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MAGNETIC NON-EQUIVALENCE OF *GEMINAL* N-METHYL GROUPS IN SOME PROTONATED ALICYCLIC DIMETHYLAMINES, AND OF BENZYLIC METHYLENE PROTONS IN SALTS OF SOME N-BENZYL HETEROCYCLIC BASES

R. W. HOROBIN, J. MCKENNA and J. M. MCKENNA
Chemistry Department, The University, Sheffield

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Abstract—The N-methyl groups in the hydrochlorides of certain dimethylamino-steroids and other suitably unsymmetrical alicyclic bases are observed as magnetically non-equivalent pairs in the NMR spectra, the non-equivalence effects being very sensitive to position and orientation of the $-\overset{+}{N}HMe_2$ groups. The benzylic protons in suitable N-benzyl heterocyclic bases and their protonated and quaternary salts likewise show magnetic non-equivalence which varies sharply with structure and orientation, particularly large chemical-shift differences being observed between the benzylic protons of one of the two N-benzyl groups in certain N-benzyl benziodides.

IT HAS been known for some time that the *geminal*, non-cyclic, "diastereomeric",[1] protons in compounds of the general type $R{\cdot}CH_2{\cdot}C^*R'R''R'''$ are often magnetically non-equivalent, and the observed effects have been discussed[2] in terms of, on the one hand, the "intrinsic" difference between the relevant protons, and, on the other, preferred rotamer populations about the C—C* bond. Furthermore,[3] (1) the asterisked carbon atom need not be asymmetric in the usual sense for display of proton non-equivalence in $-CH_2-$, one of the R-stroke groups being replaceable by $R-CH_2-$; (2) suitably unsymmetrical groupings based on other elements such as N, S or P, may take the place of the group $-C^*R'R''R'''$; (3) the *geminal* protons may themselves be replaced by other groups which give magnetic resonance signals, such as F or Me; (4) the unasterisked carbon in the above expression may be replaced by other elements (e.g., in some of our examples, N); and (5) the group containing the *geminal* pair need not be directly linked to $-C^*R'R''R'''$ (or any of its modifications indicated): a link group such as —COO— or $-CH_2-$ may be interposed. The general relevant expression is thus $R-PQ_2-(Y)-Z^*$, Q_2 representing the *geminal* pair and Z* being a group with sufficient lack of symmetry, e.g., lack of a

[1] K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon and G. H. Wall, Jr., *J. Amer. Chem. Soc.* **86**, 1710 (1964).

[2] *Inter alia* [a] J. S. Waugh and F. A. Cotton, *J. Phys. Chem.* **65**, 562 (1961); [b] H. S. Gutowsky, *J. Chem. Phys.* **37**, 2196 (1962); [c] E. I. Snyder, *J. Amer. Chem. Soc.* **85**, 2624 (1963); [d] G. M. Whitesides, J. I. Grocki, D. Holtz, H. Steinberg and J. D. Roberts, *Ibid.*, **87**, 1058 (1965), and earlier papers by Prof. Roberts *et al.*; [e] P. L. Southwick, J. A. Fitzgerald and G. E. Milliman, *Tetrahedron Letters* 1247 (1965); [f] A. H. Lewin, J. Lipowitz and T. Cohen, *Tetrahedron Letters* 1241 (1965).

[3] *Inter alia* [a] T. D. Coyle and F. G. A. Stone, *J. Amer. Chem. Soc.* **83**, 4138 (1961); [b] M. Saunders and F. Yamada, *Ibid.* **85**, 1882 (1963); [c] W. F. Reynolds and T. Schaefer, *Canad. J. Chem.* **42**, 2119 (1964); [d] J. F. Nixon, *J. Chem. Soc.* 777 (1965); [e] R. M. Moriarty, *J. Org. Chem.* **30**, 600 (1965).

