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Nitrodeiodination of Some Alkyl-substituted Iodobenzenes

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Some alkyl-substituted iodobenzenes, 2-iodomesitylene, 2-iodo-1,3,5-trineopentylbenzene and 2-iodo-4-methyl-1,3,5-trineopentylbenzene, were nitrated with nitric acid in nitromethane. In addition to nitrodeprotonation, direct nitrodeiodination was found to occur. When iodobenzene was nitrated, only nitrodeprotonation was observed.

The known examples of nitrodeiodination of aromatic iodo compounds involve compounds activated by hydroxy or methoxy substituents.[1,2] In the present paper we report direct nitrodeiodination of aromatics activated by alkyl groups. The compounds which were nitrated are iodobenzene (IB), 2-iodomesitylene (IM), 2-iodo-1,3,5-trineopentylbenzene (ITNB) and 2-iodo-4-methyl-1,3,5-trineopentylbenzene (IMeTNB). In a recent publication,[3] nitrodeiodination of 2-bromo-4-iodo-1,3,5-trineopentylbenzene (BrITNB) is reported.

The nitrations have been carried out with 90 % nitric acid in nitromethane. Nitrodeiodination is not the single reaction, it accompanies nitrodeprotonation. In the case of IM, there is still another reaction. IM reacts almost quantitatively with the iodonium ions from the nitrodeiodination to yield 2,4-diiodomesitylene. The corresponding reaction is not observed with the 1,3,5-trineopentylbenzene derivatives, in accordance with the resistance of ITNB towards reaction with "iodonium perchlorate".[4] This resistance is believed to be caused by steric hindrance, and should then be more pronounced in IMeTNB and BrITNB. In the nitration of iodobenzene no nitrodeiodination could be detected.

In Table 1 it can be seen that the rate ratio a of nitrodeiodination to nitrodeprotonation, each per position, is constant during the course of the reactions. This indicates that the nitrodeiodination does not take place in an indirect way, such as *via* protodeiodination of nitrodeprotonated products. The possibility of a slow protodeiodination, followed by a fast nitrodeprotona-

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tion, has been ruled out by means of isotopic labeling in the case of BrITNB in connection with related work in this laboratory.[3] A possible nitrosodeiodination, followed by oxidation, cannot be operating since a did not change when the nitric acid used had previously been treated with urea, and urea was present in the reaction mixture (Table 1).

Table 1. The composition (in mol %) of the nitration mixtures at different times during the reactions. The symbol a denotes the ratio of the rate of nitrodeiodination per position to the rate of nitrodeprotonation per position.

Reactant	Composition of reaction mixture				a
ITNB	ITNB	INO_2TNB	NO_2TNB		
	78.7	15.8	5.5		0.70
	68.1	23.5	8.4		0.71
	48.1	37.9	14.0		0.74
	21.3	58.3	20.4		0.70
	7.9	67.7	24.3		0.72
IMeTNB	IMeTNB	$IMeNO_2TNB$	$MeNO_2TNB$		
	65.6	30.6	3.8		0.12
	53.0	42.3	4.7		0.11
	29.7	62.4	7.9		0.13
	17.1	73.4	9.5		0.13
	0	89.3	10.7		0.12
IM	IM	INO_2M	NO_2M	I_2M	
	86.1	7.1	3.6	3.2	1.01*
	75.1	12.9	6.2	5.8	0.96
	63.0	18.6	9.5	8.9	1.02
	35.3	32.6	16.9	15.2	1.04
IM (with urea added to the reaction mixture)	IM	INO_2M	NO_2M	I_2M	
	0	53.0	26.7	20.3	1.01
BrITNB	Mean value of a from Ref. 3.				0.24

**Added in proof.* 2,4-Diiodomesitylene was nitrated under the same conditions as used for the determination of the a values. 2-Iodo-4-nitromesitylene, 2,4-diiodo-6-nitromesitylene and 2,4,6-triiodomesitylene were formed in the approximate relative amounts 83 : 7 : 10. This reaction was found to be sufficiently slow so as not to disturb the determination of the a value for 2-iodomesitylene by affecting the produced 2,4-diiodomesitylene.

