to note that shifts to longer wavelengths in the paracyclophane series were also associated with broadened bands and decreased absorption intensities.

The properties of 1 are thus vastly different from the perpendicular isomer **2** or other analogous *trans*-alkenes. The difference appears attributable to the transannular repulsions between the π bond and the cyclopropane ring. These repulsions distort the π bond and thus greatly alter its chemical reactivity. Further studies on these and related distorted alkenes should clarify the precise nature of the distortion process and the chemical consequences of such distortions. Finally, it is apparent that the unique features of the trans,trans arrangement present in these compounds offer many opportunities for chemical study of previously unavailable molecular arrangements.[20]

Registry No.—**1a,** 36217-82-0; **1b,** 36217-84-2; **2a,** 36217-81-9; **2b,** 36217-83-1; **6,** 1552-12-1; **9a,** 36217-85-3; **9a** oxide, 53447-31-7; **9b,** 53447-32-8; **9c,** 36217-86-4; **13b,** 53384-96-6; **13c,** 53432-89-6; **13d,** 53384-97-7; **13e,** 53384-98-8; **13f** (X = I), 53384-99-9; **13f** (X = Cl), 53385-02-7; **13g,** 36217-87-5; **15,** 53447-33-9; **16,** 5259-71-2; **18,** 36217-88-6; **19,** 53447-34-0; **20,** 53385-00-5; **21,** 53447-36-2; **22,** 53447-35-1; **23,** 53447-37-3; phenyl azide, 622-37-7; sodium methylsulfinyl methide, 15590-23-5; cuprous chloride, 7758-89-6; *p*-methoxyphenyl azide, 2101-87-3; di-*tert*-butyl *trans*-4-octene-1,8-dioate, 53432-90-9; di-*tert*-butyl 2,2,7,7-tetradeuterio-*trans*-4-octene-1,8-dioate, 53385-01-6; triphenylphosphine, 603-35-0; sodium iodide, 7681-82-5; *p*-toluenesulfonyl chloride, 98-59-9; dimethyl *trans*-4-octene-1,8-dioate, 32456-97-6; sodium trichloroacetate, 650-51-1.

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Synthesis of Some *cis*- and *trans*-2-Dimethylaminomethyl Cyclic Amines and Related Diamines[1]

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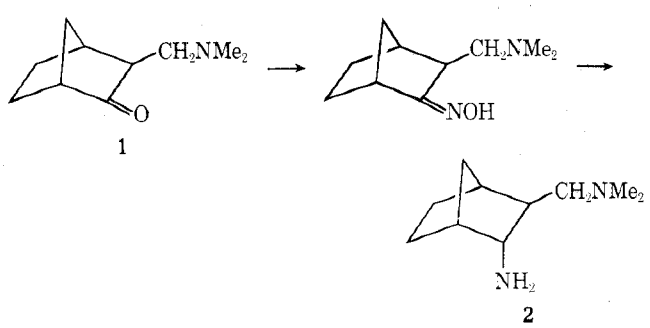
The preparation of *N,N,* 2,2-tetramethyl-1,3-propanediamine, *cis*- and *trans*-2-(dimethylaminomethyl)cyclohexylamine, and 3-*exo*-dimethylaminomethyl-2-*endo*-norbornanamine has been accomplished by the Mannich reaction on the appropriate carbonyl compound, followed by oximation and reduction. The reactions of methacrolein and 3-methylene-2-norbornanone with methylhydrazine gave pyrazolines whose methiodides were reduced to *N,N,* 2-trimethyl-1,3-propanediamine and 3-*endo*-dimethylaminomethyl-2-*endo*-norbornanamine, respectively.

The dedeuteration of acetone-d_6 has been shown to be catalyzed bifunctionally by the monoprotonated form of *N,N*-dimethyl-1,3-propanediamine.[2,3] Examination of models of the transition state of the rate-controlling step in the reaction showed that in the two most stable conformers the carbon-1–nitrogen bond from the diamine was approximately eclipsed with a carbon-2–hydrogen or carbon-2–carbon-3 bond. The greatly increased bifunctional catalytic activity of both the cis and trans isomers of 2-(dimethylaminomethyl)cyclopentylamine experimentally demonstrated the importance of conformational effects.[2,3] To study such effects in more detail we have synthesized several additional conformationally constrained derivatives of *N,N*-dimethyl-1,3-propanediamine and also two 1,4-diamines.

