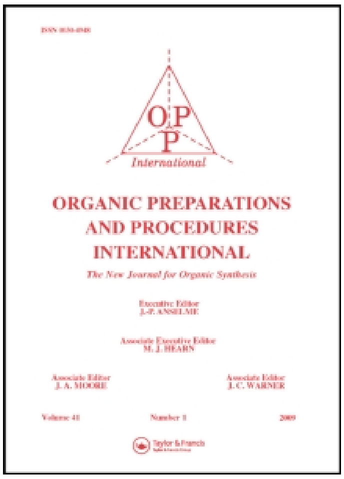

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cis- AND trans-N,N'-DIMETHYL-1,4-CYCLOHEXANEBIS(METHYLAMINE) BY METHYLATION OF THE BENZALDEHYDE IMINES

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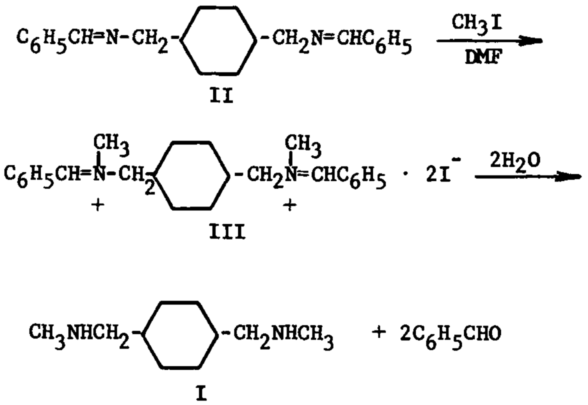
N,N'-Disubstituted 1,4-cyclohexanebis(methylamines) were required for a study of partially N-substituted polyamides. cis-N,N'-Dimethyl-1,4-cyclohexanebis(methylamine) (Ia) was prepared by methylation of the corresponding di(benzenesulfonamide), followed by removal of the benzenesulfonyl group with hydrobromic acid in phenol.[1] However, this method proved impractical since the cleavage conditions are drastic and the work-up procedure is tedious.

Both Ia and the trans isomer, Ib, were prepared by methylation of the benzaldehyde imine (II) of the corresponding 1,4-cyclohexanebis(methylamine) (IV) followed by hydrolysis of the intermediate immonium salt (III).[2,3,4,5]



a = cis-
b = trans-

Initially, IIb was alkylated at 100° in benzene with methyl iodide, using a small tubular bomb, following Wazonek's procedure for N-methylethylamine.[2] Only a low yield (12%) of Ib was obtained, perhaps because of low solubility of the immonium salt, IIIb, or because of incomplete reaction. Dimethylformamide was used as a solvent in subsequent experiments in order to produce a homogeneous reaction mixture and in hopes of increasing the reaction rate by greater stabilization of the charge separation in the transition state. Thus, alkylation of the trans imine IIb with dimethyl sulfate[5] at 110-135° gave a 67% yield of crude Ib. Gas chromatography indicated the presence of about 2-3% of a more volatile impurity; recrystallization from pentane gave pure material, m.p. 47-49°.

cis-N,N'-Dimethyl-1,4-cyclohexanebis(methylamine) (Ia) was prepared in similar yield in the same manner using methyl iodide or dimethyl sulfate. As in the case of the trans isomer, a few percent of impurity was found by gas chromatography. Ia, a liquid, was purified by fractional distillation. A lower boiling impurity, not completely removed by distillation, appeared to be amine Va since no IVa was detected by gas chromatography, although i.r. indicated the presence of primary amine.

Va

In connection with the preparation of secondary amines, it is worth noting that attempts to prepare the N,N'-n-butyl-1,4-cyclohexanebis(methylamines) from the butyraldehyde imines of IV by reduction in all cases gave complex mixtures of compounds arising from redistribution of alkyl groups. Thus, catalytic hydrogenation with palladium or platinum catalysts under a variety of conditions gave products boiling over a wide range, although N,N'-dibenzylidene-IV has been reported to yield N,N'-dibenzyl-IV smoothly by catalytic hydrogenation.[6]

cis AND trans-N,N'-DIMETHYL-1,4-CYCLOHEXANEBIS (METHYLAMINE)

Experimental

Melting points are uncorrected. Gas chromatography was performed using a Beckman GC-4 chromatograph equipped with dual flame ionization detectors; 6', 1/8" dia. stainless steel columns packed with 20% SE-30 on Celite 545 were employed. Microanalyses (duplicates) were performed by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. The starting amines IVa and IVb were supplied by Aldrich Chemical Co.

cis- and trans-N,N'-Dibenzylidene-1,4-cyclohexanebis(methylamine), (IIa and IIb)

IIa and IIb were prepared from the amines IVa and IVb and benzaldehyde by refluxing in benzene, using a Dean and Stark trap to collect the water formed. The cis isomer, IIa, after three recrystallizations from n-hexane, melted at 60.5-61.5°.