TABLE 1. τ-VALUES[a] OF *geminal* N-METHYL GROUPS IN PROTONATED ALICYCLIC DIMETHYLAMINES $R\overset{+}{N}HMe_2\ \overset{-}{Z}$

Formula	R	Solvent[b]	τ		
			Me^a	$Me^a + Me^b$	Me^b
I	5α-Cholestanyl-3α-yl	TFA		6·96	
II	5α-Cholestanyl-3β-yl[c]	TFA		7·04	
III	Cholest-5-en-3α-yl[d]	TFA	7·00		7·04
IV	Cholest-5-en-3β-yl[c]	TFA		6·98	
XV	Lanost-8-en-3β-yl	TFA	6·93		7·05
V	5α-Cholestan-4α-yl	$CHCl_3$/HCl	7·14		7·38
VI	5α-Cholestan-4β-yl	$CHCl_3$/HCl		7·02	
VII	5α-Cholestan-6α-yl[e,f]	$CHCl_3$/HCl	7·08		7·28
VIII	5α-Cholestan-6β-yl[g]	TFA	6·85		6·90
IX	3α,5-Cyclocholestan-6β-yl	$CHCl_3$/HCl	6·93		7·08
X	5α-Cholestan-7α-yl[h]	TFA	6·86		6·91
XI	5α-Cholestan-7β-yl	TFA	6·90		7·04
XII	3β-Acetoxypregn-5-en-20α-yl[d]	TFA	7·00		7·19
XIII	5α-Pregnan-18-yl[i]	TFA	6·83		6·88
XVI	Bornyl	TFA		6·95	
XVII	*neo*-Bornyl	TFA	6·85		7·02

[a] Room temp. measurements. Doublets (J, ca. 5 c/s) due to interaction with $\overset{+}{N}$—H.

[b] TFA: trifluoroacetic acid, used to dissolve either bases or hydrochlorides. $CHCl_3$–HCl:$CHCl_3$ previously shaken with aqueous 5NHCl, used to dissolve hydrochlorides or hydriodides.

[c] Equivalent methyl groups were also observed for salts of other bases containing protonated 3β-dimethylamino groups in 5α-H or 5-ene steroidal frameworks: conessine, dihydroconessine, dioxyconessine, chlorodihydroconessine.

[d] Only unresolved multiplet patterns seen in the N-methyl signal area for solutions of the hydrochloride in $CHCl_3$–HCl at room temp.

[e] Hydrochloride showed equivalent N-methyl groups, without spin-doubling, in nitrobenzene at 150° (intermediate signal displays seen at lower temp.) or in $CHCl_3$ containing a little alcohol and pyridine at room temp. (intermediate displays in $CHCl_3$ containing varying proportions of alcohol). The isomeric 7β-hydrochloride also lost the spin-doubling in $CHCl_3$, but, with increasing proportions of alcohol or even pyridine in this solution, the N-methyl groups were less readily rendered equivalent than in the case of the 6α-isomer.

[f] The analogous 6α-methylethylamino hydriodide in $CHCl_3$–HCl showed two N-methyl signals (each a doublet: J, 5 c/s) at τ, 7·10 and 7·32. In the same solvent only one N-methyl singlet was seen with a solution of the 6β-isomer, and shortage of material unfortunately prevented examination of this salt (as also 5α-cholestanyl-4β-yldimethylamine) in more strongly acidic solvents. Only one singlet N-methyl peak was observed for 5α-cholestan-6α-ylmethylethylamine hydriodide in nitrobenzene.

[g] Lit[4], τ, 6·84; 6·90, in TFA.

[h] Lit[4], τ, 6·84; 6·88, in TFA.

[i] In some analogous protonated 19-dimethylamino steroids, the relevant part of the NMR spectra could not readily be analysed because of partial superposition of N-methyl and N-methylene signals. The N-methyl groups of 19-dimethylamino-5α-cholestan-6β-ol seem, however, to be non-equivalent, and those in the corresponding 6-keto base to be equivalent, in a mixture of chloroform and trifluoroacetic acid.

plane of symmetry along the P—Z or the Y—Z bond. There has been much recent interest in observations of non-equivalence for non-cyclic *geminal* pairs, as indicated e.g. by the typical references to the 1965 literature quoted in the present paper, several important communications appearing while our own work was being prepared for press. Our work deals with non-equivalence effects observed in derivatives of a variety of alicyclic and heterocyclic bases, and, in the sequel, R—PQ_2— of the above general expression is usually either $HNMe_2^+$— attached to a steroidal or other alicyclic framework, or Ph·CH_2— attached to heterocyclic nitrogen. Our results are of interest for two reasons: (1) the dependence of the non-equivalence effect on structure, and on steric orientation of the *geminal* group, and (2) the near-record size of the non-equivalence effects in one of the two benzyl-methylene groups in certain heterocyclic N-benzyl benziodides. Results are summarized in Tables 1 and 2.

