Registry No.—**2d**, 65899-17-4; **13**, 65899-18-5; **14**, 66142-11-8; C_8K, 12081-88-8; cyclohexylamine, 108-91-8; nonanal, 124-19-6; 1-phenylpropan-2-one, 103-79-7.

References and Notes

(1) E. C. Blossey and D. C. Neckers, Ed., "Solid Phase Synthesis", Dowden, Hutchinson and Ross, Stroudsburg, Pa., 1975.
(2) D. C. Neckers, *J. Chem. Educ.*, **52**, 695 (1975).
(3) (a) M. E. Vol'pin, Y. N. Novikov, N. D. Lapkina, V. I. Kasatochkin, Y. T. Struchkov, M. E. Kazakov, R. A. Stukan, V. A. Povitskij, Y. S. Karimov, and A. V. Zvarikina, *J. Am. Chem. Soc.*, **97**, 3366 (1975); (b) H. B. Kagan, *CHEMTECH*, **6**, 510 (1976).
(4) J. Bertin, H. B. Kagan, J. L. Luche, and R. Setton, *J. Am. Chem. Soc.*, **96**, 8113 (1974).
(5) J. M. Lalancette, M. J. Fournier-Breault, and R. Thiffault, *Can. J. Chem.*, **52**, 589 (1974).
(6) J. M. Lalancette, G. Rollin, and P. Dumas, *Can. J. Chem.*, **50**, 3058 (1972).
(7) G. A. Olah and J. Kaspi, *J. Org. Chem.*, **42**, 3046 (1977).
(8) M. C. Robert, M. Oberlin, and J. Mering, *Chem. Phys. Carbon*, **10**, 141 (1973).
(9) M. A. M. Boersma, *Catal. Rev.*, **10**, 243 (1974).
(10) H. Podall and W. E. Foster, *J. Org. Chem.*, **23**, 401 (1958).
(11) C. Ungurenasu and M. Palie, *J. Chem. Soc., Chem. Commun.*, 388 (1975).
(12) D. Savoia, C. Trombini, and A. Umani-Ronchi, *J. Chem. Soc., Perkin Trans. 1*, 123 (1977).
(13) D. Savoia, C. Trombini, and A. Umani-Ronchi, *Tetrahedron Lett.*, 653 (1977).
(14) Recently the alkylation of 1- and 2-tetralone with allyl bromide in the presence of C_8K has been reported: H. Hart, B.-I. Chen and C.-T. Peng, *Tetrahedron Lett.*, 3121 (1977).
(15) (a) G. Wittig, H. D. Frommeld, and P. Suchanek, *Angew. Chem., Int. Ed. Engl.*, **2**, 683 (1963); (b) G. Wittig and H. F. Frommeld, *Chem. Ber.*, **97**, 3548 (1964); (c) G. Wittig and H. Reiff, *Angew. Chem., Int. Ed. Engl.*, **7**, 7 (1968); (d) T. Cuvigny, H. Normant, and P. Hullot, *Bull. Soc. Chim. Fr.*, 3976 (1970).
(16) (a) T. Cuvigny and H. Normant, *Synthesis*, 198 (1977); (b) M. Larchevêque, G. Valette, and T. Cuvigny, *ibid.*, 424 (1977).
(17) A. I. Meyers, A. Nabeya, H. W. Adickes, I. R. Politzer, G. R. Malone, A. C. Kovelesky, R. L. Nolen, and R. C. Portnoy, *J. Org. Chem.*, **38**, 36 (1973).
(18) The general observed trend in alkylation of imines and *N,N*-dimethylhydrazones leads to the introduction of the new alkyl group on the less alkylated side:[18a] G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963); T. Cuvigny, M. Larchevêque, and H. Normant, *Tetrahedron Lett.*, 1237 (1974); E. J. Corey and D. Enders, *ibid.*, 3 (1976); M. E. Jung and T. J. Shaw, *ibid.*, 3305 (1977).
(19) Amines are freed by the aqueous acid after imine hydrolysis with solid KOH and extracted with ether. The identification of *N*-alkylated cyclohexylamine is accomplished through the enhancing of the gas chromatographic peak with an authentic sample obtained by independent synthesis, on different stationary phases: SF96, FFAP, and Carbowax 20M (poly(ethylene glycol)).
(20) T. Takeshima, M. Muraoka, H. Asaba, and M. Yokoyama, *Bull. Chem. Soc. Jpn.*, **41**, 506 (1968).
(21) D. J. Curran and S. Siggia, "The Chemistry of the Carbon-Nitrogen Double Bond", S. Patai, Ed., Interscience, London, 1970, Chapter 3.