Anal. Calcd. for $C_{22}H_{26}N_2$: C, 82.97; H, 8.23; N, 8.80. Found: C, 83.15; H, 8.09; N, 8.64.

The trans imine, IIb, was recrystallized four times from n-heptane to give an analytical sample, m.p. 109.2-110.2°.

Anal. Found: C, 83.18; H, 8.41; N, 8.71.

trans-N,N'-Dimethyl-1,4-cyclohexanebis(methylamine) (Ib)

A solution of 95.6 g (0.30 mole) of IIb, m.p. 107.5-109° in 680 ml of purified DMF (dried over CaH_2) was heated to 110° and 68 ml (90.7 g, 0.72 mole) of dimethyl sulfate was added over 0.5 hr. with stirring under nitrogen. The temperature rose to 120°; after 20 min. the exothermic reaction subsided, and the reaction mixture was heated to 135° for 2-2.5 hrs. As much DMF as possible was removed under aspirator vacuum using a steam bath, and 200 ml of 3N HCl was added to the residue, followed by 200 ml of water. The mixture was extracted with three portions of methylene chloride, heated to remove traces of solvent, cooled, and solid NaOH pellets were added until a second layer formed. The amine was separated by extraction with three portions of ether; the combined ether layers were dried over NaOH pellets, concentrated, and the residue was vacuum distilled through a Vigreux column. Four fractions totaling 34.2 g (66.7%) were obtained:

Fraction	B.p.	Wt., g	n_D^{25}	% Impurity
1	74°(0.08 mm)	3.78	1.4722	3.2
2	70.5°(0.08 mm)	12.32	1.4724	3.3
3	70.5°(0.08 mm)	15.81	1.4724	2.4
4	53°(0.05 mm)	2.24	1.4725	1.7

Gas chromatography of the four fractions (0.5μl sample; 175° to 275°, 1 min. isothermal, then 25°/min.) showed the presence of an impurity as a small shoulder appearing just before the main peak. Fractions 1-3 solidified upon standing, m.p. 28-32° (fraction 1). Fraction 2 was recrystallized from 50 ml of pentane, by cooling in ice and pressure filtration with nitrogen, to give 7.57 g of product (vacuum-dried at room temperature), m.p. 47-49°. G.c. of a 33% soln. of recrystallized Ib in xylene indicated no perceptible impurity (155°to 205°; 2 min. isothermal, then 12.5°/min.). A second crop was obtained, 0.92 g, m.p. 47-49° (68% total recovery). Fractions 3 and 4 were combined and recrystallized to give 10.35 g of purified Ib, m.p. 47.5-49° (57.3% recovery). Three recrystallizations from pentane gave an analytical sample.

Anal. Calcd. for $C_{10}H_{22}N_2$: C, 70.53; H, 13.02; N, 16.45. Found: C, 70.78; H, 12.71; N, 16.23.

I.r. (KBr pellet) showed bands at 3240 cm^{-1}, shoulder at 3260 cm^{-1} (N-H stretching); 2800 cm^{-1} (CH_3NH- stretching); 2700 cm^{-1}; no $-NH_2$ bending at 1600 cm^{-1}; 1510 cm^{-1}(strong) (-NH-bending ?); several at 1082 cm^{-1}, 1130-40 cm^{-1} (C-N stretching); 865-880 cm^{-1} (strong, broad).

cis AND trans-N,N'-DIMETHYL-1,4-CYCLOHEXANEBIS (METHYLAMINE)

cis-N,N'-Dimethyl-1,4-cyclohexanebis(methylamine) (Ia). A. Alkylation of IIa with Methyl Iodide

A solution of IIa, 31.85 g (0.10 mole), m.p. 52.4-53.1°, in 200 ml of DMF (dried over CaH_2) was placed in a 400-ml split ring bomb, and 13.7 ml (31.2 g, 0.22 mole) of methyl iodide was added. The bomb was heated with magnetic stirring in a bath of boiling water for 11 hrs. The bomb was cooled, and the contents were worked up by the procedure given for Ib. The crude product was vacuum distilled through a small Vigreux column to give 4 fractions totalling 11.33 g (66.5%).

Fraction	B.p.	Wt., g	n_D^{25}
1	62°(0.08 mm)	0.69	1.4768
2	62°(0.08 mm)	2.87	1.4764
3	62°(0.08 mm)	7.32	1.4763
4	62°(0.07 mm)	0.45	1.4767

G.c. showed a few percent impurity as a small peak at the beginning of the main peak. A sample of fraction 3 was submitted for microanalysis.