Geminal *Methyl groups in protonated alicyclic dimethylamines* (Table 1). Magnetic non-equivalence of N-methyl groups is not observed (on a 60 Mc/s instrument) in salts (I and II) containing —$HNMe_2^+$ attached to the 3α- or 3β-position in 5α-cholestane, no doubt because of the symmetry associated with the presence of unsubstituted methylene groups at C_2 and C_4, and absence of sufficiently strong unsymmetrical effects at greater distances from C_3. The same is true for the salt IV of cholest-5-en-3β-yl dimethylamine. In the 3α-isomer (III), however, the protonated dimethylamino group, positioned under ring A, is nearer to the unsymmetrical environment associated with the 5,6-double bond, and magnetic non-equivalence thus develops in the *geminal* dimethyl pair. The results just quoted indicate that the observed non-equivalence in the proton salt (XV) of lanost-8-en-3β-yl dimethylamine is particularly associated with the unbalance between —CH_2— and —CMe_2— flanking C_3.

In the equatorial 4α (V), 6α (VII), and 7β (XI) salts derived from 5α-cholestane, the marked magnetic non-equivalence in each *geminal* dimethyl pair suggests that the equatorial ring-methylene group adjacent (on one side only) to each equatorial —$HNMe_2^+$ has a considerable unsymmetrical effect on the environment of the nitrogenous group, more so than on that of the epimeric axial —$HNMe_2^+$ group, 4β (VI), 6β (VIII), or 7α (X) where a lower or no difference between the chemical shifts for N-methyl groups for each *geminal* pair is observed. The 6β-substituted 3,5-cyclosteroid (IX), with partly deformed ring B, gives a qualitatively intermediate pattern. In the broadest sense one can understand these results: the axial —$HNMe_2^+$ groups are more subject than the equatorial to the levelling environmental effects of the remainder of the alicyclic system, so that the unsymmetrical influence of the adjacent equatorial ring-methylene groups may be reduced. A more detailed qualitative conformational interpretation does not seem useful.

In a very recent paper,[4] written in another context, Ma and Warnhoff have also commented on magnetic non-equivalence in the *geminal* dimethyl pairs of the proton salts of some cholestanyldimethylamines, and, where direct comparison can be made (Table 1), the chemical shifts quoted by these authors agree quite closely with those measured in this laboratory. Non-equivalence was apparently not observed for the 2α- and the 2β-salts, for which the structural position is rather similar (symmetry of

[4] J. C. N. Ma and E. W. Warnhoff, *Canad. J. Chem.* **43**, 1849 (1965).

