organic layer was dried over anhydrous sodium sulfate. The solvent was removed *in vacuo*. The product mixture, oil or crystalline, was analyzed by nmr for isomer distribution. Purification was achieved on an alumina column eluted with dichloromethane or benzene–hexane (2:3 v/v). This solvent was removed, and the isomers were fractionally crystallized with ethanol. In general, the cis isomers were more insoluble in ethanol. Elemental analyses were consistent with the assigned structures. Yields were reported for the combined isolated isomers.

Isomerization of *cis*- and *trans*-1,4-Diphenyl-3-chloro-2-azetidinone (1).—The *cis*- or *trans*-**1** (5.0 g, 1.9×10^{-2} mol) was dissolved in 50 ml of DMF. To this was added 1.8 ml (1.9×10^{-2} mol) of phosphoryl chloride and 1.8 g (1.9×10^{-2} mol) of monochloroacetic acid. The solution was stirred at reflux and sampled every 2 hr. The 5-ml samples were dissolved in 10 ml of dichloromethane and extracted with 10 ml of water. The organic layer was evaporated and dissolved in chloroform-d_1 for nmr determination of the isomer distribution. The equilibrium isomer mixture was established within 7 hr from the cis isomer, but 22 hr were required for the trans isomer to reach the 53% cis–47% trans relationship.

2-Chloro-*N*-(α-chlorobenzyl)acetanilide (11).—A benzene solution of 30 g (0.16 mol) of benzalaniline was cooled to 0° with an ice bath. To this was added, dropwise, 18.7 g (0.16 mol) of chloroacetyl chloride over 2 hr while maintaining 0°. Moisture will cause hydrolysis of **11**, and chloroacetanilide may precipitate if the reaction is not performed under a dry atmosphere. Recent evidence indicated that adducts such as **11** may be in equilibrium with acyl chloride and imine.[5] The solvent was removed under reduced pressure and a white solid (46.5 g, 96%) was obtained, mp 50–52°. Since the product hydrolyzed readily, it was stored under dry nitrogen. Two characteristic nmr signals (chloroform-d_1) were obtained: nmr δ 3.76 (2 H, s, CH_2Cl), and 7.85 (1 H, s, ClCHN); ir ($CHCl_3$) 1661 cm^{-1} (carbonyl). For comparison, the carbonyl absorbance for chloroacetanilide ($CHCl_3$) was 1681 cm^{-1}.

Anal. Calcd for $C_{15}H_{13}Cl_2NO$: C, 61.2; H, 4.42; N, 4.7. Found: C, 60.7; H, 4.56; N, 5.06.

2-Chloro-*N*-(α-chloro-*o*-nitrobenzyl)-*p*-acetanisidide (13).—The adduct was prepared in a similar manner as **11**. Hydrolysis of **13** did not occur as readily as **11**. A light yellow solid (92%) was recovered: mp 115–117° dec; nmr (chloroform-d_1) δ 3.81 (2 H, s, CH_2Cl), 3.77 (3 H, s, OCH_3), 8.27 (1 H, s, ClCHN); ir ($CHCl_3$) 1686 (carbonyl), 1533 (asymmetrical nitro), and 1352 cm^{-1} (symmetrical nitro).

Anal. Calcd for $C_{16}H_{14}Cl_2N_2O_4$: C, 52.0; H, 3.79; N, 7.6. Found: C, 52.2; H, 3.97; N, 7.7.

Registry No.—**1b**, 27348-77-2; **3a**, 33281-33-3; **3b**, 33281-34-4; **4a**, 33949-24-5; **4b**, 33276-88-9; **5a**, 33949-26-7; **6b**, 33276-92-5; **7a**, 33949-28-9; **7b**, 33276-93-6; **8b**, 33949-30-3; **9a**, 33949-31-4; **9b**, 33276-96-9; **10a**, 33949-33-6; **10b**, 33276-97-0; **11**, 33949-35-8; **13**, 33949-36-9.