Anal: Calcd. for $C_{10}H_{22}N_2$: C, 70.53; H, 13.02; N, 16.45. Found: C, 70.35; H, 13.01; N, 16.35.

I.r. of a redistilled sample showed bands at 3300 cm^{-1} (NH); 2920 and 2855 cm^{-1} (CH_2 stretching); 2795 cm^{-1} (strong, CH_3NH-); 2720 cm^{-1} (weak); no $-NH_2$ bending peak at 1600 cm^{-1}; C-N stretching at 1110-1150 cm^{-1}; band at 750 cm^{-1} (strong, very broad).

B. Alkylation of IIa with Dimethyl Sulfate

The reaction was run in the same manner as in the preparation of Ib, using 62.7 g (0.20 mole) of IIa, m.p. 55.5-57°, 660 ml of dry DMF, and 45 ml (60.6 g, 0.48 mole) of dimethyl sulfate. The crude product was vacuum distilled; the first three fractions totalled 22.84 g (67%), n_D^{25}

1.4775-1.4777, b.p. 67-67.5°(0.02 mm). G.c. indicated the presence of up to 8-9% impurity. Fractionation of combined fractions 1-3 with a Nestor-Faust spinning band (Teflon) column gave two small fractions containing about 50% impurity; i.r. spectra were similar to that of Ia from methyl iodide, except for the following: shoulder at 3380 cm^{-1}, NH_2 bending band at 1610 cm^{-1}, sharp band (med) at 1030-1040 cm^{-1}, shoulder at 845 cm^{-1}. IVa showed the same bands in the i.r. spectrum but had a different g.c. retention time (0.85 min. for IVa vs 2.6 min. for Ia and the impurity at about 2.5 min.). Moreover, Ia and IVa should be readily separable by distillation.

Ia via the Hinsberg Reaction

IVa di(benzenesulfonamide) was prepared from IVa (0.20 mole) and benzenesulfonyl chloride (0.42 mole) in the presence of 10% NaOH (0.42 mole) at 5-10° for 1 hr. A sample of crude product (VIa) was recrystallized from ethanol, m.p. 143-144.5°. I.r. 3320-3280 cm^{-1} (NH); 3070 cm^{-1} (aromatic CH); 1327 cm^{-1} and 1170-1150 cm^{-1} (sulfonamide).

Anal. Calcd. for $C_{20}H_{26}N_2O_4S_2$: C, 56.86; H, 6.20; N, 6.63; S, 15.18. Found: C, 56.75; H, 6.27; N, 6.73; S, 15.20.

Crude VIa, 0.2 mole, was suspended in 250 ml. of methanol and 105 ml. of Claisen's alkali (25% KOH) was added. After all of the solid dissolved, 28 ml. (0.45 mole) of methyl iodide was slowly added with stirring; the temperature rose and a white solid formed. The reaction mixture was heated at 40-45° for 6-7 hrs; the crude cis-N,N'-1,4-cyclohexanedimethylbis(benzenesulfonamide) (VIIa) was isolated by filtration, m.p. 161-162.5° (34.6% yield from IVa; considerable unchanged VIa was recovered). VIIa was recrystallized 3 times from 2:1 EtOH-$CHCl_3$, m.p. 165.5-166.8°. The infrared spectrum was similar to that of VIa, except that there was no 3320-3280 cm^{-1} band.

<u>cis</u> AND <u>trans</u>-N,N'-DIMETHYL-1,4-CYCLOHEXANEBIS (METHYLAMINE)

Anal. Calcd. for $C_{22}H_{30}N_2O_4S_2$: C, 58.64; H, 6.71; N, 6.22; S, 14.20. Found: C, 58.60; H, 6.80; N, 6.44; S, 14.44.

VIIa, 20.0 g (0.0444 mole), was cleaved with 48% HBr in phenol[1] to give 5.28 g (69.9%) of Ia, b.p. 64-66° (0.06 mm), n_D^{25} 1.4760.

References

1. H. R. Snyder and R. E. Heckert, J. Am. Chem. Soc., 74, 2006 (1952).
2. S. Wazonek, W. McKillip, and C. J. Peterson, "Organic Syntheses", Vol. 44, ed. by W. E. Parham, John Wiley and Sons, N.Y., 1964, p. 75.
3. A. L. Morrison and H. Rinderknecht, J. Chem. Soc., 1478 (1950).
4. H. Decker and P. Becker, Ann., 395, 362 (1913).
5. J. Lucier, A. D. Harris, and P. S. Korosec, "Organic Syntheses", Vol. 44, ed. by W. E. Parham, John Wiley and Sons, N.Y., 1964, p. 72.
6. L. G. Humber, J. Med. Chem., 7, 826 (1964).

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