Results

The method used previously for the preparation of the 2-(dimethylaminomethyl)cyclopentylamines, in which the Mannich reaction is used to introduce a dimethylaminomethyl substituent into a carbonyl compound that is then transformed to its oxime and reduced,[3] was used to prepare *N,N*,2,2-tetramethyl-1,3-propanediamine and the 2-(dimethylaminomethyl)cyclohexylamines, which were obtained as a mixture containing about 60% of the major and 40% of the minor isomer. After separation by fractional crystallization of the oxalate salts, the major product was assigned the cis and the minor one the trans configuration on the basis of their pmr spectra. The carbon-1 proton of the cis isomer, which should be largely equatorial, absorbed at about 0.5 ppm lower field than the carbon-1 proton of the trans isomer, which should be largely axial.[4a] In the presence of the shift reagent Eu(fod)$_3$[5] the widths at half-height for the carbon-1 proton peaks were *ca.* 12 and *ca.* 30 Hz for the cis and trans isomers, respectively. The peak for the largely axial carbon-1 proton of the trans isomer is broadened by two large axial–axial vicinal coupling constants, whereas the peak for the largely equatorial carbon-1 proton of the cis isomer is much less extensively split.

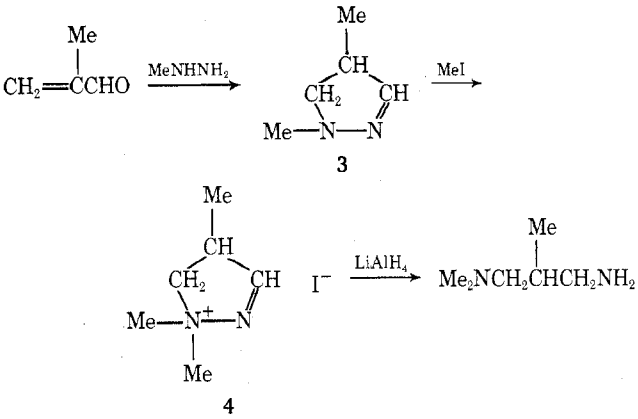
Application of the same method of synthesis to 2-norbornanone as the starting material gave, as the product of the first step, the 3-(dimethylaminomethyl)-2-norbornanone (1) that has been shown by Krieger to be exo.[6] This stereochemical assignment is supported by pmr measurements using a shift reagent. Oximation of the ketone and lithium aluminum hydride reduction gave 3-*exo*-dimethylaminomethyl-2-*endo*-norbornanamine (2). The pmr peak for

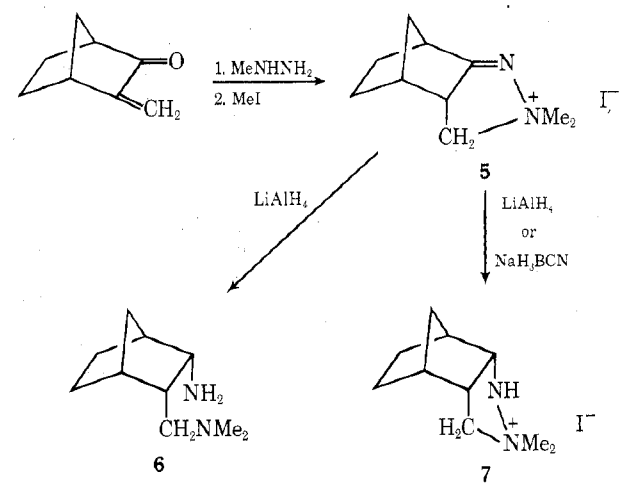


the carbon-2 proton was split with coupling constants of about 1, 4.5, and 4.5 Hz. The latter two coupling constants are plausible for vicinal exo–bridgehead coupling and exo–endo coupling.[4b,7] The coupling constant of *ca.* 1 Hz probably arises from long-range splitting by the exo proton on carbon-6. If the new primary amino group had been exo the carbon-2 proton peak would have been split by the carbon-3 proton with a coupling constant of about 7 Hz and by no other coupling constant larger than 3 Hz.[4b,7]

Since the synthesis of **2** gave no clearly observable amount of a cis isomer, we devised a stereospecific synthesis to obtain such a compound. The required groups would be held cis by being in a five-membered ring, whose cleavage would be the last step of the reaction. The preparation of *N,N*,2-trimethyl-1,3-propanediamine was used as a proving ground for this new stereospecific synthesis. By analogy to the reaction of α-methylene ketones with methylhydrazine to give pyrazolines,[8,9] methacrolein was transformed to 1,4-dimethyl-2-pyrazoline (**3**), which was methylated with methyl iodide at its saturated nitrogen atom.[10] Lithium aluminum hydride reduction of the resulting pyrazolinium salt **4** gave the desired diamine in 19% yield (not optimized).

When this method of synthesis was applied to 3-methylene-2-norbornanone, lithium aluminum hydride reduction of the pyrazolinium salt **5** gave 15% 3-*endo*-dimethylaminomethyl-2-*endo*-norbornanamine (**6**) and 22% of the product **7** in which only the double bond had been reduced.

