimethylformamide, 1.8 ml (56 g, 35 mmol) of bromine in 5 ml of the same solvent was added and the mixture was kept at room temperature for 2 h in the dark. Completion of reaction was verified by GLC. The reaction mixture was added to a solution of 10 g of sodium sulphite and 10 g of sodium carbonate in 100 ml of water, extracted with cyclohexane, washed with water, and dried with magnesium sulphate. After the solvent was evaporated, the product was recrystallized from nitromethane. The yield was 2.0 g (83 %). M.p. 49 – 52.5°C. Reported 50.0 – 50.5°C. NMR and IR data agreed with the reported ones. Dr. Martinson has given the information that the reported IR spectrum is misprinted. 1271m should be read 1257m. MS: 41(10), 43(10), 57(100), 198(25), 200(25), 264(28), 266(27), 301(14), 312(14), 351(9), 353(5), 366(11.6), 367(2.7), 368(11.4), 369(2.7), 370(0.3).

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2,4-Dibromo-1,3,5-trineopentylbenzene (Br₄TNB) was prepared according to a modified version of the synthesis described by Márton and Martinson.⁴

TNB (3.0 g, 10.4 mmol) was dissolved in 70 ml of carbon tetrachloride, 170 mg of iron powder, and 1.3 ml (4.0 g, 25 mmol) of bromine in 17 ml of carbon tetrachloride were added. The reaction mixture was stirred at room temperature for 3 h in the dark and then worked up as described for the preparation of Br₂TNB. The product was recrystallized from absolute ethanol and 3.9 g (84 %) was obtained. M.p. 89 - 91°C. The reported melting point is misprinted and should be read 90.5 - 91.0°C. The last information is a private communication from Dr. Martinson. NMR and IR data agreed with the reported ones.⁶ MS: 41(48), 43(48), 57(100), 71(22), 276(32), 278(61), 280(30), 332(21), 334(41), 336(21), 388(18), 389(12), 390(32), 391(17), 392(16), 444(7.8), 445(1.7), 446(16.2), 447(3.4), 448(7.5), 449(1.6), 450(0.2).

2-Iodo-1,3,5-trineopentylbenzene (ITNB) was synthesized according to a modified form of the method described by Márton and Martinson.⁷

ITNB (2.9 g, 10.0 mmol), 2.6 g (12.5 mmol) of silver perchlorate and 0.5 ml (5.8 mmol) of 70 % perchloric acid were dissolved in 60 ml of acetic acid/dioxane 5/1 by volume and 3.3 g (13 mmol) of iodine in 65 ml of the same solvent (the iodine was dissolved by warming) was added. The reaction mixture was stirred for 1 h at room temperature and completion of reaction was verified by GLC. The reaction mixture was poured into a mixture of 20 g of sodium sulphite in 200 ml of water and 50 ml of cyclohexane. After the precipitate was filtered off, the organic phase was separated off and the water phase was extracted with cyclohexane. The combined organic phases were washed with water until neutral and dried with magnesium sulphate. The product was decolorized by adsorption chromatography (aluminium oxide, hexane) and recrystallized from nitromethane. The yield was 3.1 g (75 %). M.p. 65.5 - 68°C. Reported ⁸ 63.0 - 63.5°C. NMR and IR data agreed with the reported ones.⁹ MS: 41(22), 43(21), 57(100), 71(7), 119(9), 240(27), 302(31), 358(14), 399(5), 414(23.1), 415(5.4), 416(0.6).

2-Bromo-4-iodo-1,3,5-trineopentylbenzene (Br₂ITNB) was prepared according to a modification of the synthesis described by Márton and Martinson.⁶

ITNB (4.96 g, 12.0 mmol), 2.8 g (13.5 mmol) of silver perchlorate and 1.7 ml (20 mmol) of 70 % perchloric acid were dissolved in 100 ml of acetic acid/dioxane 5/1 by volume and 0.7 ml (2.2 g, 14 mmol) of bromine in 20 ml of the same solvent was added. The reaction mixture was stirred for 1 h at room temperature and it was checked by GLC that the reaction was complete. The work-up was performed as described for the synthesis of ITNB. After decolourisation by adsorption chromatography (aluminium oxide, hexane) and recrystallization from nitromethane, 4.6 g (78 %) was obtained. M.p. 78 - 80°C, reported ¹ 73.0 - 73.5°C. NMR and IR data agreed with the reported ones.⁸ MS: 41(19), 43(21), 57(100), 71(10), 324(19), 326(18), 380(12), 382(11), 436(13), 438(12), 477(2), 479(2), 492(10.0), 493(2.3), 494(10.0), 495(2.2), 496(0.3).

2,4-Dibromomostylylene (Br₂RM) was prepared by bromination of mesitylene with bromine in N,N-dimethylformamide.

Mesitylene (0.64 g, 5.3 mmol) was dissolved in 5 ml of N,N-dimethylformamide and 1.1 ml (3.4 g, 21 mmol) of bromine was dissolved in 5 ml of the same solvent. The solutions were cooled to 0°C and combined. The reaction mixture was stirred in the dark and allowed to warm to room temperature. After 3 h completion of reaction was verified and the same work-up procedure as described for Br₂TNB was applied. After recrystallization from nitromethane, 1.2 g (81 %) was obtained. M.p. 63 - 64°C, reported ¹ 65.5°C.