Conformational Studies of Some 2-*exo*-Alkyl-3-benzyl-3-azabicyclo[3.3.1]nonanes

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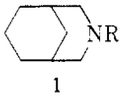
The conformations of three 3-benzyl-3-azabicyclo[3.3.1]nonanes substituted with 2-*exo*-alkyl groups have been studied by analysis of their proton and carbon-13 nuclear magnetic resonance spectra. These compounds were prepared by stereoselective alkylation of aldimmonium ion **4** with Grignard reagents. The presence of 2-methyl and 2-ethyl substituents was shown to cause the ring system to prefer a flattened double-chair conformation similar to that of the unsubstituted compound (**3a**). Introduction of a 2-isopropyl substituent, however, caused a change in favor of the chair–boat conformation.

Considerable attention has been directed toward synthesis and conformational analysis of substituted bicyclo[3.3.1]-nonanes and heterocyclic analogues, compounds which have potential as models for extension of the concepts and theories of stereochemistry.[1] In this connection, our interest has been centered on the 3-azabicyclo[3.3.1]nonane ring system (**1**). According to relative energy minima, **1** may exist in any of four conformations: double chair, chair–boat, boat–chair, and double boat. The most stable conformer of **1** is the double chair, as is the case with its *N*-alkyl analogues.[2] However, in this and in the conformationally similar diazabicyclic compound **2a**,[3a] minor structural modifications have been shown



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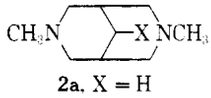
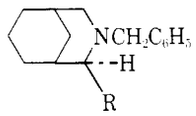


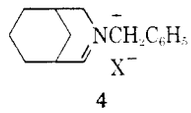
2a, X = H
b, X = OH

to cause conformational changes. For example, the methiodide of **1** (R = CH_3) and *N,N'*-dimethylbispidinol (**2b**) appear to prefer chair–boat conformations.[3b,c] While there have been a number of conformational studies of symmetrical derivatives of **1** and isomers, less information is available concerning the conformational preferences of unsymmetrical derivatives. Accordingly, we have investigated the effect of 2-*exo*-alkyl substituents on the conformation of **1**.

Among other methods, proton magnetic resonance (^{1}H NMR) spectrometry has proven to be effective in resolving configurational and conformational features in azabicyclic systems.[4] More recently, carbon-13 nuclear magnetic resonance (^{13}C NMR) spectrometry has been shown to be a particularly powerful tool in such studies.[5] In this paper, we report the synthesis of 3-benzyl-3-azabicyclo[3.3.1]nonane (**3a**) and three of its 2-*exo*-alkyl analogues (**3b–d**) and some conclusions regarding the preferred conformations of these last compounds as determined from analysis of their ^{1}H and ^{13}C NMR spectral features.



3a, R = H
b, R = CH_3
c, R = CH_2CH_3
d, R = *i*-C_3H_7



4

Results and Discussion

Compounds **3b–d** were each prepared from **3a** in two steps.[6] Oxidation of **3a** with bromine in methylene chloride[7] furnished aldimmonium salt **4** (X = bromide or perchlorate).