A comparison of iodobenzene with the alkylated derivatives reveals that the iodo-substituted carbon is subject to attack by the nitronium ion in the alkyl-substituted aromatics only. Inherent in this conclusion is the assumption that nearly every cyclohexadienyl cation formed by attack of nitronium

ion on the iodo-substituted carbon will proceed into product by expelling an iodonium ion (most certainly by attack of a nucleophile in an S_N2 process on iodine). This is likely because the iodonium ion has a much higher leaving ability than the nitronium ion.[2] Two observations in the 1,3,5-trineopentylbenzene system support this assumption. Iodination of 1,3,5-trineopentylbenzene with positive iodine in acetic acid – dioxane (10:1 by volume) proceeds with an appreciable isotope effect [5] ($k_D/k_H = 0.38 \pm 0.02$), showing that in this medium the iodonium ion has a higher leaving ability than the proton. Nitration of 1,3,5-trineopentylbenzene with 90 % nitric acid in nitromethane shows an isotopic rate ratio k_D/k_H of 1.057 ± 0.005, however.[3] This latter fact means that the proton has a higher leaving ability than the nitronium ion under nitration conditions. If transitivity is assumed, the iodonium ion has a higher leaving ability than the nitronium ion.

In the series IM, ITNB, IMeTNB, and BrITNB, the values for a were determined using identical reaction conditions. BrITNB is enough sterically crowded to make proton expulsion kinetically significant in nitrodeprotonation.[3] This may also be the case for IMeTNB. The rate of nitrodeprotonation is then dependent on the concentration of the base that accepts the proton. This dependence cannot be established without further investigations concerning the kinetics and as long as the kinetics are unknown, a comparison of the a values is of little importance.

The first step in nitrodeiodination might be facilitated by a sterically induced increase in the energy of the ground state, not paralleled by a similar increase in the energy of the transition state. This step is assumed to be rate-limiting and thus the steric effects should tend to increase a in the series IM, ITNB, IMeTNB, and BrITNB, provided that the kinetics are comparable for the nitrodeprotonations.

When bromo analogues of the compounds investigated here, 2-bromo-1,3,5-trineopentylbenzene, 2,4-dibromo-1,3,5-trineopentylbenzene and 2,4-dibromomesitylene, were nitrated, no nitrodebromination could be detected.[3] This reaction was not observed in the nitration of 2-bromo-4-iodo-1,3,5-trineopentylbenzene.[3] This is in accordance with the result that nitrodeiodination is easier to bring about than nitrodebromination.[1,2]

In the preparation of IMeTNB from MeTNB with iodine and silver perchlorate in acetic acid – dioxane (5:1 by volume), 2-acetoxymethyl-1,3,5-trineopentylbenzene was isolated as a by-product. Possibly it had been formed by oxidation by iodonium ion of the ring methyl group in MeTNB to form a benzyl cation, followed by reaction with the acetic acid in the medium. Somewhat similar acetoxylations have been reported during anodic oxidation of mesitylene.[6] The fact that the methylene groups in the neopentyl groups were not oxidized is in accordance with the known relative difficulty of oxidizing aromatic neopentyl groups.[7]

We cannot, however, exclude other possibilities, as an attack of iodonium ion at C-1 or C-3 with a concomitant collapse of the cyclohexadienyl cation thus formed into 2-iodomethyl-1,3,5-trineopentylbenzene which undergoes acetoxylation in the medium.[8]

EXPERIMENTAL

The NMR spectra were recorded on a Varian A 60 spectrometer. About 10% (by weight) solutions in carbon tetrachloride were used. The probe temperature was 35°C. The chemical shifts are reported in ppm downfield from tetramethylsilane as internal standard. The multiplicities of the peaks are reported as singlet (s) or broad (b).

The IR spectra were recorded on a Beckman IR 9 spectrophotometer using 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).

The mass spectra (MS) were determined on an AEI MS 902 mass spectrometer, using the direct inlet system. The following conditions were used: inlet temperature 25°C, ion chamber temperature 100°C, electron energy 70 eV, accelerating voltage 8 kV and emission 100 μA .The intensities of the peaks are reported in parentheses as percentages of the base peak. Only the most abundant peaks are reported, together with the parent peaks and the isotope peaks corresponding to them.