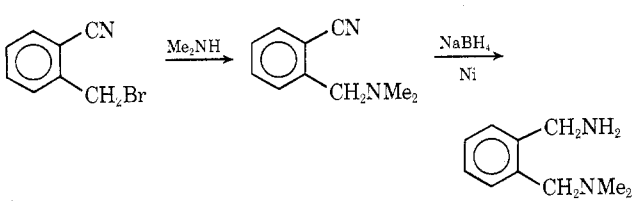




The latter was the only product obtained (in 46% yield) when **5** was reduced with sodium cyanoborohydride in methanol at about pH 4. The C-2 proton peak for **6** was a doublet of doublets (J = 9.5, 4.5 Hz). The larger of these coupling constants shows that **6** must be a cis isomer and very probably an endo cis isomer.[4b,7] The smaller coupling constant, which is too large for any possible long-range coupling or for bridgehead–endo vicinal coupling in the norbornane series, is perfectly plausible for bridgehead–exo vicinal coupling.

We believe that the pyrazoline route we have used may prove to be a rather general method for the stereospecific synthesis of derivatives of *cis*-(2-aminomethyl) cyclic amines.

Also prepared was *o*-(dimethylaminomethyl)benzylamine, which was synthesized from *o*-cyanobenzyl bromide by reaction with dimethylamine followed by sodium borohydride–Raney nickel reduction.[11]



Reductive methylation of the appropriate primary–tertiary diamines was used to prepare *o*-bis(dimethylaminomethyl)benzene, which has been made in other ways,[12,13] and *N,N,N',N'*,2,2-hexamethyl-1,3-propanediamine.

Experimental Section[14]

2,2-Dimethyl-3-dimethylaminopropylamine.--A concentrated aqueous solution of 14.1 g of sodium carbonate was added dropwise to a cold mixture of 34.3 g of 2,2-dimethyl-3-dimethylaminopropanal and a saturated aqueous solution of 20.3 g of hydroxylamine hydrochloride. After about 1 hr of stirring 18.9 g (49%) of the oxime was obtained as white crystals: mp 51--55°; ir (KBr) 3050, 3150 (s, O-H), 1630 (w, C=N), 954 (s, N-O), 1470 (m), 1450 (m), 1420 (m), 1350 (w), 1300 (m), 1230 (w), 1165 (m), 1105 (w), 1040 (m), 1026 (s), 996 (w), 927 (s), 870 (m), 775 (m), 635 (w), 508 cm^{-1} (w); pmr ($CDCl_3$) δ 1.10 (s, 6, CH_3C), 2.28 (s, CH_2N) and 2.30 (s, CH_2)--8.2 protons, and 7.37 ppm (s, 1, CH=N).

After slow addition of 9 g (0.063 mol) of oxime to 4.94 g (0.130 mol) of lithium aluminum hydride in 250 ml of ether with stirring, the solution was refluxed for 48 hr. Addition of 10% aqueous sodium hydroxide gave a white precipitate that was removed by filtration. Distillation of the filtrate gave 4.71 g (58%) of 2,2-dimethyl-3-dimethylaminopropylamine: bp 152.5--153°; ir (neat) 3370 and 3280 (w, NH_2), 2940, 2860, 2810, and 2760 (all s, C-H), 1590 (w), 1450 (m), 1340 (w), 1370 (w), 1240 (w), 1155 (w), 1100 (w), 1050 (s), and 850 cm^{-1} (m); pmr ($CDCl_3$) δ 0.83 (s, 6, CH_3C), 1.43 (s, 2, NH_2), 2.05 (s, 2, CH_2NMe_2), 2.20 (s, 6, CH_2N), and 2.43 ppm (s, 2, CH_2NH_2); exact mass of parent ion, calcd 130.14698, found 130.14725.