TABLE 2. τ-VALUES[a] OF *Geminal* BENZYLIC METHYLENE PROTONS IN N-BENZYL HETEROCYCLIC BASES AND DERIVATIVES

Compound and formula number[b]	Solvent	τ		
		H^a(J)	$H^a + H^b$	H^b(J)
Derivatives of 1-*Benzyl-2-methylpiperidine*:				
Base[c]	$CDCl_3$	6·02		6·82
Protonated base (XVIIIa,[a] R = H; major isomer)[d]	$CDCl_3$–TFA	5·40(2·85)		6·02(7·15)
Protonated base (XVIIIb; minor isomer)[d]	$CDCl_3$–TFA		5·85	
Methiodide (XVIIIa; R = Me)[e,f]	$CDCl_3$		5·01	
Methiodide (XVIIIc)[5,6e,f]	$CDCl_3$	5·20		5·56
Benziodide (XVIIIa; R = CH_2Ph)	$CDCl_3$	5·03 4·40[g]		5·23 6·06[g]
Derivatives of 1-*Benzyl-2-methylpyrrolidine*:				
Base[c]	$CDCl_3$	5·98		6·86
Protonated base (XIXa; R = H; major isomer)	TFA	5·38(5·4)		5·73(7·3)
Methiodide (XIXa; R = Me)[e]	$CDCl_3$		5·08	
Methiodide (XIXb; R = Me)[e]	$CDCl_3$	5·47		5·65
Benziodide (XIXa or XIXb; R = CH_2Ph)[f]	$PhNO_2$	4·81 4·25[g]		5·17 5·55[g]
	$CDCl_3$	5·13 4·48[g]		5·50 5·78[g]
Derivatives of 1-*Benzyl*-trans-*decahydroquinoline*:				
Base[c]	$CDCl_3$	5·96		6·89
Protonated base (XXa; R = H; major isomer)	$CDCl_3$–TFA	5·55(2·7)		6·17(7·3)
Methiodide (XXa; R = Me)[e,f]	$CDCl_3$		4·98	
Methiodide (XXb; R = Me)[e,f]	$CDCl_3$	5·27		5·55
Benziodide (XXa or XXb; R = CH_2Ph)	$CDCl_3$	4·93 4·33[g]		5·09 6·11[g]
Derivatives of 4-*Benzyl-4-aza-5α-cholestane*:				
Base[c]	$CDCl_3$	6·01		6·94
Protonated base (XXIa; R = H)	$CDCl_3$–TFA	5·50[h]		5·80[h]
Methiodide (XXIa; R = Me)[e]	$CDCl_3$	Narrow unresolved multiplet centered on τ, 4·9–5·0		
Methiodide (XXIb; R = Me)[e]	$CDCl_3$	Broad unresolved multiplet centered on τ, 5·5–5·6.		

[a] From spectra run at room temp. J between non-equivalent *geminal* protons ca. 12–13 c/s. In protonated salts, J for the coupling $H^c—C—\overset{+}{N}—H^a$ and/or[b] varied considerably (as is to be expected) for the non-equivalent *geminal* protons, and the values are given in brackets in the Table. J for the same coupling for equivalent pairs was ca. 6 c/s where measurable.

[b] Energetically more favoured conformations only (in idealized representations) given for piperidines.

[c] Magnetically averaged conformations, mainly as in major protonated configurations. On addition of increasing proportions of TFA (trifluoroacetic acid) to solutions of bases in $CDCl_3$, the methylene multiplets were characteristically narrowed at first and shifted downfield and then became more complex by spin-interaction with $\overset{+}{N}—H$ and in appropriate cases by separation into separate spectra for major and minor components of the cation mixture.

[d] The observed proportion of the stereochemically less-favoured configurational isomer in this and

1- *vs.* 3-ring methylene groups) to that of the 3-substituted analogues discussed above.

We have also observed two N-methyl peaks for 6α-methylethylamino-5α-cholestane in acid solution: these are associated with the two enantiomeric configurations of the dissymmetric cationic nitrogen atom.

The non-equivalence of *geminal* methyl groups in the proton salt of 18-dimethylamino-5α-pregnane (hexahydro*apo*conessine; XIII) provides an example of the effect for a compound $R^*CH_2\overset{+}{N}HMe_2\ \overset{-}{X}$ where the unsymmetrical R* is separated from the nitrogenous group by a methylene bridge (i.e. $CH_2 = Y$ in the generalized expression given above). Less satisfactory analogous examples, derivatives of 19-amino-5α-cholestane (XIV) are also referred to in Table 1.

A sufficiently slow proton-exchange rate between nitrogen and solvent is required for the display of *gem*-methyl non-equivalence in the NMR spectra of the protonated bases, as configuration at nitrogen is inverted by valency-"flip" in the free amines, which can arise if the free amine has a long enough equilibrium life in the system studied (an interesting quantitative application of the relevant theory is discussed in Ref. 3*b*). In our work we found (Table 1, footnote d) that, for some compounds, *gem*-methyl non-equivalence and spin-coupling between N—H and N-methyl was clearly displayed in trifluoroacetic acid, but, in a weaker acid system (chloroform previously shaken with aqueous hydrochloric acid), only unresolved multiplet patterns were observed. With other compounds, notably 5α-cholestan-6α-yldimethylamine, an interesting range of spectra between one extreme (2 spin-doublets for the N-methyl groups) and the other (one singlet) were observed by suitable control of temperature or solvent (Table 1, footnote e).