Gas chromatographic (GLC) analyses were carried out on a Perkin-Elmer 900 gas chromatograph, fitted with flame ionization detector. The outer diameter of the columns 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 nitrogen was 30 ml/min. The quantitative gas chromatographic analyses were made on a Perkin-Elmer F 11 instrument, fitted with hot wire detector. The dimensions of the columns were: outer diameter 1/4 inch, length 2 m. The stationary phase was the same as above and the flow rate of helium was 30 ml/min. The areas of the peaks were determined with a Perkin-Elmer D2 electronic integrator.

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

For column chromatography, Merck neutral silica gel with activity 2 – 3 was used with a grain size of 0.05 – 0.2 mm.

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. Anhydrous silver perchlorate was stored over phosphorus pentoxide. All other chemicals were of reagent grade and were used without further purification.

The purities of all substances prepared were checked by gas chromatography and were found to be at least 99.5 %, as estimated from the peak heights.

2-Methyl-1,3,5-trineopentylbenzene was prepared as described previously [3] as was 2-iodo-1,3,5-trineopentylbenzene.[4] 2-Iodomesitylene was prepared as described by Keefer and Andrews.[9]

Synthesis of 2-iodo-4-methyl-1,3,5-trineopentylbenzene. 2-Methyl-1,3,5-trineopentylbenzene (3.25 g, 10.7 mmol) and 2.8 g (13.5 mmol) of silver perchlorate were dissolved in 65 ml of acetic acid – dioxane (5:1 by volume). By warming, 3.4 g (13.4 mmol) of iodine was dissolved in 65 ml of the same solvent. After the last-mentioned solution was cooled to room temperature, the solutions were combined and stirred overnight. Completion of reaction was checked by GLC, and two products appeared in the chromatogram. The reaction mixture was poured into a mixture of 10 g of sodium sulphite in 100 ml of water and 50 ml of cyclohexane. The mixture was filtered and the aqueous phase of the filtrate was extracted with cyclohexane. The combined organic phases were washed with water and dried with magnesium sulphate. After evaporation of the solvent, the two products were separated by means of column chromatography. With hexane as eluent 2-iodo-4-methyl-1,3,5-trineopentylbenzene was obtained, and after recrystallization from nitromethane, the yield was 2.3 g (50 %). M.p. 68 – 70.5°C. With dichloromethane, an oil was obtained, identified as 2-acetoxymethyl-1,3,5-trineopentylbenzene. It was not further purified, and the yield was 0.58 g (15 %).

Spectral characteristics for 2-iodo-4-methyl-1,3,5-trineopentylbenzene:

NMR: 6.79 (s, 1 H, aromatic), 3.19 (b, 2 H, methylene), 2.89 (b, 2 H, methylene), 2.53 (b, 2 H, methylene), 2.34 (s, 3 H, methyl), 1.00 (s, 18 H, *tert*-butyl), 0.94 (s, 9 H, *tert*-butyl).

MS: 41(41), 43(43), 57(100), 133(12), 173(12), 245(11), 260(39), 316(41), 371(24), 372(27), 428(28.1), 429(6.5) 430(0.8).

IR: 2950vs, 2860s, 1478s, 1466w, 1430w, 1391m, 1362s, 1230m, 1199w, 1169w, 1145w, 1109m, 1026w, 984m, 926w, 874m.

Spectral characteristics for 2-acetoxymethyl-1,3,5-trineopentylbenzene:

NMR: 6.74 (s, 2 H, aromatic), 5.17 (s, 2 H, oxymethylene), 2.62 (s, 4 H, methylene), 2.42 (s, 2 H, methylene), 1.96 (s, 3 H, methyl), 0.94 (s, 27 H, *tert*-butyl).

MS: 41(33), 43(21), 57(100), 71(10), 131(7), 132(15), 173(10), 187(22), 188(45), 189(9), 243(19), 244(50), 245(12), 261(8), 285(11), 300(21), 301(8), 360(19.3), 361(4.8), 362(0.8).