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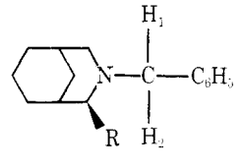
Table I. ^{1}H NMR Spectral Features of 2-Alkyl-3-benzyl-3-azabicyclo[3.3.1]nonanes[a]

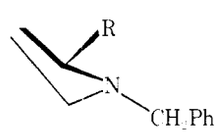


Compd	Registry no.	Chemical shifts, ppm (J, Hz)[a]		
		CCH_3 of R	Aliphatic NCH_2 and NCH	H_1; H_2
3a	19015-40-8		1.95–2.29 (dd,[b] 2 H), 2.65–3.00 (dd,[b] 2 H)	3.28 (s); 3.28 (s)
3b	66224-91-7	0.97 (d) (7)	2.52–3.17 (m, 3 H)	3.42 (d); 3.62 (d) (14)
3c	66224-92-8	0.75 (t) (7)	2.50–2.90 (m, 3 H)	3.45 (d); 3.65 (d) (14)
3d	66224-93-9	0.88 (d) (7), 1.00 (d) (7)	2.15–2.45 (m, 2 H), 2.90–3.20 (m, 1 H)	3.50 (d); 4.07 (d) (14)

[a] Spectra were taken at 60 MHz using chloroform-*d* as solvent and 1% tetramethylsilane as an internal standard. Aromatic protons were seen as broad singlets centered at 7.31 ppm (average value). [b] J_1 = 10.5 Hz and J_2 is unresolved.

Addition of this salt to an excess of the appropriate Grignard reagent gave **3b–d**. The relative configurational assignment of the alkyl groups in these compounds is based on the assumption that nucleophilic attack will be from the less hindered exo side of **4**, in analogy with the reported preference for addition of various nucleophiles to bicyclo[3.3.1]non-2-ene and bicyclo[4.3.1]dec-2-ene derivatives.[8]

^{1}H NMR Studies. The extent of chemical shift nonequivalence in benzylic methylene protons in ^{1}H NMR spectra[9] has been utilized not only in determination of relative configurations of piperidines,[10a] piperazines,[10] and 1-azadecalins[11] but also in qualitative conformational analysis of heterocyclic and azabicyclic systems.[3,12] From these investigations it has become clear that nonequivalence will be observed in these cyclic systems if the benzyl group is vicinal to a single equatorial alkyl substituent, as in **5**.[10c,12] However, if this substituent is axial as in **6**, nonequivalence will not be seen.[10c]



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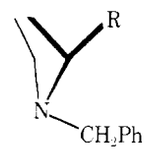


6

Salient features in the ^{1}H NMR spectra of **3a–d** are shown in Table I. The benzylic methylene protons of **3b–d** exhibit observable nonequivalence. The chemical shift difference between these protons is 0.20 ppm in **3b** and **3c** and is increased to 0.57 ppm in **3d**. Based on the above analysis, two explanations may be offered to account for this increase. The isopropyl group could cause an increased disparity in benzyl rotamer populations in **3d** relative to **3b** and **3c**,[13] assuming that all three compounds prefer the conformation in which their alkyl groups are equatorial, as represented by partial structure **5**. This in turn would result from a more severe steric interaction of the isopropyl substituent with the benzyl group in **3d**, as compared with that of the methyl and ethyl substituents with this group in **3b** and **3c**, respectively. In support of this, inspection of molecular models of these compounds showed that the methyl and ethyl substituents should have about the same influence on benzyl group rotamer populations, with the isopropyl substituent having an increased influence. Alternatively, the greater $\Delta\delta$ could be due to a predominance, in **3d**, of conformer **5** over conformer **6**, with a relatively smaller percentage of **5** (greater percentage of **6**) representing both **3a** and **3b**.

Consideration of the region of the spectra in which aliphatic *N*-methylene and *N*-methine protons are found lends further support to the contention that **5** best represents the heterocyclic ring in **3d** but casts doubt as to the conformations of this ring in **3b** and **3c**. The spectrum of **3d** features a broad one proton multiplet centered at 3.05 ppm and a two proton multiplet at 2.15–2.45 ppm. From analysis of the ^{1}H NMR spectra of numerous related cyclic and polycyclic compounds, it has been suggested that protons anti to the nitrogen lone pair electrons appear below 2.50 ppm and those gauche to these electrons between 2.70 and 3.10 ppm.[14] Therefore, **3d** has two protons anti and one proton gauche to the lone pair, indicative of the predominance of conformer **5**. The spectra of **3b** and **3c** exhibit no signals indicative of anti protons, but multiplets integrating for three protons are present in the region of the spectra where gauche protons are generally found. These data do not seem to support the presence of either **5** or **6** as being representative of the heterocyclic ring of **3b** and **3c**.