NMR: 6.94 (singlet, 1 H, aromatic), 2.60 (singlet, 3 H, CH₃), 2.31 (singlet, 6 H, CH₂). IR: 2965m, 1461m, 1384m, 1221w, 1049s, 1035s, 969s, 862m, 642s, 520w. MS: 51(26), 58(24), 59(23), 91(23), 115(33), 117(37), 118(21), 197(60), 199(59), 276(44.5), 277(9.4), 278(100.0), 279(12.4), 280(48.8), 281(5.3), 282(0.2).

Nitro compounds (for calibration and identification purposes) were prepared by nitration with nitric acid in nitromethane.

1,3,5-Trineopentyl-2-nitrobenzene (NO₂TNB) has been synthesized by Dr. Per Martinson under different nitrating conditions, and will be discussed in a forthcoming publication by him.

TNB (5.0 g, 17.4 mmol) was dissolved in 300 ml of nitromethane by warming. The solution was cooled to 0°C and a mixture of 150 ml (3.2 mol) of 90 % nitric acid and 50 ml of nitromethane, cooled to 0°C, was added. The reaction mixture was stirred at 0°C for 2 h and then poured into 500 ml of water. Concentrated aqueous ammonia was added.

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and the mixture was cooled and shaken until it became homogeneous. The solution was extracted with cyclohexane, the organic phase was washed with water until neutral and dried with magnesium sulphate. The product was decolorized by adsorption chromatography (silica gel, hexane) and recrystallized from nitromethane. The yield was 4.45 g (77 %) of pure NO₂TNB. M.p. 113 - 114°C.

NMR: 6.88 (singlet, 2 H, aromatic), 2.53 (singlet, 4 H, CH₂), 2.47 (singlet, 2 H, CH₂), 0.93 (singlet, 9 H, C(CH₃)₃), 0.90 (singlet, 18 H, C(CH₃)₃). IR: 2965 vs, 2865s, 1595m, 1540s, 1530s, 1477s, 1447m, 1391m, 1364vs, 1271m, 1237s, 1200m, 1158w, 1142w, 1087w, 915w, 880m, 832s, 786w, 753w, 740w, 668w, 600w, 548w. MS: 41(29), 43(10), 57(100), 204(42), 260(50), 277(21), 318(21), 333(5.5), 334(1.3), 335(0.2).

2-Methyl-1,3,5-trineopentyl-4-nitrobenzene (MeNO₂TNB). MeTNB (0.5 g, 1.7 mmol) was dissolved in 125 ml of nitromethane and the solution was cooled to 0°C. Nitric acid (100 ml 90 %, 2.1 mol) was added and the mixture was stirred at 0°C for 3.5 h. The work-up procedure was the same as for NO₂TNB. The product contained, as indicated by GLC, approximately equal amounts of two components. A separation by adsorption chromatography (silica gel, cyclohexane) was performed, and the products were identified as MeNO₂TNB and 1-methyl-2,4,6-trineopentyl-3,5-dinitrobenzene (MeNO₃TNB). After recrystallization from nitromethane, 0.2 g (34 %) of MeNO₂TNB was obtained. M.p. 98 - 99.5°C. After recrystallization from nitromethane, 0.3 g (45 %) of MeNO₃TNB was obtained. M.p. 121 - 123°C.

Spectral characteristics for MeNO₂TNB. NMR: 6.86 (singlet, 1 H, aromatic), 2.72 (singlet, 2 H, CH₂), 2.60 (singlet, 2 H, CH₂), 2.48 (singlet, 2 H, CH₂), 2.31 (singlet, 3 H, CH₃), 0.97 (singlet, 9 H, C(CH₃)₃), 0.90 (singlet, 18 H, C(CH₃)₃). IR: 2970vs, 2870s, 1534vs, 1480s, 1397w, 1368vs, 1239m, 1202w, 1186w, 1154w, 1068w, 1042w, 914w, 893w, 836m, 790w, 780w, 724w. MS: 41(29), 43(10), 57(85), 218(58), 274(100), 291(30), 332(18), 347(8.1), 348(1.9), 349(0.3).

Spectral characteristics for MeNO₃TNB. NMR: 2.79 (singlet, 4 H, CH₂), 2.70 (singlet, 2 H, CH₂), 2.44 (singlet, 3 H, CH₃), 0.92 (singlet, 18 H, C(CH₃)₃), 0.83 (singlet, 9 H, C(CH₃)₃). IR: 2960vs, 2915s, 2870s, 1550vs, 1478vs, 1400w, 1364vs, 1231m, 1200w, 1152m, 896w, 840s, 783w, 760w, 676w. MS: 41(20), 57(100), 263(11), 280(7), 319(3), 336(4), 377(6), 392(22), 393(0.6).