IR: 2955vs, 2910s, 2865s, 1739vs, 1606w, 1574w, 1475m, 1466w, 1389w, 1374w, 1360s, 1280w, 1230vs, 1200w, 1139w, 1033m, 976m, 895w, 811w.

Relative rates of nitrodeiodination versus *nitrodeprotonation, determination of a.* In order to determine the relative rates of the reactions observed, nitrations were carried out under the following standard conditions. The aromatic substrate (25 mg) 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 mixture was stirred at 0°C. Aliquots were withdrawn at proper time intervals, worked up as described below for the nitration of IM, and the raw product was analyzed by gas chromatography. The relative rates of the competing reactions were obtained as the molar ratios of the products, corrected for the number of equivalent positions. The results are given in Table 1.

Nitration of 2-iodomesitylene. 2-Iodomesitylene (1.23 g, 5 mmol) was dissolved in 40 ml of nitromethane and the solution was cooled to 0°C. A mixture of 7.5 ml of 90 % nitric acid (160 mmol) and 2.5 ml of nitromethane, cooled to 0°C, was added, and the reaction solution was stirred at 0°C for 7 h. The solution was poured into water, and concentrated aqueous ammonia was added until the mixture became homogeneous. The mixture was extracted with hexane, the organic phase was then washed with water until neutral, and dried with magnesium sulphate. After evaporation of the solvent, the yield was 1.25 g (89 %). Three products were obtained and separated by column chromatography. With hexane, 2,4-diiodomesitylene (I_2M) was eluted, followed by 2-iodo-4-nitromesitylene (INO_2M). With dichloromethane, 2-nitromesitylene (NO_2M) was eluted.

2,4-Diiodomesitylene was recrystallized from nitromethane. Yield 0.18 g (10 %). M.p. 82 – 83.5°C. The crystals underwent a transition around 70°C. Reported m.p.[10] 82 – 83°C.

NMR: 6.92 (s, 1 H, aromatic), 2.89 (s, 3 H, methyl), 2.39 (s, 6 H, methyl).

MS: 39(12), 50(5), 51(12), 63(6), 65(6), 77(8), 91(12), 103(8), 115(13), 117(30), 118(40), 245(33), 372(100.0), 373(9.5), 374(0.4).

IR: 2940m, 1443s, 1375s, 1300w, 1212m, 1038w, 1016s, 959s, 863m, 604m, 584w, 519w.

2-Iodo-4-nitromesitylene was recrystallized from absolute ethanol. Yield 0.41 g (28 %). M.p. 97.5 – 98°C. Reported[11] 96 – 97°C.

NMR: 6.99 (s, 1 H, aromatic), 2.47 (s, 3 H, methyl), 2.41 (s, 3 H, methyl), 2.20 (s, 3 H, methyl).

MS: 39(19), 51(17), 65(11), 77(18), 78(12), 91(35), 103(16), 104(11), 115(18), 117(38), 118(53), 119(54), 147(31), 274(85), 291(100.0), 292(10.8), 293(1.3).

IR: 2990m, 2930m, 2880m, 1526vs, 1460m, 1435m, 1381vs, 1369vs, 1221w, 1104m, 1047m, 981s, 877s, 855vs, 640vs, 560w, 528w.

2-Nitromesitylene was recrystallized from absolute ethanol. Yield 0.05 g (6 %). M.p. 43 – 44°C. Reported[10] 44°C.

NMR: 6.85 (s, 2 H, aromatic), 2.30 (s, 3 H, methyl), 2.24 (s, 6 H, methyl).

MS: 39(25), 40(29), 41(46), 43(27), 77(53), 79(25), 91(69), 93(55), 103(28), 119(39), 120(40), 150(100), 165(76.3), 166(8.5).

IR: 2980m, 2925m, 2860m, 1608s, 1530s, 1370s, 1304m, 1189w, 1097w, 1049m, 866s, 840s, 722m, 608s, 580m, 511w.

In another experiment, 2-iodomesitylene was nitrated as described above but with urea present in the reaction mixture and with nitric acid that had been treated with urea until it became colourless. The rate ratio *a* obtained was the same as found with the ordinary nitric acid (Table 1).