The *A* Value of the Deuterioamino Group Determined by the Nuclear Magnetic Resonance Peak Area Method at −93°

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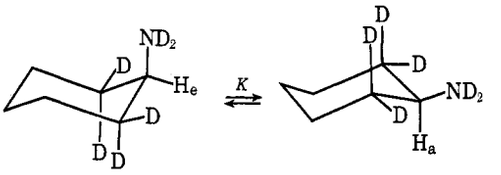
Although there have been many reports concerning the measurement of the axial *vs.* equatorial conformational preference of the hydroxyl group in cyclohexanol,[3] similar data concerning the amino group is relatively scarce, having been derived from indirect kinetic, pK_a, and nuclear magnetic resonance (nmr) techniques which necessarily involve the use of model compounds.[4] There have been no reports concerning the direct measurement of the conformational preference of the amino group in cyclohexylamine itself free from the constraints and possible distortions of locking substituents.[4]

This report concerns the direct measurement of the *A* value[5] (eq 1–2) of the deuterioamino group (ND_2)



(1)

$$A \text{ value} = -\Delta G^\circ = \frac{RT \ln K}{1000} \qquad (2)$$

in cyclohexylamine-*N*,*N*,2,2,6,6-d_6 (**1**) using the low-temperature nmr method. **1** was prepared from cyclohexanol-2,2,6,6-d_4 by the method of Streitwieser and Coverdale[6] and was purified by preparative glpc.

Examination of the ^1H nmr spectrum (60 or 100 MHz) of **1** in CD_3OD revealed broadening or coalescence of the various complex $(CH_2)_3$ resonances from about −40 to −70° and subsequent sharpening of the complex $(CH_2)_3$ spectrum at lower temperatures. Likewise, the HCN resonance broadened and sharpened as the temperature was lowered, separating into a large singlet resonance at δ 2.49 (H_a, eq 1) and a much smaller singlet at δ 3.02 (H_e, eq 1). Such spectral behavior is completely consistent with a slowing of the axial ⇄ equatorial equilibration in **1** (eq 1) on the nmr time scale and the direct observation of axial and equatorial conformers. The observed chemical shifts for axial and equatorial HCN protons in **1** are in good agreement with axial (δ 2.50) and equatorial (δ 3.09) HCN chemical shifts in *trans*- and *cis*-4-*tert*-butylcyclohexylamine, respectively (95% ethanol at room temperature).[4a]

Thus, we examined the ^1H nmr spectrum of **1** at −93° in three solvent systems at different concentrations obtaining the axial:equatorial conformer ratio (eq 1) by weighing cut-outs of the HCN proton resonances and by hand planimeter integration. The various equilibrium constants (*K*, eq 1) and associated free energy differences are compiled in Table I. It should be noted that the large equilibrium constants (Table I) at least by nmr standards necessitated the use of relatively high radiofrequency power levels, introducing the possibility of differential saturation effects.[5]

The various *A* values compiled in Table I are in remarkably good agreement with those obtained by more indirect methods.[4] Although the *A* value of ND_2 does

(1) Alfred P. Sloan Research Fellow, 1971–1973.

(2) Supported by Worcester Polytechnic Institute Undergraduate Work-Study Program, Summer 1971.

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TABLE I
A VALUE OF ND_2 AS A FUNCTION OF CONCENTRATION AND SOLVENT AT −93°

Solvent	Concn, mol/l.	K[a]	A value, kcal/mol
CD_3OD	0.5	34 ± 5	1.3 ± 0.1
	1.0	42 ± 7	1.3 ± 0.1
	1.5	56 ± 9	1.4 ± 0.1
	2.0	55 ± 9	1.4 ± 0.1
50% Pyridine–50% CH_2CHCl (v/v)	2.0	26 ± 4	1.2 ± 0.1
50% CD_2Cl_2–50% toluene-d_8 (v/v)	2.0	55 ± 10	1.4 ± 0.1

[a] According to eq 1; the error assigned to K is the maximum deviation in the measured value.