1,3-Dimethyl-2,4,6-trineopentyl-5-nitrobenzene (Me₂NO₂TNB). Me₂TNB (0.6 g, 1.9 mmol) was dissolved in 400 ml of nitromethane and the solution was cooled to 0°C. Nitric acid (50 ml 90 %, 1.1 mol) was added and the reaction mixture was stirred at 0°C for 0.5 h. The work-up procedure was the same as for NO₂TNB. After purification by means of adsorption chromatography (silica gel, hexane) and recrystallization from nitromethane the yield was 0.57 g (83 %). M.p. 133 - 134°C.

NMR: 2.82 (singlet, 2 H, CH₂), 2.07 (singlet, 4 H, CH₂), 2.34 (singlet, 6 H, CH₃), 0.98 (singlet, 9 H, C(CH₃)₃), 0.99 (singlet, 18 H, C(CH₃)₃). IR: 2965vs, 2870s, 1528s, 1477s, 1392w, 1382s, 1230m, 1200m, 1160w, 1145w, 1061w, 1022w, 896w, 829m, 787w, 734w. MS: 41(44), 43(11), 57(100), 176(12), 232(74), 249(11), 288(32), 346(11), 361(9.8), 362(2.3), 363(0.4).

2-Bromo-1,3,5-trineopentyl-4-nitrobenzene (BrNO₂TNB). BrTNB (0.4 g, 1.1 mmol) was dissolved in 160 ml of nitromethane and 50 ml (1.1 mol) of 90 % nitric acid was dissolved in 32 ml of the same solvent. The solutions were cooled to 0°C and combined. The reaction mixture was stirred for 8 h and worked up as described for NO₂TNB. The product was purified by preparative thin-layer chromatography (silica gel, hexane) and recrystallized from nitromethane. The yield was 0.3 g (66 %). M.p. 84 - 87°C.

NMR: 6.97 (singlet, 1 H, aromatic), 3.03 (singlet, 2 H, CH₂), 2.86 (singlet, 2 H, CH₂), 2.50 (singlet, 2 H, CH₂), 1.01 (singlet, 9 H, C(CH₃)₃), 0.95 (singlet, 9 H, C(CH₃)₃), 0.91 (singlet, 9 H, C(CH₃)₃). IR: 2955 vs, 2870s, 1532vs, 1478s, 1395m, 1364vs, 1260w, 1230m, 1200w, 1148w, 1086w, 1030w, 996w, 882w, 833m, 799w, 682w. MS: 41(24), 43(6), 57(100), 282(21), 284(20), 338(18), 340(18), 355(8), 357(8), 396(4), 398(4), 411(0.4), 412(0.1), 413(0.4), 414(0.1).

1,3-Dibromo-2,4,6-trineopentyl-5-nitrobenzene (Br₂NO₂TNB). Br₂TNB (0.9 g, 2.0 mmol) was dissolved in 200 ml of nitromethane, 80 ml (1.7 mol) of 90 % nitric acid was added and the reaction mixture was allowed to react at 55°C for 4 h. The work-up procedure was the same as described for NO₂TNB. The product was purified by absorption chromatography (silica gel, hexane) and recrystallized from absolute ethanol. The yield was 0.8 g (81 %), m.p. 137 - 139°C.

NMR: 3.42 (singlet, 2 H, CH₂), 3.02 (broad singlet, 4 H, CH₂), 1.09 (singlet, 9 H, C(CH₃)₃), 0.96 (singlet, 18 H, C(CH₃)₃). IR: 2960vs, 2870s, 1550s, 1478s, 1400w, 1370s, 1228m, 1202w, 1153m, 1093w, 1032w, 991w, 934w, 865m, 838m, 764w, 694w. MS: 41(19), 43(4), 57(100), 360(5), 362(9), 364(4), 377(2), 379(4), 381(2), 433(2), 435(4), 437(2), 489(0.1), 491(0.2), 493(0.1).

1-Bromo-3-iodo-2,4,6-trineopentyl-5-nitrobenzene (BrINO₂TNB). BrTNB (1.0 g, 2.0 mmol) was dissolved in 200 ml of nitromethane, 80 ml (1.7 mol) of 90 % nitric acid was added and the reaction mixture was allowed to react at 60°C for 2 h. It was then worked up as described for NO₂TNB. Two products were obtained, separated by adsorption chromatography (silica gel, hexane), and then recrystallized from nitromethane. They were identified as BrNO₂TNB and BrINO₂TNB. The yields were 0.16 g (19 %) of BrNO₂TNB and 0.40 g (37 %) of BrINO₂TNB. M. p. for BrINO₂TNB 117–118°C.

Spectral data for BrINO₂TNB: NMR: 3.62 (doublet, 2 H, CH₂), 3.15 (multiplet, 2 H, CH₂), 3.00 (multiplet, 2 H, CH₂), 1.11 (singlet, 9 H, C(CH₃)₃), 0.99 (singlet, 9 H, C(CH₃)₃), 0.97 (singlet, 9 H, C(CH₃)₃). IR: 2955vs, 2900s, 2865s, 1550s, 1477s, 1398w, 1368s, 1357s, 1225m, 1200w, 1152w, 1051w, 1033w, 989w, 865w, 839m, 694w. MS: 41(28), 43(7), 44(9), 55(4), 56(7), 57(100), 58(5), 408(7), 410(7), 425(4), 427(4), 464(3), 466(3), 481(6), 483(5), 537(0.10), 538(0.03), 539(0.12), 540(0.03).