Geminal *Benzylic-methylene protons in some* N-*benzyl heterocyclic bases and derivatives* (Table 2). The NMR spectra of the free bases are magnetically averaged, with the N-benzyl group (which is capable of rapid conformational inversion by valency "flip") being mostly in the same orientation as is adopted in the more stable proton-salt configuration. The methylene chemical-shift patterns for a base and for the preferred configuration of its proton salt are qualitatively similar in all cases studied: magnetic non-equivalence is observed for these species in contrast to equivalence for one less-stable hydrochloride configuration. An important factor in determination of the methylene chemical-shift pattern is the dihedral angle between the strongly anisotropic benzene ring and each methylene C—H bond, and alteration in the NMR signal-pattern may be caused by either (a) variation in the orientation of the whole N-benzyl group, e.g. from N-axial to N-equatorial, or (b) variation of

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Footnotes to Table 2. *Contd.*

in some related systems is much higher than would be estimated from consideration of the energetics of analogous carbocyclic systems. This point will be discussed in a later paper.

[e] The spectra of diastereoisomeric methiodides were for convenience taken together (in mixtures containing the components in different proportions, corresponding to the product ratios in different preparations). The spectra of the diastereoisomeric pairs of protonated N-benzyl bases were of course necessarily taken together, but in most cases no difficulty was caused by partial overlapping of signals.

[f] When nitrobenzene solutions were heated from room temp. to 120°, no significant qualitative changes in chemical shifts or coupling constants were observed.

[g] Probably equatorial methylene group (see Text).

[h] Spin-interaction with $\overset{+}{N}$—H not fully resolved.

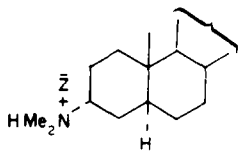
the other exocyclic group on nitrogen (lone-pair, hydrogen, or methyl). The striking reversals displayed in Table 2 are therefore broadly intelligible: *either* reversal of the orientation of an N-benzyl group in the systems studied, *or* replacement of lone-pair or hydrogen by an N-methyl group, alters a non-equivalent to an equivalent pattern, or *vice-versa*, and making two such changes, i.e. in moving from a protonated base with N-benzyl equatorial to a methiodide with N-benzyl axial (or *vice-versa*) does not alter the observed spectral pattern qualitatively.

We were at first rather disturbed to find such a regular qualitative correspondence in N-methylene chemical-shift patterns between N-benzyl methiodides and N-benzyl proton salts which, on the basis of empirical arguments[5] previously elaborated in this laboratory were assigned opposite rather than corresponding configurations at N^+. As examination of Dreiding models for the hydrogen- and the quaternary salts, however, does not allow sufficiently unambiguous choices to be made from conformations which would (qualitatively) seem to accord with the spectroscopic results (including coupling constants) quoted, and also be acceptable on other steric grounds, we feel that the results afford no reason for alteration of our previous views; these views are in any case being currently checked by X-ray crystallographic analysis and by other methods, one of which (based on NMR spectroscopic examination of the N-benzyl benziodides) is indicated below.

Analogous to the non-equivalent benzyl-methylene patterns noted for the relevant compounds quoted in Table 2, we have observed that the methylene protons at C_{19} in the 6β-hydroxy derivative of 19-amino-5α-cholestane (XIV) also afford an AB pattern (τ, 6·98, 7·26; J, 14 c/s), and parts of similar patterns (the remainders obscured in each case by other signals) are seen in the spectra of 19-dimethylamino-5α-cholestan-6β-ol, the corresponding ketone, and 18-dimethylamino-5α-pregnane (hexahydro-*apo*conessine). The methylene protons in the group-$CH_2.CO_2H$ attached to C_3 in 5α-cholestane-3α-acetic acid, 5α-cholestane-3β-acetic acid, 5β-cholestane-3β-acetic acid, and cholest-5-en-3α-acetic acid appeared only as fairly broad singlets (half-height width ca. 3–4 c/s for chloroform solutions) probably because of the symmetry of the ring near C_3 (compare the results for 3-dimethylamino steroids in acid solution).