Nitration of 2-iodo-4-methyl-1,3,5-trineopentylbenzene. 2-Iodo-4-methyl-1,3,5-trineopentylbenzene (0.5 g, 1.17 mmol), 50 ml (1.07 mol) of 90 % nitric acid and 355 ml of nitromethane were used in the same procedure as described for the nitration of 2-iodomesitylene. The temperature was 0°C and the reaction time 3 h. The two products, 2-methyl-1,3,5-trineopentyl-4-nitrobenzene ($MeNO_2TNB$) and 1-iodo-3-methyl-2,4,6-

trineopentyl-5-nitrobenzene ($IMeNO_2TNB$), were separated by means of column chromatography (hexane).

1-Iodo-3-methyl-2,4,6-trineopentyl-5-nitrobenzene was recrystallized from nitromethane. Yield 0.35 g (64 %). M.p. 104 – 105.5°C.

NMR: 3.30 (b, 2 H, methylene), 3.14 (b, 2 H, methylene), 2.68 (s, 2 H, methylene), 2.45 (s, 3 H, methyl), 1.05 (s, 9 H, *tert*-butyl), 0.98 (s, 9 H, *tert*-butyl), 0.91 (s, 9 H, *tert*-butyl).

MS: 41(25), 43(8), 57(100), 58(6), 288(8), 305(6), 344(48), 361(31), 400(30), 458(5), 473(7.9), 474(2.3), 475(0.3).

IR: 2960vs, 2865s, 1540s, 1474s, 1396w, 1364s, 1226m, 1201w, 1152w, 1128m, 1029w, 862w, 830m.

2-Methyl-1,3,5-trineopentyl-4-nitrobenzene was recrystallized from nitromethane. Yield 0.03 g (7 %). The melting point and the NMR and IR spectra were identical with the reported ones.[3]

Nitration of 2-iodo-1,3,5-trineopentylbenzene. 2-Iodo-1,3,5-trineopentylbenzene (4.0 g, 9.7 mmol) was dissolved in 2.3 l of nitromethane and the solution was cooled to 0°C. Nitric acid (300 ml, 90 %, 6.4 mol) was added, and the reaction mixture was kept at 0°C for 3 h. The mixture was washed twice with 1 l of water and then extracted three times with hexane. The hexane phase was washed with water until neutral and dried with magnesium sulphate. After the solvent was evaporated the residue weighed 3.9 g (98 %, the composition of the mixture was used when this figure was calculated). Two products, 1,3,5-trineopentyl-2-nitrobenzene (NO_2TNB), and 2-iodo-1,3,5-trineopentyl-4-nitrobenzene (INO_2TNB), were obtained and separated by means of column chromatography (hexane).

1,3,5-Trineopentyl-2-nitrobenzene was recrystallized from nitromethane. The yield was 0.41 g (13 %). The melting point and the NMR and IR spectra were identical with the reported ones.[3]

2-Iodo-1,3,5-trineopentyl-4-nitrobenzene was recrystallized from nitromethane and the yield was 2.49 g (56 %). M.p. 83 – 84°C.

NMR: 6.97 (s, 1 H, aromatic), 3.17 (s, 2 H, methylene), 2.98 (s, 2 H, methylene), 2.50 (s, 2 H, methylene), 1.03 (s, 9 H, *tert*-butyl), 0.98 (s, 9 H, *tert*-butyl), 0.92 (s, 9 H, *tert*-butyl).

MS: 41(25), 43(5), 57(100), 58(5), 274(4), 291(3), 330(40), 347(14), 386(40), 403(22), 444(7), 459(5.1), 460(1.3), 461(0.2).

IR: 2965vs, 2950vs, 2865s, 1530vs, 1476vs, 1450m, 1396w, 1362vs, 1230s, 1200w, 1159w, 1090w, 1043w, 1001w, 895w, 846m, 686w, 621w.

Nitration of iodobenzene. Iodobenzene (1.02 g, 5 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. Since no reaction could be detected by GLC after 12 h, the temperature was raised. At 65°C the reaction was complete in 3 h as determined by GLC. The work-up procedure described for the nitration of 2-iodomesitylene was applied. No nitrobenzene could be detected by GLC in the product.

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