2,4-Dibromo-6-nitromesitylene (Br₂NO₂M). Br₂M (1.2 g, 4.3 mmol) was dissolved in 100 ml of nitromethane and 50 ml (1.1 mol) of 90 % nitric acid was added. The reaction mixture was kept at 60°C for 6 h and was then worked up as described for NO₂TNB. The product was recrystallized from hexane and 1.0 g (72 %) was obtained. The crystals melted at 197–198°C, and underwent a reversible transition at 188°C.

NMR: 2.09 (singlet, 3 H, CH₃), 2.51 (singlet, 6 H, CH₂), 1.11 (singlet, 9 H, C(CH₃)₃). IR: 2930m, 1540vs, 1530vs, 1470m, 1386s, 1358s, 1108w, 1022w, 964s, 844s, 660m, 639m, MS: 43(15), 50(18), 51(40), 53(38), 65(27), 75(22), 77(29), 89(27), 91(32), 115(90), 116(66), 117(96), 118(39), 196(27), 197(34), 198(31), 199(29), 225(24), 227(23), 276(11), 278(22), 280(11), 304(52), 306(100), 308(50), 321(26), 322(3), 323(50), 324(5), 325(25), 326(3).

1,3,5-Trineopentylbenzene-2,4,6-d₃ (TNB-d₃) was prepared according to a modification of a method described by Márton.

TNB (4.0 g, 13.9 mmol) was dissolved in a mixture of 2.5 ml of carbon tetrachloride and 6.5 ml (10 g, 87 mmol) of deuter trifluoroacetic acid and equilibrated at 45°C for 2 days in a closed flask. Then the deuter trifluoroacetic acid—carbon tetrachloride mixture was distilled off. The equilibration was repeated three times, the product was decolorized by absorption chromatography (aluminium oxide, hexane) and then recrystallized from nitromethane. The yield was 3.8 g (95 %). No aromatic protons could be detected by NMR spectroscopy.

2-Methyl-1,3,5-trineopentylbenzene-4,6-d₄ (MeTNB-d₄). MeTNB (2.0 g, 6.6 mmol) was treated three times with 1.3 ml of carbon tetrachloride and 3.4 ml (5.2 g, 45 mmol) of deuter trifluoroacetic acid as described for TNB-d₄. The yield was 1.6 g (80 %) of MeTNB-d₄ with no aromatic protons detectable by NMR spectroscopy.

A mixture of 2,4-dimethyl-1,3,5-trineopentylbenzene-6-d (Me₂TNB-d) and Me₂TNB (0.4 g, 1.3 mmol) was treated with deuter trifluoroacetic acid—carbon tetrachloride as described for MeTNB. One equilibration was made and the product was a mixture of ca. 80 % Me₂TNB-d and 20 % Me₂TNB as determined by NMR spectroscopy. The yield was quantitative.

2-Bromo-1,3,5-trineopentylbenzene-4,6-d₄ (BrTNB-d₄) was prepared by bromination of TNB-d₄ according to the procedure given for BrTNB. No aromatic protons could be detected in the product by NMR spectroscopy.

2,4-Dibromo-1,3,5-trineopentylbenzene-6-d (Br₂TNB-d₄) was prepared by bromination of TNB-d₄ according to the procedure given for Br₂TNB. No aromatic protons could be detected by NMR spectroscopy.

2-Bromo-4-iodo-1,3,5-trineopentylbenzene-6-d (ITNB-d₄) was obtained by iodination of TNB-d₄ according to the procedure given for ITNB.

2-Bromo-4-iodo-1,3,5-trineopentylbenzene-6-d (ITNB-d₄) was obtained by bromination of ITNB-d₄ according to the procedure given for BrITNB. No aromatic protons could be detected by NMR spectroscopy.

Mesitylene-2,4,6-d₃, Mesitylene (10 g, 83 mmol) was mixed with 26.5 g (257 mmol) of deuterated sulphuric acid and 6.7 g (335 mmol) of deuterium oxide and the mixture was stirred at room temperature for 4 days. It was then poured into 300 ml of ice water.

The aqueous solution was extracted with carbon tetrachloride. The organic phase was washed with a 10% aqueous solution of sodium carbonate and then with water until neutral. It was finally dried with magnesium sulphate. The solvent was evaporated and the whole procedure was repeated twice. The product was finally distilled. Yield 6.0 g (59%). NMR spectroscopy indicated 98.5% deuterium in the aromatic ring.

A mixture of 2,4-dibromomesitylene-6-d (Br₂M-d) and Br₂M was prepared by bromination of a mixture of mesitylene and mesitylene-2,4,6-d₄ in the same way as described for the synthesis of Br₂M.

Competitive nitration were always carried out with recrystallized mixtures of deuteriated and non-deuteriated materials to ensure homogeneity of the substrates. The isotopic composition of the starting material was determined by mass spectroscopy (see above). After the competitive reaction the isotopic composition of the recovered unreacted starting material was determined in the same way.

All these nitrations were carried out in the same way, and the reaction with TNB/ TNB-d₄ is typical.