2-(Dimethylaminomethyl)cyclohexylamines.--The oxime of 2-(dimethylaminomethyl)cyclohexanone has been reduced catalytically[15] and with sodium in liquid ammonia,[16] but the products were not separated into cis and trans isomers nor was their stereochemistry studied. A solution of 8.67 g (0.051 mol) of this oxime was refluxed with 7.6 g (0.20 mol) of lithium aluminum hydride in 500 ml of ether. After the usual work-up vacuum distillation gave 6.0 g (76%) of liquid: bp 39--42° (0.11 mm); ir (neat) 3285 and 3360 cm^{-1} (NH_2). Glpc of this liquid on a 12-ft column containing 20% mannitol and 5% potassium hydroxide on Chromosorb-P at 155° showed two overlapping peaks, of which the first was 50% larger than the second. When the oxalate salts were crystallized from 9:1 methanol--water the salt of the major isomer crystallized first. Repeated crystallization of the remaining salt mixture from ethanol gave the pure salt of the minor isomer. The amines were liberated from their oxalates with potassium hydroxide. The major isomer is taken to be cis-2-(dimethylaminomethyl)cyclohexylamine: pmr ($CDCl_3$) δ 2.12 (s, 6, CH_2N), 3.00 (multiplet about 12 cps wide at half-height, 1, H-1), 1.0--2.1 ppm (m, ~13); exact mass of parent ion, calcd 156.16264, found 156.16278. The minor isomer was taken to be trans-2- (dimethylaminomethyl)cyclohexylamine: pmr ($CDCl_3$) δ 2.12 (s, 6, CH_2N), 2.0--2.6 (m, ~3, H-1 and CH_2N), 0.9--2.0 ppm (m, ~11); in the presence of $Eu(fod)_3$ the H-1 peak had a width at half-height of 30 cps.

Anal. Calcd for $C_9H_{20}N_2$: C, 69.17; H, 12.90; N, 17.93. Found: C, 68.83; H, 13.03; N, 17.81.

3-exo-Dimethylaminomethyl-2-norbornanone.--This compound was made from 2-norbornanone by the Mannich reaction.[8] Although the pmr spectra in chloroform-*d* and benzene-d_6 were consistent with the structure assigned previously,[8] they added no evidence for it. However, in the presence of enough (less than 0.3 mol per mol of compound) $Eu(fod)_3$ to shift the 6-proton peak for the dimethylamino group to δ 6.90 there was a 1-proton broadened doublet (J = 12 cps) of doublets (J = 7 cps) at δ 5.99, a 1-proton broadened triplet (~7 cps) at δ 4.57, a 1-proton broad (8 cps at half-height) singlet at δ 3.51, and a 1-proton doublet (J = 12.5 cps) of doublets (J = 8 cps) at δ 2.82, in addition to the large multiplet stretching from δ 1.0 to 2.5 ppm. Since the coupling constant of 12.5 cps is plausible only for geminal coupling in the present case, and since the peak due to at least one of the two nonequivalent hydrogen atoms of the methylene part of the dimethylaminomethyl group should be shifted about as much as that for the dimethylamino hydrogen atoms, the peaks at δ 5.99 and 2.82 ppm must arise from these two hydrogen atoms. They split the peak for the vicinal hydrogen atom on carbon-3 of the ring system into the apparent triplet seen at δ 4.57 ppm. If this hydrogen atom were exo its peak should also be split by the vicinal bridgehead hydrogen atom with a coupling constant of 3--4 cps.[4b] No additional splitting of this magnitude could be seen in our spectrum, which is consistent with a coupling constant in the range 0--2 cps to be expected for vicinal splitting between a bridgehead hydrogen atom and an endo hydrogen atom.[4b]

Reaction of 34.0 g (0.200 mol) of 3-exo-dimethylaminomethyl-2-norbornanone with 14 g (0.20 mol) of hydroxylamine hydrochloride overnight at room temperature, followed by treatment with 8 g (0.20 mol) of sodium hydroxide gave 30 g (82%) of a white powder; mp (after recrystallization from methanol) 184--191°; ir (KBr) 3050, 3175 (s, OH), 2945, 2910, 2850, 2820, 2775 (all s, CH), 1650 (w, C=N), 1430 (s, CH_2), 1279, 1250 (w), 1165 (m), 1100, 1042 (w), 1012 (m), 933 (s, NO), 912, and 820 cm^{-1} (m); pmr ($CDCl_3$) showed peaks at δ 2.25 and 2.35, attributed to the dimethylamino protons of syn and anti isomers, and other absorption from 1.0 to 3.6 ppm (the solution being dilute because of the low solubility of the oxime); exact mass of parent ion, calcd 182.14189, found 182.14223.

Anal. Calcd for $C_{10}H_{18}N_2O$: C, 65.90; H, 9.95; N, 15.37. Found: C, 65.89; H, 9.96; N, 15.12.