In order to clarify the conformational preferences of the ring systems in **3a–d** in general and in **3b** and **3c** in particular, a comparison of their ^{13}C NMR spectra was made.

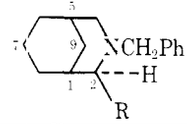
^{13}C NMR Studies. The sensitivity of carbon-13 chemical shifts to changes in molecular geometry is the basis for the application of ^{13}C NMR spectrometry in conformational analysis.[5,15]

In Table II are listed the carbon-13 chemical shifts of compounds **3a–d**. Assignments were made in the following manner. Off resonance decoupled spectra were obtained in order to distinguish between methyl, methylene, and methine carbon atoms. Most of the individual assignments of methylene and methine carbons of **3b–d** could be made by consideration of the ^{13}C NMR shift values of **3a** and related bicyclo[3.3.1]nonanes,[16] taking into account the anticipated substituent parameters.

In addition to the greater complexity of the spectra of **3b–d** in relation to that of **3a**, consistent differentiating features are the positions of C-4, C-9, and the benzylic methylene carbons, which are found at 6.1–7.5, 5.3–6.2, and 4.6–5.8 ppm upfield from the corresponding carbons in the spectrum of **3a**, respectively. The upfield shift of the benzylic methylene carbons is indicative of steric congestion due to the presence of the 2-alkyl groups; those of C-4 and C-9 seem to be due to stereochemical features which will be discussed below.

The spectral positions of C-7 and C-2′ appear to provide the most unambiguous evidence regarding the ring system conformations of **3b–d**. A 5.0 ppm upfield shift of C-7 is seen in **3d** relative to **3a**. Based on the ^{1}H NMR spectral characteristics of **3d** (see above), which suggested that its piperidine ring was mainly in the boat conformation, we attribute this difference to a gauche relationship of the 7-*endo*-hydrogen with the endo hydrogens at C-2 and C-4. This interaction has been proposed to account for the ca. 5 ppm upfield shift of C-7 in the spectra of chair–boat conformers with respect to those of

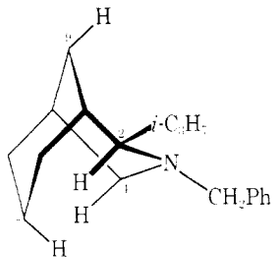
Table II. ^{13}C Chemical Shifts of 2-Alkyl-3-benzyl-3-azabicyclo[3.3.1]nonanes[a]



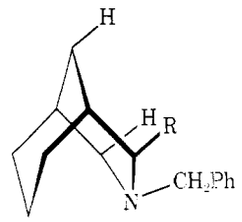
Compd	R	C-1	C-2	C-4	C-5	C-6	C-7	C-8	C-9	C-2′	CH_2Ph[e]
3a	H[b]	29.7	59.9	(59.9)	(29.7)	31.5	22.6	(31.5)	34.4		64.3
3b	CH_3	35.5	57.7	52.4	29.6	32.8[c]	22.1	32.0[c]	28.3	10.1	59.7
3c	C_2H_5	29.9[c]	65.1	52.9	29.3[c]	32.7[d]	22.0	32.0[d]	28.2	15.4[f]	59.5
3d	i-C_3H_7	27.7[c]	67.2	53.8	29.1[c]	33.0[d]	17.6	31.6[d]	29.1	27.2[c,f]	58.5

[a] Spectra were taken using chloroform-*d* as solvent. Shifts are given in ppm downfield from internal tetramethylsilane. [b] Chemical shifts of symmetry-related atoms are enclosed in parentheses. [c,d] These assignments are interchangeable. [e] Phenyl ring carbons were found at 140.3 (α-C), 128.7 (σ-C), 128.0 (m-C), and 126.4 (p-C) ppm (average values). [f] Chemical shifts for C–CH_3: **3c**, 11.8 ppm; **3d**, 16.2 and 19.8 ppm.

chair–chair conformers in the closely related 9-azabicyclo[3.3.1]nonan-3-ols.[16b] This implies that the cyclohexane ring of **3d** prefers the chair conformation and that the overall ring system may be best represented by I. Since the



I



II

position of C-7 in **3b** and **3c** does not differ greatly from that in **3a**, the gauche endo hydrogen relationship must not be present, and the rings of all of these compounds therefore appear to prefer a flattened double-chair conformation (II; R = H, CH_3, and C_2H_5).