A mixture of TNB and TNB-d₄ (50 mg, 0.173 mmol) was dissolved in 40 ml of nitromethane, and the solution was cooled to 0°C. A mixture of 7.5 ml (160 mmol) of 90% nitric acid and 2.5 ml of nitromethane, cooled to 0°C, was added, and the reaction solution was stirred at 0°C for a time which varied between 75 and 105 min in the different experiments. The reaction was quenched by pouring the solution into 50 ml of water, concentrated aqueous ammonia was added, and the mixture was shaken until it became homogeneous. The solution was extracted with cyclohexane. The organic phase was washed with water and dried with magnesium sulphate. After the solvent was evaporated the extent of nitration was determined by GLC. The mixture of product and unreacted starting material was then separated by adsorption chromatography (silica gel, hexane).

In Table 1 data for the different competitive nitrations are summarized.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Amount of substrate</th>
<th>Amount of 90% nitric acid</th>
<th>Nitromethane</th>
<th>Reaction time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg</td>
<td>mmol</td>
<td>ml</td>
<td>mmol</td>
</tr>
<tr>
<td>TNB/TNB-d₄</td>
<td>50</td>
<td>0.173</td>
<td>7.5</td>
<td>160</td>
</tr>
<tr>
<td>MeTNB/MeTNB-d₄</td>
<td>50</td>
<td>0.165</td>
<td>7.5</td>
<td>160</td>
</tr>
<tr>
<td>Me₂TNB/Me₂TNB-d</td>
<td>50</td>
<td>0.158</td>
<td>7.5</td>
<td>160</td>
</tr>
<tr>
<td>BrTNB/BrTNB-d₄</td>
<td>50</td>
<td>0.136</td>
<td>7.5</td>
<td>160</td>
</tr>
<tr>
<td>Br₂TNB/Br₂TNB-d</td>
<td>50</td>
<td>0.112</td>
<td>30</td>
<td>640</td>
</tr>
<tr>
<td>Br₂TNB/Br₂TNB-d</td>
<td>50</td>
<td>0.102</td>
<td>15</td>
<td>320</td>
</tr>
<tr>
<td>Br₂M/Br₂M-d</td>
<td>50</td>
<td>0.181</td>
<td>7.5</td>
<td>160</td>
</tr>
</tbody>
</table>

Proof of direct nitrodeiodination of BrITNB. BrITNB-d (98% deuterium in the ring positions) was nitrated as described for the competitive nitration of BrITNB/BrITNB-d. In the product BrNO₂TNB-d the deuterium content was the same as in the starting material as determined by mass spectroscopy. This result rules out the possibility of a slow protodeiodination followed by a fast nitrodeprotonation. The possibility of protodeiodination of the product BrNO₂TNB can be excluded since the relative amounts of BrNO₂TNB and BrINO₂TNB are constant through the reaction (see next paragraph).

Determination of the relative rates of nitrodeiodination and nitrodehydrogenation of BrITNB. BrITNB was nitrated under the same conditions as for the competitive runs. Aliquots were withdrawn, worked up as described for the competitive nitrations, and analyzed with GLC. In this way, $m = k_H/k_I$, where $k_H$ and $k_I$ are the rate constants for nitrodehydrogenation and nitrodeiodination, respectively, was obtained as the molar ratio of the two products. The result was: overall extent of reaction/m: 0.25/4.24; 0.49/4.15; 0.51/4.24; 0.63/4.20; 0.73/4.15; 0.79/4.30; 0.82/4.12; 1.00/4.17. The mean value is 4.20 ± 0.08 (standard deviation).

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Nitrations of a mixture of BrITNB and BrITNB-d. To estimate the magnitude of the possible isotope effect in the nitrodeiodination of BrITNB, a mixture of BrITNB and BrITNB-d was nitrated under the same conditions as for the competitive runs. The reaction time was 22 h. The ratio of the amount of BrNO₂TNB +BrNO₂TNB-d to the amount of BrNO₂TNB, i.e. the quantity denoted by \( q \) in the calculations, was 0.275-0.005 (standard deviation) as determined by repeated GLC analyses. By means of adsorption chromatography (silica gel, hexane), BrNO₂TNB + BrNO₂TNB-d was separated from the product mixture. Mass spectroscopy gave 54.5 % BrNO₂TNB, i.e. the quantity denoted by \( z \) was 0.545 ± 0.001.

Check against hydrogen exchange. To ascertain that no hydrogen exchange accompanies the nitrations, TNB-d₄, MeTNB-d₃ and BrTNB-d₄ were nitrated as described for the competitive experiments. No aromatic protons could be detected in the products by NMR spectroscopy, indicating the absence of hydrogen exchange.

Absence of hydrogen exchange during the adsorption chromatography was proved as follows. A mixture of MeTNB and MeTNB-d₃, with known composition, was chromatographed on silica gel with hexane, and the composition was then determined by mass spectroscopy. No difference in composition could be detected.

Check against unfair competition due to high reaction rate. A necessary condition for fair competition to occur is that the mixing of reagent and substrate is not rate-determining. For the present competitive nitrations the time for mixing is completely negligible. This was proved by repeating the reactions with non-deuteriated materials under the same conditions as for the competitive runs and following the conversion. At proper time intervals aliquots were withdrawn and analyzed by GLC.