3-exo-Dimethylaminomethyl-2-endo-norbornanamine.--A solution of 7.1 g (0.039 mol) of the oxime of 3-exo-dimethylaminomethyl-2-norbornanone[8] was refluxed with 6.0 g (0.15 mol) of lithium aluminum hydride in 700 ml of ether under nitrogen for 44 hr. After the usual work-up, vacuum distillation gave 5.0 g (76%) of colorless liquid, bp 49° (0.12 mm), whose glpc showed traces of several impurities. Recrystallizations of the oxalate salt from methanol--ethanol and liberation of the free amine with potassium hydroxide gave pure 3-exo-dimethylaminomethyl-2-endo-norbornanamine: ir (neat) 3290, 3365 (m, NH_2), 2950, 2870, 2820, 2770 (s, CH), 1570 (m), 1450 (s, CH_2), 1365 (m, CH_2), 1320 (m), 1180, 1158 (w), 1043 (s), and 837 cm^{-1} (m); pmr ($CDCl_3$) δ 2.67 (broadened triplet, 1, J~4.5, 1 cps, $CHNH_2$) 2.12 (s, ~6, CH_2N), 1.75--2.7 (m, ~4, $CHCH_2N$ and H-1), 0.67--1.67 ppm (m, ~9); exact mass of parent ion, calcd 168.16264, found 168.16288. Amine hydrochloride, mp 309--311 (d) from EtOH--MeOH (1:1).

Anal. of the hydrochloride. Calcd for $C_{10}H_{22}N_2Cl_2$: C, 49.80; H, 9.19; N, 11.61. Found: C, 49.75; H, 9.14; N, 11.53.

1,4,4-Trimethyl-3-pyrazolinium Iodide.--The method of Ioffe and Zalevin[17] was used to prepare 1,4-dimethyl-2-pyrazoline: ir (neat) 3060 (w, sp^2-CH), 2750--3000 (s, sp^3-CH), 1630 (w, C=N), 1560 (w), 1430 (m), 1360 (w, CH_3), 1298, 1279 (w), 1220, 1200, 1165, 1128 (m), 1080, 1065, 1045 (w), 963, 940 (m), 886, 859, 832, 810, 775 (m), 739, 655, and 608 cm^{-1} (w); pmr ($CDCl_3$) 1.13 (d, 3, J = 6.2 cps, CH_3C), 2.42 (m, 1, NH=CH), 2.77 (s, 3, CH_3N), 2.83--3.37 (m, 2, CH_2N), and 6.58 ppm (broad s, 1, NH=CH). After 30.5 g (0.31 mol) of this pyrazoline and 59.6 g (0.42 mol) of methyl iodide in 150 ml of benzene had stood overnight at room temperature, 67.5 g (90%) of crude yellow 1,1,4-trimethyl-2-pyrazolinium iodide had seperated. Two recrystallizations from methanol gave pure light yellow crystals: mp 142--145°, ir (KBr) 2975, 2875 (s, CH), 1610 (w, C=N), 1280, 1260, 1230 (m), 1112, 1058, 990 (w), 930 (s), 875 (w), 825, 765, and 705 cm^{-1} (m); pmr (D_2O)[18] δ 1.38 (d, 3, J = 6.5 cps, CH_3C), 3.37 (s, one CH_2N), 3.52 (s, the other CH_2N), 3.33--4.50 (m, CH_2CH), and 8.13 ppm (broad s, 1, N=CH).

2-Methyl-1-dimethylaminopropylamine.--A suspension of 33 g (0.137 mol) of 1,1,4-trimethyl-2-pyrazolinium iodide and 7.9 g (0.2 mol) of lithium aluminum hydride in 400 ml of ether was refluxed for two days and worked up in the usual manner. Distillation gave 2.97 g (19%) of 2-methyl-3-dimethylaminopropylamine: bp 141--142° (lit.[19] 148--150°); ir (neat) 3275 and 3350 cm^{-1} (NH_2); pmr ($CDCl_3$) δ 0.89 (d, 3, CH_3C), 1.32 (s, 2, NH_2), 1.63 [m, 1, $CH(C)_2$], 2.11 (m, 2, CH_2NMe_2), 2.17 (s, 6, CH_2N), and 2.52 ppm (m, 2, CH_2NH_2); exact mass of parent ion, calcd 116.13137, found 116.13148.

Anal. Calcd for $C_6H_{16}N_2$: C, 62.01; H, 13.88; N, 24.11. Found: C, 61.38; H, 13.78; N, 24.09.

4-Methyl-3,4-diazatricyclo[5.2.1.$0^{2,6}$]-8-decene.--A solution of 20 g (0.164 mol) of 3-methylene-2-norbornanone[8] in 100 ml of methanol was added dropwise to 14.8 g (0.32 mol) of methylhydrazine in 60 ml of methanol and refluxed for 3 hr. The solvent and excess methylhydrazine were removed at reduced pressure and the residue vacuum distilled to give 20.1 g (82%) of clear yellow liquid product; bp 56--58° (0.21--0.22 mm); ir (neat) no NH absorption, 2955 (s), 2875 (m), 2830, 2780 (w), 1630 (w, C=N), 1430 (m), 1350, 1226, 1191, 1160 (w), 1137, 1123 (m), 1102, 953, 932 (w), 905 (m), 869, 832 (w), 807 (s), and 759 cm^{-1} (w); pmr ($CDCl_3$) δ 2.72 (s, 3, CH_3) and absorption from 1.17 to 2.67 ppm; uv max (*n*-hexane) 255 nm, (95% ethanol) 246 nm. This hypsochromic shift is in the range of those observed with some other pyrazolines on going from *n*-heptane to ethanol and water.[20]