Additional evidence in favor of these conformational representations is provided by the position of C-2′: methyl, methylene, and methine in the spectra of **3b–d**, respectively. The methyl carbon of **3b** is seen at 10.1 ppm, which is about 10 ppm upfield from its position in 2-methylpiperidine derivatives in which it assumes an equatorial orientation.[17] We attribute this high-field position to a gauche relationship of it with the 4-*exo*- and 9-*syn*-hydrogens, as a result of its being in an axial orientation (conformer II; R = CH_3). When one of the hydrogens of this group is replaced with a methyl group, the resulting methylene is shifted downfield by 5.3 ppm. Since the substituent parameter for α-CH_3 in piperidines is 5.4 ppm,[17b] the downfield shift of this methylene seems to be due primarily to the influence of the methyl group and not to any reduction in its proximity with respect to the 4-*exo*- and 9-*syn*-hydrogens. Replacement of another hydrogen with a methyl group, giving **3d**, would be expected to result in a further shift of C-2′ to about 20.6 ppm. However, C-2′ is found at least 6.6 ppm farther downfield, presumably as a result of the relief of steric crowding due to a shift in favor of conformer I.

The positions of C-2, C-4, and C-9 in the spectra may be interpreted in a manner consistent with the above analysis. In **3b** and **3c** the C-4 carbon is shifted 7.5 and 7.0 ppm upfield relative to its position in **3a** due to the gauche interaction of the 2-*exo*-alkyl groups with the respective 4-*exo*-hydrogens.[17b] This effect is partially offset at C-2 in **3b** by the downfield shift caused by the α-CH_3 contribution, resulting in a net upfield shift of only 2.2 ppm relative to C-2 in **3a**; in **3c** the effect at C-2 is overridden by downfield α-CH_2 and β-CH_3 contributions, resulting in a net downfield shift of 5.2 ppm. In **3d**, C-4 is shifted 6.1 ppm upfield relative to its position in **3a** due to the gauche 2,4,7-*endo*-hydrogen interaction. This relationship also undoubtably causes C-2 to appear upfield from where it would appear in the absence of such an interaction, but the magnitude of the relative difference cannot be reliably estimated due to the lack of a suitable reference compound.

The upfield shift of C-9 in **3b** and **3c** relative to its position in **3a** is due to the *syn*-9-hydrogen–2-*exo*-alkyl interaction, and in **3d** relative to **3a** is probably due to transannular shielding by the nitrogen lone pair electrons on the 9-*syn*-hydrogen.[18]

Conclusion

The ^1H and ^{13}C NMR spectral features of **3d** indicate that it prefers a chair–boat conformation (I). Analysis of the ^{13}C NMR spectra of **3b** and **3c** shows them to prefer flattened double-chair conformations, similar to that of **3a**, while the observable nonequivalence of the benzylic methylene protons in the ^1H NMR spectra of these compounds implies the presence of the chair–boat conformer. However, in these compounds this nonequivalence, suggestive of close proximity of the 2-alkyl and 3-benzyl substituents, seems to result from conformational flattening rather than from the presence of equatorial alkyl groups.