CALCULATIONS AND RESULTS

The isotope effect in nitration was determined by observing the competition between fully deuteriated (with respect to the pertinent positions) and non-deuteriated molecules, and thus the competition was purely intermolecular.

When the extent of reaction and the isotopic compositions of the starting material and the recovered unreacted starting material are known, the following equation is applicable for the determination of the isotopic rate ratio \( k_D/k_H = \frac{\{\log[y_D(1-x)/y_H']\}}{\{\log[y_H(1-x)/y_H']\}} \)

(1)

In this equation \( y_D \) and \( y_D' \) denote the fraction of deuteriated molecules in the recovered unreacted starting material and in the initial starting material, respectively. In the same way \( y_H \) and \( y_H' \) denote the corresponding fractions of non-deuteriated molecules, and \( x \) denotes the overall extent of reaction.

In the nitration of BrITNB, the nitrodehydrogenation is accompanied by nitrodeiodination, which complicates the calculation of the isotopic rate ratio. According to experimental evidence presented above (m independent of the extent of reaction) it seems legitimate to assume that the two nitrations have analogous kinetics. It is necessary to know the magnitude of the possible isotope effect in the nitrodeiodination reaction. To determine this, the following method was used.

The scheme below is applicable to the competitive reactions of BrITNB and BrITNB-d. The \( k' \)'s denote rate constants.

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\[ \text{BrITNB} \begin{cases} \frac{k_H}{k_1} \rightarrow \text{BrINO}_2\text{TNB} \\ \frac{k_1}{k_1} \rightarrow \text{BrNO}_2\text{TNB} \end{cases} \]

\[ \text{BrITNB-d} \begin{cases} \frac{k_D}{k_2} \rightarrow \text{BrINO}_2\text{TNB} \\ \frac{k_2}{k_2} \rightarrow \text{BrNO}_2\text{TNB-d} \end{cases} \]

The following equation holds:

\[ [\text{BrINO}_2\text{TNB}] = (k_H/k_1)[\text{BrNO}_2\text{TNB}] + (k_D/k_2)[\text{BrNO}_2\text{TNB-d}] \tag{2} \]

where square brackets denote concentration.

This can be rewritten in the following way:

\[
1 = \frac{k_H}{k_1} \times \frac{[\text{BrNO}_2\text{TNB}]}{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]} \times \frac{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]}{[\text{BrINO}_2\text{TNB}]} + \frac{k_D}{k_2} \times \frac{[\text{BrNO}_2\text{TNB-d}]}{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]} \times \frac{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]}{[\text{BrINO}_2\text{TNB}]} \tag{3} \]

It is now convenient to introduce the following symbols:

\[
k_H/k_1 = m \\
(k_D + k_2)/(k_H + k_1) = l \\
\frac{[\text{BrNO}_2\text{TNB}]}{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]} = z \\
\frac{[\text{BrNO}_2\text{TNB-d}]}{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]} = 1 - z \\
\frac{[\text{BrNO}_2\text{TNB}] + [\text{BrNO}_2\text{TNB-d}]}{[\text{BrINO}_2\text{TNB}]} = q \]

From eqn. (3) it is possible to derive the following expression:

\[
k_1/k_2 = \{1 + q[1 - z(m + 1)]\}/\{l(m + 1)(1 - z)q\} \tag{4} \]

The ratio \( l \) can be obtained by means of a modified form of eqn. (1):

\[
l = (k_D + k_2)/(k_H + k_1) = \{\log[y_D(1 - x)/y_D']\}/\{\log[y_H(1 - x)/y_H']\} \tag{5} \]

where \( x \) denotes the overall extent of reaction, now including both types of reaction, and the other symbols are the same as used before.

The magnitude \( l \) was determined by competitive nitration of a mixture of BrITNB and BrITNB-d with known isotopic composition and was found to be equal to \( 0.751 \pm 0.007 \) (the error is the maximum deviation from the mean). The magnitude \( m \) was determined by nitration of BrITNB and analysis of the product distribution, and the value \( 4.20 \pm 0.08 \) (the error is the standard deviation) was found (see above). The magnitudes \( l \) and \( m \) are constants and were determined by repeated experiments. Values for \( z \) and \( q \) were determined by nitration of a mixture of BrITNB and BrITNB-d. Analysis of the product distribution gave \( q = 0.275 \pm 0.005 \) (standard deviation) and analysis of the isotopic composition of the resulting nitrodeiodinated product gave \( z = 0.545 \pm \)

0.001 (standard deviation). The magnitudes \( q \) and \( z \) are covariant variables and were determined for a single experiment only. When these values are put into eqn. (4), \( k_1/k_2 = 1.0 \pm 0.1 \) is obtained. The error is the maximum error calculated from the errors of \( l \), \( m \), \( q \), and \( z \). Thus there is no isotope effect within this limit in the nitrodeiodination of BrITNB, as could perhaps have been anticipated.