The methiodide (5) was made from 3.47 g (0.023 mol) of this pyrazoline in 5 ml of benzene by adding 2 ml of methyl iodide in 10 ml of benzene dropwise with cooling. After several hours at room temperature filtration and recrystallization from methanol gave 4.34 g (65%) of methiodide; mp 175--178°; ir (KBr) 2940, 2870 (s, CH), 1620 (m, C=N), 1420 (m, CH_3), 1390, 1265 (m), 1235, 1120 (w), 1098 (m), 1057, 1010, 992, 955, 945 (w), 870 (m), 800, 763 (w), and 636 cm^{-1} (m); pmr (D_2O)[18] δ 3.31 (s, 3, one CH_2N), 3.48 (s, 3, the other CH_2N), 3.58--4.33 (m, 2, CH_2N), and broad absorption from 1.0 to 3.33 ppm.

3-endo-Dimethylaminomethyl-2-endo-norbornanamine.--Gradual addition of 36 g (0.123 mol) of the methiodide 5 to 9.5 g (0.25 mol) of lithium aluminum hydride in 600 ml of ether was followed by 56 hr of refluxing under nitrogen. After addition of 10 ml of water, 10 ml of 15% aqueous sodium hydroxide, and 30 ml of water with agitation, the ether layer was separated and the residue extracted with ether. Concentration and vacuum distillation of the ether solutions gave 3.5 g of material whose glpc showed it to be about 90% pure. Glpc purification on a 12-ft, 20% mannitol, 5% potassium hydroxide, Chromosorb P column gave pure 3-endo-dimethylaminomethyl-2-endo-norbornanamine: ir (neat) 3300, 3370 (w, NH_2), 2945 (s), 2865, 2850, 2810, 2760 (m, CH), 1590 (w), 1450 (m, CH_2), 1370, 1350 (w), 1290, 1262, 1190, 1162, 1105, 1050 (w), 1022 (m), and 855 cm^{-1} (m); pmr ($CDCl_3$) δ 3.33 (d of d, 1, J = 9.5, 4.5 cps, $CHNH_2$), 2.18 (s, 6, CH_2N), and 1.1--2.9 ppm (m, 13); exact mass of the parent ion, calcd 168.16264, found 166.16283.

The ether-insoluble material from the lithium aluminum hydride reduction was extracted with warm methanol. After several recrystallizations from 1:1 methanol--ethanol these extracts yielded 7.84 g (22%) of **7** as white needles: mp 192--193°; ir (KBr) 3125 (m, NH), 3150 (s), 2999, 2960, 2900, 2870 (s, CH), 1700 (w), 1450 (s, CH_2), 1425, 1380, 1340, 1300, 1292, 1252 (m), 1237, 1215, 1194, 1168 (w), 1124 (m), 1087, 1052 (w), 1020 (s), 989, 963, 938 (m), 933 (w), 921, 917 (m), 885 (w), 860 (m), 842, 817, 799 (w), 772 (m), 735 (m), 695 (m), 582, 529, and 457 cm^{-1} (w); pmr (D_2O)[18] δ 4.02 (d of d, J = 10.5, 5 cps, one CH_2N proton), 3.63 (d of d, J = 10.5, 2 cps, the other CH_2N proton), 3.42 (s, one CH_2N), 3.34 (s, the other CH_2N), and broad absorption from 1.33 to 3.50 ppm.

Anal. Calcd for $C_{10}H_{18}N_2I$: C, 40.83; H, 6.51; N, 9.52. Found: C, 40.63; H, 6.63; N, 9.25.

A solution of 4.34 g (0.015 mol) of **5** and 1.7 g (0.027 mol) of sodium cyanoborohydride in 100 ml of methanol at about pH 4.4 was stirred for 4.5 hr at room temperature, then concentrated, added to water, and made basic with 1 *N* sodium hydroxide. Several extractions with ether, concentration, and recrystallizations from ethanol--methanol gave 2 g (46%) of **7**, ir and pmr identical to that obtained as described in the preceding paragraph.