Experimental Section

Melting points were taken in a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared (IR) and 60-MHz proton magnetic resonance spectra were obtained using Beckman IR 33 and Hitachi R 20A spectrometers. Carbon-13 magnetic resonance spectra were measured at 25.035 MHz with a Joel JNM PS-100 spectrometer interfaced with a Jeol JEC-980A computer, using 10-mm tubes. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Ga. Analytic gas–liquid chromatography (GLC) was done using a Perkin-Elmer 881 gas chromatograph equipped with flame ionization detection: carrier gas, helium (30 mL/min); detector gasses, hydrogen (40 mL/min) and compressed air (250 mL/min); temperatures, injection port (210 °C), oven (150 °C), and detector (210 °C); 6 ft × 0.125 in stainless steel column containing 3% OV-17 on Gas Chrom Q (80–100 mesh), ca. 2400 theoretical plates (calcd). Reactions were monitored by thin-layer chromatographic analysis, which was carried out using 5 × 10 cm glass plates precoated with 0.25-mm layers of silica gel GF (Analtech): developing solvent, chloroform–methanol–28% aqueous ammonia (95:5:0.5) unless stated otherwise; spots were visualized with iodine vapor.

General Methods. All reactions were carried out under dry nitrogen. Solutions of products were concentrated on a Buchi Rotavapor (10–40 mm) at water bath temperatures of 40 °C or less. Free bases of hydrochloride salts were prepared by partitioning them between ether and 10% aqueous sodium hydroxide, followed by drying (anhydrous sodium sulfate) and concentration as above. Traces of water in the samples were removed azeotropically with benzene in vacuo.

3-Benzyl-3-azabicyclo[3.3.1]nonane (3a) was prepared as described previously.[19] Its hydrochloride salt was crystallized from chloroform–carbon tetrachloride, mp 215–216 °C subl (lit.[19] 217 °C subl).

3-Benzyl-3-azoniabicyclo[3.3.1]non-2-ene Bromide (4). To 200 mL of methylene chloride was added 7.52 g (35 mmol) of **3a** and 31.5 g (296 mmol) of anhydrous sodium carbonate. To the magnetically stirred mixture was added dropwise a solution of 6.76 g (42 mmol) of bromine in 100 mL of methylene chloride over a period of 1.5 h. After stirring for another 2 h, the mixture was filtered and concentrated to give a red solid, which separated from ethyl acetate–ether as white crystals: 3.5 g (34%); TLC showed one spot, R_f 0.5. A small amount of this was converted to the perchlorate salt and crystallized from ethanol: mp 126–127.5 °C; IR (KBr) 1680 cm^{-1} (C=N$^+$) (lit.[20] mp 122 °C, IR (KBr) 1669 cm^{-1}).

2-*exo*-Methyl-3-benzyl-3-azabicyclo[3.3.1]nonane (3b). To a cold (0 °C) 1 M solution of methylmagnesium bromide in tetrahydrofuran (5 mL) was added 0.185 g (0.5 mmol) of **4** bromide in one portion. The stirred suspension was allowed to warm to room temperature, and after 15 h excess Grignard reagent was destroyed by the addition of 30% aqueous ammonium chloride. The supernatant was decanted and the precipitate washed with tetrahydrofuran. The combined organic extracts were concentrated. The residue was dissolved in ether and dried (anhydrous sodium sulfate), and the solution was treated with excess ethereal hydrogen chloride. The precipitate was crystallized from chloroform–carbon tetrachloride: 0.06 g (35%); mp 197–202 °C (darkening).

Anal. Calcd for $C_{16}H_{24}ClN$: C, 72.29; H, 9.10; N, 5.27. Found: C, 72.32; H, 9.12; N, 5.35.

This salt was converted to the free base: GLC retention time of 5.8 min and ca. 100% purity.

2-*exo*-Ethyl-3-benzyl-3-azabicyclo[3.3.1]nonane (3c). To 1.0 mL of 1.3 M ethereal ethylmagnesium bromide was added 0.056 g (0.18 mmol) of **4** perchlorate in one portion. After stirring for 24 h, the reaction mixture was found to contain no starting material by TLC analysis. Excess Grignard reagent was destroyed as above, the residual solvent decanted, and the precipitate washed well with ether. The combined extracts were dried (anhydrous sodium sulfate) and concentrated to give 0.02 g (46%) of a colorless oil: GLC retention time of 7.7 min and >99% purity. This was dissolved in ether and, excess ethereal hydrogen chloride was added. The precipitate was crystallized from chloroform–carbon tetrachloride, mp 204.5–207 °C (darkening).