Eqn. (5) with \( k_1 = k_2 \) was applied to determine the isotopic rate ratio for the nitrodeiodination. The value of \( k_D/k_H \) was calculated from the measured values of \( l \) and \( m \) by means of equation (6).

\[
k_D/k_H = [\{l(m + 1) - 1\}/m]
\]  

(6)

The results of the various calculations of the isotopic rate ratios are summarized in Table 2.

**Table 2. Summary of the various isotopic rate ratios. The errors given are the maximum deviations from the mean values. For symbols, see the text.**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>( x )</th>
<th>( y_H' )</th>
<th>( y_H )</th>
<th>( l )</th>
<th>( k_D/k_H )</th>
<th>( k_D/k_H \ mean \ value )</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNB</td>
<td>0.426</td>
<td>0.608</td>
<td>0.616</td>
<td>1.062</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNB</td>
<td>0.470</td>
<td>0.608</td>
<td>0.616</td>
<td>1.054</td>
<td>1.057 ± 0.005</td>
<td></td>
</tr>
<tr>
<td>TNB</td>
<td>0.500</td>
<td>0.608</td>
<td>0.617</td>
<td>1.056</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeTNB</td>
<td>0.401</td>
<td>0.622</td>
<td>0.623</td>
<td>1.008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeTNB</td>
<td>0.488</td>
<td>0.622</td>
<td>0.621</td>
<td>0.994</td>
<td>0.999 ± 0.009</td>
<td></td>
</tr>
<tr>
<td>MeTNB</td>
<td>0.511</td>
<td>0.622</td>
<td>0.621</td>
<td>0.994</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeOTNB</td>
<td>0.429</td>
<td>0.410</td>
<td>0.412</td>
<td>1.015</td>
<td></td>
<td>1.015 ± 0.004</td>
</tr>
<tr>
<td>MeOTNB</td>
<td>0.504</td>
<td>0.410</td>
<td>0.413</td>
<td>1.018</td>
<td></td>
<td>1.015 ± 0.004</td>
</tr>
<tr>
<td>MeOTNB</td>
<td>0.531</td>
<td>0.410</td>
<td>0.412</td>
<td>1.011</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrTNB</td>
<td>0.474</td>
<td>0.612</td>
<td>0.618</td>
<td>1.040</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrTNB</td>
<td>0.488</td>
<td>0.612</td>
<td>0.618</td>
<td>1.038</td>
<td>1.041 ± 0.004</td>
<td></td>
</tr>
<tr>
<td>BrTNB</td>
<td>0.655</td>
<td>0.612</td>
<td>0.623</td>
<td>1.045</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrTNB</td>
<td>0.453</td>
<td>0.605</td>
<td>0.587</td>
<td>0.882</td>
<td></td>
<td>0.872 ± 0.010</td>
</tr>
<tr>
<td>BrTNB</td>
<td>0.505</td>
<td>0.605</td>
<td>0.582</td>
<td>0.871</td>
<td></td>
<td>0.872 ± 0.010</td>
</tr>
<tr>
<td>BrnTB</td>
<td>0.521</td>
<td>0.605</td>
<td>0.579</td>
<td>0.862</td>
<td></td>
<td>0.862</td>
</tr>
<tr>
<td>BrnTB</td>
<td>0.286</td>
<td>0.608</td>
<td>0.555</td>
<td>0.745</td>
<td></td>
<td>0.692 ± 0.008</td>
</tr>
<tr>
<td>BrnTB</td>
<td>0.449</td>
<td>0.608</td>
<td>0.568</td>
<td>0.751</td>
<td></td>
<td>0.692 ± 0.008</td>
</tr>
<tr>
<td>BrnTB</td>
<td>0.574</td>
<td>0.608</td>
<td>0.552</td>
<td>0.758</td>
<td></td>
<td>0.692 ± 0.008</td>
</tr>
<tr>
<td>BrnM</td>
<td>0.391</td>
<td>0.518</td>
<td>0.520</td>
<td>1.016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BrnM</td>
<td>0.742</td>
<td>0.518</td>
<td>0.522</td>
<td>1.012</td>
<td>1.017 ± 0.006</td>
<td></td>
</tr>
<tr>
<td>BrnM</td>
<td>0.826</td>
<td>0.518</td>
<td>0.528</td>
<td>1.023</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

The two-step mechanism for electrophilic aromatic substitutions will be taken as a basis for the discussion.10,11

\[
\text{ArH} + \text{E}^+ \overset{1}{\underset{-1}{\rightleftharpoons}} \left\{ \text{Ar} \right\} \overset{2}{\underset{\text{base}}{\rightarrow}} \text{ArE} + \text{H}^+ (\text{base})
\]

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The following picture of the mechanism is accepted for nitration with
nitric acid of an aromatic species with no special features such as steric crowding.
The intermediate exists as a high-energy species and step 1 is rate-determining,
\textit{i.e.} the rate of step 2 is much larger than that of step \( -1 \). The attacking
electrophile is the nitronium ion and it is possible that it forms a \( \pi \)-complex
with the aromatic species in a kinetically indistinguishable pre-equilibrium.
The information that allows such a picture of the reaction mechanism to be
constructed will be mentioned in the following.