o-(Dimethylaminomethyl)benzonitrile.--Dropwise addition of 40 g (0.204 mol) of *o*-cyanobenzyl bromide in 150 ml of benzene to about 100 g of cold dimethylamine was followed by 3 hr of stirring at room temperature. After removal of a white precipitate by filtration the solution was concentrated and vacuum distilled to give 25.5 g (78%) of *o*-(dimethylaminomethyl)benzonitrile: bp 62--63° (0.14 mm); ir (neat) 2230 (s, C≡N), 1600 (s, aromatic C=C), 1030 and 3070 (w, aromatic C-H), 2980 (m), 2950 (m), 2860 (m), 2825 (m), 2775 (m), 1480 (w), 1450 (m), 1355 (m), 1250 (m), 1180 (m), 1155 (w), 1100 (w), 1035 (s), 850 (w), 857 (w), 770 (s), and 715 (w); pmr ($CDCl_3$) δ 2.29 (s, 6, CH_2N), 3.64 (s, 2, CH_2), and 7.2--7.8 ppm (m, 4, aromatic CH); exact mass of parent ion, calcd 160.10004, found 160.10027.

o-(Dimethylaminomethyl)benzylamine.--A solution of 3.25 g of sodium borohydride in 12 ml of 8 *N* aqueous sodium hydroxide was added dropwise to 13.3 g (0.083 mol) of *o*-(dimethylaminomethyl)benzonitrile and 5 g of Raney nickel in 40 ml of methanol. After the evolution of hydrogen had stopped the solution was filtered, concentrated, and about half of it accidentally spilled. Treatment of the remainder with 9 g of potassium hydroxide caused the separation of about 5 g of an oil that was distilled to give 4 ml of *o*-(dimethylaminomethyl)benzylamine: bp 61.5--62° (0.2 mm); ir (neat) 3260, 3350 (w, NH_2), 3060, 3010 (w, sp^2-CH), 2975, 2940, 2855, 2810, 2760 (m, sp^3-CH), 1590 (w), 1450 (m), 1350 (m), 1255, 1178 (m), 1100 (w), 1050 (m), 1025 (s), 850, 755, and 740 cm^{-1} (m); pmr ($CDCl_3$) δ 1.81 (s, 2, NH_2), 2.20 (s, 6, CH_2N), 3.43 (s, 2, CH_2), 3.84 (s, 2, CH_2), and 7.13--7.38 ppm (m, 4, aromatic CH).

Anal. of the hydrochloride. Calcd for $C_{10}H_{16}N_2Cl_2$: C, 50.64; H, 7.65; N, 11.81. Found: C, 50.03; H, 7.64; N, 11.53.

In another run in which poor quality sodium borohydride was used the product obtained contained 18% starting material, but the yield was 65% (corrected for the impurity).

N,N,N',N',2,2-Hexamethyl-1,3-propanediamine.--To 9.6 ml (0.25 mol) of ~98% formic acid was added 4.64 g (0.0357 mol) of N,N,2,2-tetramethyl-1,3-propanediamine slowly with cooling and stirring. After 11 ml (0.14 mol) of 37% formaldehyde had been added the solution was refluxed for 15 hr, cooled, acidified with 36 ml of 4 *N* hydrochloric acid, and evaporated to dryness. Solution of the residue in 20 ml of water and treatment with 20 ml of 18 *N* sodium hydroxide caused an oil to separate. The oil was combined with two 15-ml benzene extracts of the aqueous layer, dried over potassium carbonate, and distilled through a 13-cm Vigreux column to give 3.55 ml (63%) of N,N,N',N',2,2-hexamethyl-1,3-propanediamine: bp 162°; ir (neat) 2970, 2945, 2855, 2820, 2760 (s, CH), 1450 (m), 1375, 1350, 1300 (w), 1255, 1150 (m), 1120, 1100 (w), 1047 (s), and 947 cm^{-1} (m); pmr ($CDCl_3$) δ 0.88 (s, 6, CH_3C), 2.12 (s, 4, CH_2), and 2.27 ppm (s, 12, CH_2N); exact mass of parent ion, calcd 158.17828, found 158.17848.

Anal. Calcd for $C_9H_{22}N_2$: C, 68.29; H, 14.01; N, 17.70. Found: C, 68.11; H, 14.18; N, 17.90.

Although we have found no report of the synthesis or properties of this compound, its perchlorate has been patented for use as a propellant.[21]

o-Bis(dimethylaminomethyl)benzene.--Essentially the same procedure[22] described in the preceding section was applied to 19.3 g (0.098 mol) of 82% pure *o*-(dimethylaminomethyl)benzylamine to obtain 15.5 g of 86% pure (by glpc) *o*-bis(dimethylaminomethyl)benzene. Recrystallization of the hydrochloride and regeneration of the base gave 12.3 g of 95% pure material: bp 96--96.5° (8 mm); ir (neat) 3060, 3015 (w, aromatic CH), 2970, 2940, 2855, 2815 (s, sp^3-CH), 1450 (s, CH_2), 1350 (m, CH_3), 1300 (w), 1252, 1177 (m), 1152, 1100 (w), 1047 (m), 1027, 848, and 752 cm^{-1} (s); pmr ($CDCl_3$) δ 2.21 (s, 12.5, CH_3), 3.51 (s, 4.0, CH_2), and 7.0--7.5 ppm (m, 4.1, CH); monoperchlorate, white needles from H_2O, mp 188--189°.