Anal. Calcd for $C_{17}H_{26}ClN$: C, 72.96; H, 9.37; N, 5.01. Found: C, 72.85; H, 9.38; N, 5.05.

2-*exo*-Isopropyl-3-benzyl-3-azabicyclo[3.3.1]nonane (3d). The reaction of 0.58 g (2 mmol) of **4** bromide with 10 mL of 1 M ethereal isopropyl magnesium bromide was carried out in the same way as that used to prepare **3c**. After stirring for 4.5 h, TLC analysis indicated complete consumption of the starting material. Excess Grignard reagent was destroyed as before, 10-mL portions of ether and water were added, and the aqueous phase was adjusted to ca. pH 7 with 10% aqueous hydrochloric acid. The ether layer was removed, and the aqueous phase was reextracted with two 10-mL portions of ether. The combined ethereal extracts were dried (anhydrous sodium sulfate) and concentrated to give 0.34 g of a yellow oil. TLC analysis (the developing solvent was methylene chloride–methanol, 90:10) showed four components. The product was chromatographed on 26 g of 60–200 mesh silica gel. Elution with 100 mL of methylene chloride followed by 300 mL of 1% methanol in methylene chloride gave two fractions. TLC analysis of the first fraction (the developing solvent was methylene chloride–methanol, 99:1) indicated the presence of two components (R_f 0.32 and 0.63), the first of which (major) was indistinguishable from an authentic sample of **3a** and the second of which (minor) was not identified. Analysis of the second fraction revealed a single component (R_f 0.06). This fraction was concentrated, and the residue was dissolved in ether and treated with excess ethereal hydrogen chloride. The precipitate was crystallized from chloroform–carbon tetrachloride: 0.11 g (19%); mp 217–219 °C (darkening).

Anal. Calcd for $C_{18}H_{28}ClN$: C, 73.57; H, 9.60; N, 4.77. Found: C, 73.47; H, 9.60; N, 4.69.

The free base was prepared from 0.1 g of this salt: GLC retention time of 11.3 min and ca. 98% purity.

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Registry No.—**3a** HCl, 23481-98-3; **3b** HCl, 66224-94-0; **3c** HCl, 66224-95-1; **3d** HCl, 66224-96-2; **4** Br^-, 66224-97-3; **4** ClO_4^-, 66224-99-5.