The benzyl–methylene chemical-shift patterns (two per compound) noted in Table 2 for the N-benzyl benziodides are particularly interesting because of the large degree of non-equivalence between *gem*-methylene protons in one benzyl group for each salt: relevant values for $\delta_{H^a}-\delta_{H^b}$ are 1·30, 1·66 and 1·78 ppm. These values are among the highest noted for diastereomeric *non-cyclic gem*-methylene proton pairs, and may be compared with the apparently record values of 1·75, 1·85 and 1·99 ppm very recently observed[2e,f] for compounds in which the anisotropy of carbonyl or thiocarbonyl was added to that of phenyl to yield the magnetic differentiations quoted. While one cannot reach detailed qualitative conformational conclusions about the N-benylz benziodides from examination of Dreiding models, it does seem that the axial benzyl groups in the piperidine derivatives are oriented with the phenyl group away from rather than over the ring (cf. XXIII; R = other substituents, including fused rings, if any). In this position the phenyl of the axial benzyl group would be expected to affect the methylene of the equatorial benzyl group much more than

[5] J. McKenna, J. M. McKenna, A. Tulley and J. White, *J. Chem. Soc.* 1711 (1965), and three following papers; R. Lygo, J. McKenna and I. O. Sutherland, *Chem. Commun.* 356 (1965); J. McKenna, J. M. McKenna and A. Tulley, *J. Chem. Soc.* 5439 (1965).



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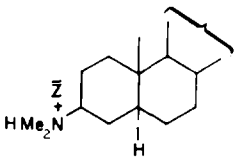

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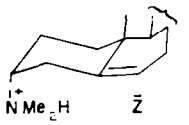

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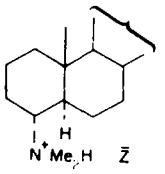

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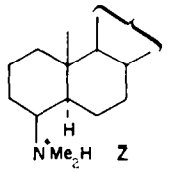

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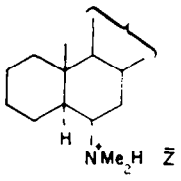

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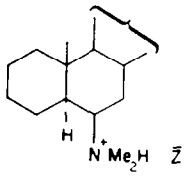

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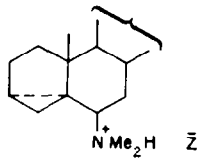

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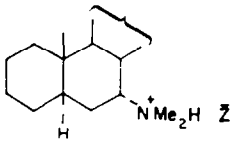

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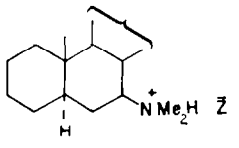

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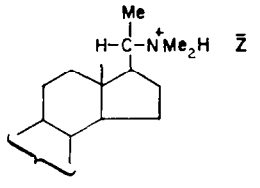

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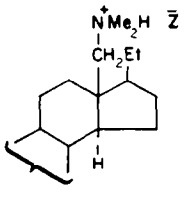

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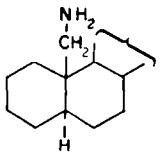
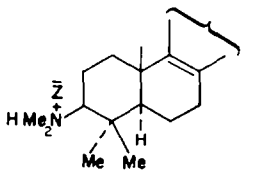


XIV



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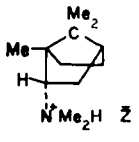

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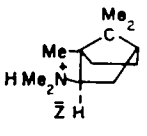

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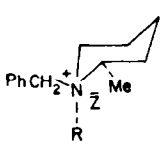

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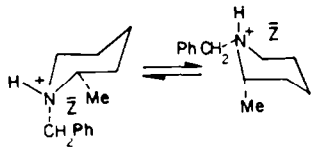

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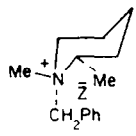

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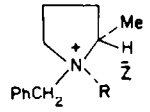

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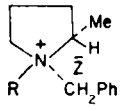

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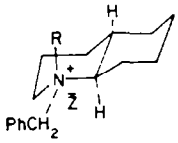
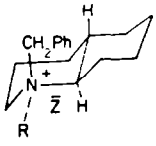
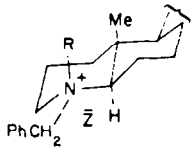


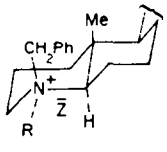
XX a



XX b



XXI a



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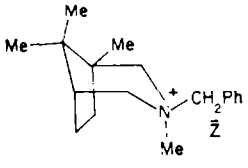