not change appreciably with concentration in CD_3OD (Table I), K (eq 1) does increase at increasing concentrations of **1**, suggesting an increasing degree of self-association by **1** in preference to complexation by CD_3OD. In those solvents which do not form as strong hydrogen bonds, *e.g.*, 50% pyridine–50% CH_2CHCl (v/v), the equatorial ND_2 conformational preference is reduced slightly in agreement with previous results.[4]

It is then instructive to compare the A value of the amino group to other functionalities having nitrogen bonded to the cyclohexane ring (Table II).[7] Although

TABLE II
PERTINENT A VALUES

Group	A Value, kcal/mol
$-ND_2$	1.2[a]
$-NO_2$	1.1[b]
$-N{=}C{=}N\text{-}C_6H_{11}$	1.0[b,c]
$-N{=}C{=}O$	0.51[b]
$-N{=}C{=}S$	0.28[b]
$-N{\equiv}C$	0.21[b]

[a] 2.0 M in 50% pyridine–50% CH_2CHCl at −93°. [b] 2.0 M in CS_2 at −80° except NO_2 at −90°; see ref 7. [c] See ref 8.

unique hybridization of nitrogen in the case of –NCO, –NCS, and $-N{\equiv}C$ apparently leads to more substituent cylindrical symmetry and a relatively low A value,[8] the A value for ND_2 is only slightly larger than that for $-NO_2$ or $-N{=}C{=}N{-}C_6H_{11}$ (Table II). Indeed, the higher A value for $-ND_2$ as compared to $-NO_2$ may reflect stronger solvent complexation of $-ND_2$ *via* hydrogen bonding and an effectively larger group.

Experimental Section

Nmr spectra were obtained using a Varian Associates HR-60A spectrometer equipped with a custom-built variable temperature probe or using a Varian HA-100 spectrometer equipped with the Varian variable temperature probe and accessories. Temperature measurement was performed using a copper–constantan thermocouple inserted into the sample (HA-100) or permanently in place in the probe (HR-60A) and is accurate to ±0.3° at the sample.

Registry No.—Cyclohexylamine-$N,N,2,2,6,6$-d_6, 33885-12-0.

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Studies on the Syntheses of Heterocyclic Compounds. CDLX.[1] Benzyne Reaction. XIII.[2] Benzyne Reaction of Halogenobenzenes with *N*-Alkylmorpholines

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In previous papers,[3-5] we reported the benzyne reaction of a number of ortho-substituted halogenobenzenes with acetonitrile or phenylacetonitrile in various organic solvents together with the appropriate amines in the presence of sodium amide to give the desired meta-substituted phenylacetonitriles in addition to the meta-substituted amino compounds. During these investigations, when *N*-methylmorpholine was used as solvent in the benzyne reaction of *o*-chloroanisole, 3-methoxy-*N*-methylaniline (**7b**)[3] was obtained as an unusual product in comparatively good yield. Although the formation of Stevens type[6-11] or Sommelet type[12] rearranged products by the reaction of amines with benzyne has been reported, formation of the *N*-alkylaniline derivative by the benzyne reaction of halogenobenzene with N-substituted alicyclic amines has not previously been described, and we have therefore studied several other cases of this reaction.

The benzyne reaction of bromobenzene, *o*-chloroanisole, and *o*-benzyloxychlorobenzene with *N*-methyl-, *N*-ethyl-, *N*-propyl-, *N*-benzylmorpholine, *N*-methylpiperidine, and *N,N'*-dimethylpiperazine was examined and found to give *N*-alkylaniline derivatives. Furthermore, in the case of the benzyne reaction of the halogenobenzenes with *N*-alkylmorpholines, 2-(*N*-alkyl-*N*-phenyl)aminoethanols were obtained in addition to the desired products. All the known products were identified with authentic specimens by comparison of spectroscopic data. The structures of the unknown products were determined by microanalyses and nmr, ir, and mass spectra. These results are shown in Table I. In the benzyne reaction of bromobenzene with *N*-methylmorpholine, when a mixture of bromo-

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