Hughes, Ingold and Reed\textsuperscript{12} studied the kinetics of nitration and proved
that the attacking species is the nitronium ion. Investigations of salt and
solvent effects on the kinetics showed that ionic charges were neither created
nor destroyed in the rate-determining step. The small solvent effects could be
rationalized by a spreading out of ionic charge in this step. These results are
in accordance with the two-step mechanism. The kinetic studies also indicated
that a ter-molecular process where proton abstraction is kinetically important
is not operative.

In order to determine whether the loss of hydrogen had any kinetic
significance or not, Melander\textsuperscript{13} introduced the isotope technique to the problem.
He nitrated various aromatic substrates and found no kinetic isotope effect.
This implies that the breaking of the carbon-hydrogen bond has not occurred
to any appreciable extent in the rate-determining transition state. It does not
show, however, whether step 1 or step 2 is rate-determining or even if there
are actually two different reaction steps. The possibility that step 2 is rate-
determining despite the lack of an isotope effect must be considered. This
situation could appear if the transition state in this step is very much like
the intermediate \( \text{ArHNO}_2^+ \). Situations like this have recently been discussed
by Melander.\textsuperscript{14} Some results concerning the transition state in nitration may
be put forward to rule out such a behaviour.

Dewar \textit{et al.}\textsuperscript{15} correlated the partial rate factors for nitration to the Dewar
reactivity number and, from the slope of the correlation line could roughly
estimate how closely the transition state in the rate-determining step re-
sembles the intermediate. It was found that, for nitration of aromatic com-
ounds, the transition state appears relatively early along the reaction path.
If, on the other hand, the rate-determining step were hydrogen abstraction,
with lack of an isotope effect as indicated above, the transition state should
have resembled the intermediate to a large extent and the slope of Dewar's
correlation line would have been quite different. It is thus justified to state
that the first step is rate-determining.

Before the two-step mechanism is accepted, a question concerning the in-
termediate ought to be considered. Is the implied intermediate a real one, \textit{i.e.}
is there actually a minimum in the potential-energy curve for the reaction, or
is the "intermediate" only a structure without stability? Melander\textsuperscript{8b,13} has
argued that if the intermediate did not exist this should mean that in the
reverse reaction (protodenitration) it would be possible to make the proton-
carbon distance equal to its final value without gaining enough energy to
balance the loss of energy caused by the stretching of the carbon-nitrogen
bond. Such a behaviour is highly improbable.

When the two-step mechanism is operating it should be possible to make

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the second step rate-determining by means of steric hindrance. If the positions ortho to the reaction site are substituted with bulky groups, the two steps in the reaction are affected differently. Since the nitro group is larger than the proton, step 2 will be retarded more than step 1, and with enough steric hindrance, step 2 will determine the overall rate. Myhre et al. found this to be the case for the nitration of derivatives of 1,3,5-tri-tert-butylbenzene.

The isotope effects found in this investigation can be correlated with the steric requirements around the reaction site. For Br₂TNB, a weak isotope effect is found. When one bromine atom is changed to an iodine, i.e. for BrI-TNB, a somewhat stronger effect is observed. When the three tert-butyl groups in Br₂TNB are changed to hydrogen atoms, i.e. for Br₂M, no appreciable isotope effect is found. For most TNB derivatives with substituents smaller than two bromine atoms, i.e. two methyl groups, one bromine and one hydrogen, or two hydrogens, only minute inverse isotope effects are found, and for one methyl and one hydrogen no measurable effect at all can be observed. The van der Waals volumes for the substituents of interest, expressed in cm³/mol, are: methyl 13.67, bromine 15.12, and iodine 19.64.

Despite their weakness, the isotope effects found for BrI-TNB and Br₂TNB are regarded as due to primary ones in a partially rate-determining second reaction step. The above good correlation to the steric requirements around the reaction site support this view. Moreover the possible effects (e.g. rehybridization, hyperconjugation, anharmonicity) that could give rise to secondary isotope effects ought to be rather insensitive to these requirements.

Electronically, 2,4-dibromomesitylene (Br₂M) should be rather similar to 2,4-dibromo-1,3,5-trineopentylbenzene (Br₂TNB), but the steric requirements should be very different. Br₂TNB shows an isotope effect, but Br₂M does not, and this indicates that steric, but not electronic effects, are responsible for the isotopic behaviour. If the observed weak isotope effects were due to a fully rate-determining, but energetically very unsymmetric, second reaction step, Br₂TNB would be expected to give a weaker effect than, for instance, Me₂TNB, because the latter compound would give less unsymmetry. (Me₂NO₂-TNB should be somewhat more basic than Br₂NO₂-TNB.)

The conclusion which can be drawn from the present work is that for the disubstituted derivatives of 1,3,5-trineopentylbenzene there seems to be a balance between the rates of step 1 and step 2. For Me₂TNB step 1 is still completely rate-determining, but, with increasing steric requirements, step 2 becomes partially responsible for the overall rate.

With a rate-determining second reaction step, the overall rate should depend on the basicity and concentration of the proton acceptor. Since the isotope effect should also depend on these variables, the same reaction medium has been chosen for all isotope effect determinations in the present investigation.

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