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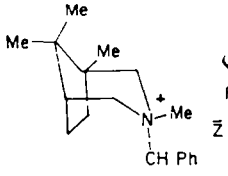
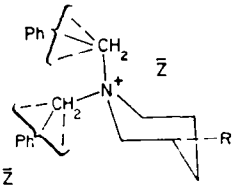


XXII b



XXIII

would the phenyl of the equatorial group affect the methylene of the axial group. The equatorially attached methylene group is probably therefore the one with the greater degree of non-equivalence, and this consideration leads to the possibility of checking the preferred direction of attack (axial or equatorial) of the N-benzyl bases on benzyl iodide, using suitable deuterium-labelling techniques, and comparison of the findings with the results of earlier work. We are actively pursuing this approach.*

* *Added in proof.* Benzylation of N-didenterobenzyl bases containing the group $>N{\cdot}CD_2{\cdot}Ph$ with benzyl iodide, and examination of the NMR spectra of the resultant quaternary salt mixtures have now indicated the preference for axial quaternization in the *trans*-decahydroquinoline and 2-methylpiperidine systems, and *cis*-quaternization in the 2-methylpyrrolidine system, in accord with the conclusions previously reached regarding the formation of diastereoisomeric cyclic quaternary salts containing N-methyl and primary N-alkyl groups.

While we were preparing this paper for press, a publication by Hill and Chan[6] appeared describing how magnetic non-equivalence in the benzyl-methylene protons of certain N-benzyl *trans*-$\alpha\alpha'$-dialkyl piperidines and pyrrolidines could be used to distinguish these bases from their *cis*-$\alpha\alpha'$-dialkylated analogues, where the protons are necessarily equivalent. The method did not work for the $\beta\beta'$-isomers (equivalent protons observed for both *cis*- and *trans*-bases) presumably because the dissymmetry in the *trans*-bases was too far removed from the nitrogen atoms. We likewise found that the benzyl-methylene protons in isomeric N-benzylcamphidine methiodides (XXIIa and b) appeared as singlets with $\tau = 4{\cdot}89$ and $4{\cdot}98$ respectively. It seems possible from our work that when the dissymmetric centre(s) in a saturated heterocyclic N-benzyl base is (are) at some distance from nitrogen, magnetic non-equivalence will be more readily demonstrated for a benzyl methylene group in the N-benzyl benziodide (if this can be prepared; it cannot in the camphidine series) rather than in the free tertiary base, and we are examining this possibility.

EXPERIMENTAL

Compounds. Nearly all the compounds examined have been described previously, and have been used in other investigations in this laboratory: some recent leading references are quoted.[5,7] Steroidal methylethylamines and lanost-8-en-3-β-yl-dimethylamine were made by standard methods and will be described in future papers in other contexts.

NMR spectra. Spectra were taken on a Varian A-60 spectrometer operating at 60 Mc/s. Concentrations of steroids in the solutions examined were typically 0·3M; concentrations of other compounds usually rather higher. Tetramethylsilane ($\tau = 10{\cdot}00$) was used as an internal standard.

Acknowledgement—We thank the D.S.I.R. for a manaintence grant (to R. W. H.) and the University of Sheffield for research facilities (to J. M. McK.)

[6] R. K. Hill and Tak-Hang Chan, *Tetrahedron* 2015 (1965).

[7] R. Ledger, A. J. Smith and J. McKenna, *Tetrahedron* 2413 (1964); J. McKenna, J. M. McKenna, R. Ledger and P. B. Smith, *Ibid.* 2423 (steroidal dimethylamines); R. Ledger and J. McKenna, *Chem. & Ind.* 1662 (1963) [derivatives of 19-amino-5α-cholestane]; H. Favre, R. D. Haworth, J. McKenna, R. G. Powell and G. H. Whitfield, *J. Chem. Soc.* 1115 (1953) and earlier papers (conessine derivatives); J. McKenna and J. B. Slinger, *J. Chem. Soc.* 2759 (1958) [dimethylbornylamine and dimethyl*neo*bornylamine]; for derivatives of N-benzyl bases (Table 2), see Ref. 5.