Anal. of the monoperchlorate. Calcd for $C_{12}H_{21}N_2ClO_4$: C, 49.23; H, 7.23; Cl, 12.11. Found: C, 49.12; H, 7.16; Cl, 12.29.

Registry No.—1, 6159-17-7; 1 oxime (*Z*), 53369-67-8; 1 oxime (*E*), 53403-31-9; 2, 53369-68-9; 2 hydrochloride, 53403-32-0; 3, 10289-77-7; 4, 53369-69-0; 5, 53403-33-1; 6, 53403-34-2; 7, 53369-70-3; 2,2-dimethyl-3-dimethylaminopropanal, 15451-14-6; hydroxylamine hydrochloride, 5470-11-1; 2,2-dimethyl-3-dimethylaminopropanal oxime, 7405-24-5; 2,2-dimethyl-3-dimethylaminopropylamine, 53369-71-4; 2-(dimethylaminomethyl)cyclohexanone oxime, 53369-72-5; *cis*-2-(dimethylaminomethyl)cyclohexylamine, 53369-73-6; *trans*-2-(dimethylaminomethyl)cyclohexylamine, 53369-74-7; 2-methyl-3-dimethylaminopropylamine, 6105-72-2; 4-methyl-3,4-diazatricyclo[5.2.1.$0^{2,6}$]-2-decene, 53369-75-8; 3-methylene-2-norbornanone, 5597-27-3; methylhydrazine, 60-34-4; *o*-(dimethylaminomethyl)benzonitrile, 53369-76-9; *o*-cyanobenzyl bromide, 22115-41-9; dimethylamine, 124-40-3; *o*-(dimethylaminomethyl)benzylamine, 53369-77-0; *o*-(dimethylaminomethyl)-benzylamine hydrochloride, 53369-78-1; *N,N,N',N'*,2,2-hexamethyl-1,3-propanediamine, 53369-79-2; *o*-bis(dimethylaminomethyl)-benzene, 53369-80-5; *o*-bis(dimethylaminomethyl)benzene monoperchlorate, 53369-81-6.

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The Intrinsic Hydrophilic Character of Organic Compounds. Correlations in Terms of Structural Contributions[1]

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Log γ, where $\gamma = c_w/c_g$, with c_w being the concentration of a compound in dilute aqueous solution at 25° and c_g the concentration in the gas phase in equilibrium with the aqueous solution (both in moles per liter), is defined as the intrinsic hydrophilicity of a compound. Values for 292 compounds are listed, and parameters for a bond contribution correlation and a group contribution correlation are determined. Major deviations from the correlations arising from distant polar interactions (interactions between halogen, oxygen, nitrogen, or sulfur substituents separated by more than one carbon atom) are observed. The significance of such deviations and of the relative magnitudes of the group contributions is discussed.

The hydrophilic and hydrophobic character of compounds[2,3] is commonly discussed in terms of data on systems involving an aqueous phase and some other liquid phase. Such data, which include water solubilities and distribution coefficients between water and some other solvent,[4,5] have been quite useful. They depend on differences in free energy (or of enthalpy or some other property) of the molecules of a compound when they are surrounded by water molecules and when they are surrounded by molecules of the other solvent. Hence they depend not only on the nature of the compound in question and on the nature of water but also on the nature of the other solvent in the system in question. The interpretation of data may be simplified somewhat if we consider the difference in free energy of molecules of a given compound when they are surrounded by water and when they are surrounded by nothing, that is, when they are in the gas phase. We shall consider the tendency of a molecule to go from the gas phase to dilute aqueous solution to be a measure of its *intrinsic hydrophilic character.*

In order to discuss the relationship between molecular structure and the intrinsic hydrophilic character of compounds in quantitative terms we have carried out correlations in terms of structural additivity schemes. Such schemes have been used in correlations of enthalpies of formation, entropies, and other thermodynamic properties.[6-8] These correlations have been largely restricted to the properties of compounds in the gas phase. They would be more useful if they were extended to the common solvents in which most reactions are run. Such extensions would consist of correlations concerning transfer processes between the gas phase and the solvents of interest. Butler and coworkers pointed out long ago that the free energy of transfer of organic compounds from the gas phase to aqueous solution is an approximately additive function of the groups present in the compounds.[9-11] Pierotti, Deal, and Derr