References and Notes

(1) (a) N. S. Zefirov and S. V. Rogozina, *Russ. Chem. Rev.* (*Engl. Transl.*), **42,** 190 (1973); (b) N. S. Zefirov, *ibid.*, **44,** 196 (1975).
(2) (a) N. W. J. Pumphrey and M. J. T. Robinson, *Chem. Ind.* (*London*), 1903 (1963); (b) M. Dobler and J. D. Dunitz, *Helv. Chim. Acta*, **47,** 695 (1964).
(3) (a) M. R. Chakrabarty, R. L. Ellis, and J. L. Roberts, *J. Org. Chem.*, **35,** 541 (1970); (b) R. Lygo, J. McKenna, and I. O. Sutherland, *Chem. Commun.*, 356 (1965); (c) P. C. Ruenitz, Ph.D. Thesis, The University of Kansas, Lawrence, Kans., 1974; *Diss. Abstr. B*, **36,** 735 (1975).
(4) (a) J. B. Lambert, *Acc. Chem. Res.*, **4,** 87 (1971); (b) C.-Y. Chen and R. J. W. LeFèvre, *J. Chem. Soc. B*, 539 (1966); see also ref 14a.
(5) N. K. Wilson and J. B. Stothers, *Top. Stereochem.*, **8,** 1 (1974).
(6) The absolute configurations of chiral compounds discussed in this paper have been assigned arbitrarily.
(7) For the method, see A. Picot and X. Lusinchi, *Synthesis*, 109 (1975).
(8) (a) L. Stéhelin, L. Kanellias, and G. Ourisson, *J. Org. Chem.*, **38,** 847 (1973). (b) J. K. MacLeod and R. J. Wells, *J. Am. Chem., Soc.*, **95,** 2387 (1973). (c) R. T. LaLonde, J.-Y. Ding, and M. A. Tobias, *ibid.*, **89,** 6651 (1967), and references cited. (d) Treatment of **4** with sodium borodeuteride in methanol gave a product which was indistinguishable by TLC from **3a**. Its IR spectrum (CCl_4) was identical with that of **3a**, except for decreased intensity of the Bohlmann (trans) bands centered at 2800 cm^{-1} and the presence of a band at 2040 cm^{-1} (ν_{C-D}). In related systems, ν_{C-D} occurs in this region when C–D is anticoplanar to the nitrogen lone pair electrons and at a higher wavenumber (ca. 2170 cm^{-1}) when it is gauche to them: M. Wiewiórowski, O. E. Edwards, and M. D. Bratek-Wiewiórowska, *Can. J. Chem.*, **45,** 1447 (1967). Therefore, the C–D bond is exo in this compound as a result of exo attack of borodeuteride on **4**.
(9) For a review on chemical shift nonequivalence of geminal groups in ^1H NMR spectra, see W. B. Jennings, *Chem. Rev.*, **75,** 307 (1975).
(10) (a) R. K. Hill and T. H. Chan, *Tetrahedron*, **21,** 2015 (1965); (b) R. E. Lyle, J. J. Thomas, and D. A. Walsh in "Conformational Analysis", G. Chiurdoglu, Ed., Academic Press, New York, N.Y., 1971, pp 157–164; (c) R. E. Lyle and J. J. Thomas, *Tetrahedron Lett.*, 897 (1969).
(11) D. A. Walsh and E. E. Smissman, *J. Org. Chem.*, **39,** 3705 (1974).
(12) L. N. Pridgen, Ph.D. Thesis, University of New Hampshire, Durham, N.H., 1972; *Diss. Abstr. B*, **33,** 3559 (1973).
(13) Observed chemical shift nonequivalence in related compounds has been suggested to be due to unequal proportions of benzyl group rotamers.[10]
(14) (a) F. Bohlmann, D. Schumann, and H. Schulz, *Tetrahedron Lett.*, 173 (1965); (b) F. Bohlmann, D. Schumann, and C. Arndt, *ibid.*, 2705 (1965).
(15) J. R. Wiseman, H. O. Krabbenhoft, and B. R. Anderson, *J. Org. Chem.*, **41,** 1518 (1976), and references cited therein.
(16) (a) A. Heumann and H. Kolshorn, *Tetrahedron*, **31,** 1571 (1975); (b) J. R. Wiseman and H. O. Krabbenhoft, *J. Org. Chem.*, **40,** 3222 (1975); (c) S. F. Nelson, G. R. Weisman, E. L. Clennan, and V. E. Peacock, *J. Am. Chem. Soc.*, **98,** 6893 (1976); (d) H.-J. Schneider and W. Ansorge, *Tetrahedron*, **33,** 265 (1977); (e) J. A. Peters, J. M. van der Toorn, and H. van Bekkum, *ibid.*, **33,** 349 (1977).
(17) (a) A. J. Jones, A. F. Casy, and K. M. J. McErlane, *Tetrahedron Lett.*, 1727 (1972); (b) A. J. Jones and M. M. A. Hassan, *J. Org. Chem.*, **37,** 2332 (1972); (c) L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley, New York, N.Y., 1972.
(18) For this reason the analogous bridge carbon in sparteine, which is also found in a boat piperidine ring, is shifted 9.1 ppm upfield relative to its position in α-isosparteine in which the corresponding piperidine ring is in the chair conformation: F. Bohlmann and R. Zeisberg, *Chem. Ber.*, **108,** 1043 (1975).
(19) For the preparation, see W. Schneider, and H. Goetz, *Arch. Pharm. Ber. Dtsch. Pharm. Ges.*, **294,** 506 (1961), and references cited therein.
(20) W. Schneider and H. Goetz, *Justus Liebigs Ann. Chem.*, **653,** 85 (1962).