ASYMMETRIC INDUCTION OF MAGNETIC NONEQUIVALENCE OF THE PROTONS OF THE AZIRIDINE RING

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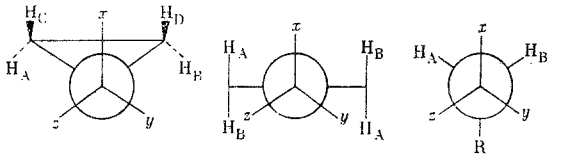
The disposition of ring protons (A) and (B) in aziridines with an asymmetric center in the nitrogen substituent is the same as that of the geminal protons in substituted ethanes (C). Thus under the conditions of slow nitrogen inversion (on the NMR time scale) vicinal nonequivalence of the ring protons and carbons (A) can be detected



Compounds in earlier studies showed marked nonequivalence of the protons cis to the N substituent ($\Delta\nu_{CD} > \Delta\nu_{AB}$) and identical geminal coupling constants ($J_{AC} = J_{BD}$) [1]. We have now found that 1-(α-phenylethyl)aziridine [2] is an exception: $\Delta\nu_{AB} > \Delta\nu_{CD}$ and $J_{AC} > J_{BD}$ (Fig. 1), i.e., the difference $\Delta\nu_{vid}$ cannot act as an independent criterion for assigning the PMR signals of the cis and trans protons.

Under the conditions of rapid nitrogen inversion (B) the ring carbon atoms are equivalent. Thus we can determine the activation parameters for nitrogen inversion at the coalescence temperature of the ^{13}C signals of these carbons [1, 3]. Under conditions (B) the ring protons should be nonequivalent. The PMR spectra of the aziridines described in [1] and of 1-(α-phenylethyl)aziridine above 100°C show a singlet from the ring

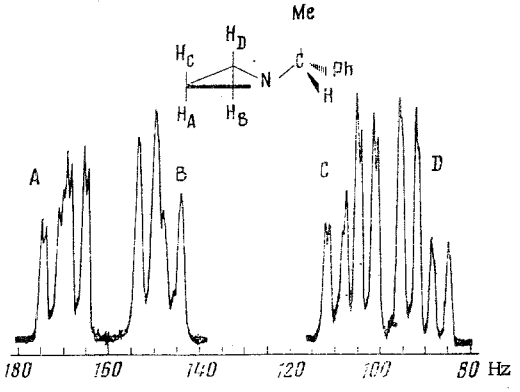


Fig. 1. PMR spectrum of the ring protons of 1-(α-phenylethyl)aziridine (100 MHz, CCl_4, δ, Hz): 92.2 (D), 106.8 (C), 148.9 (B), 169.1 (A), 127.8 (Me), 211 (CH, J_{MeCH} = 6.5, J^{cis}_{CD} = 7.0, J^{cis}_{AB} = 5.6, J^{trans}_{AD} = 3.75 Hz, J^{gem}_{AC} = 0.9, J^{gem}_{BD} < 0.5 Hz.

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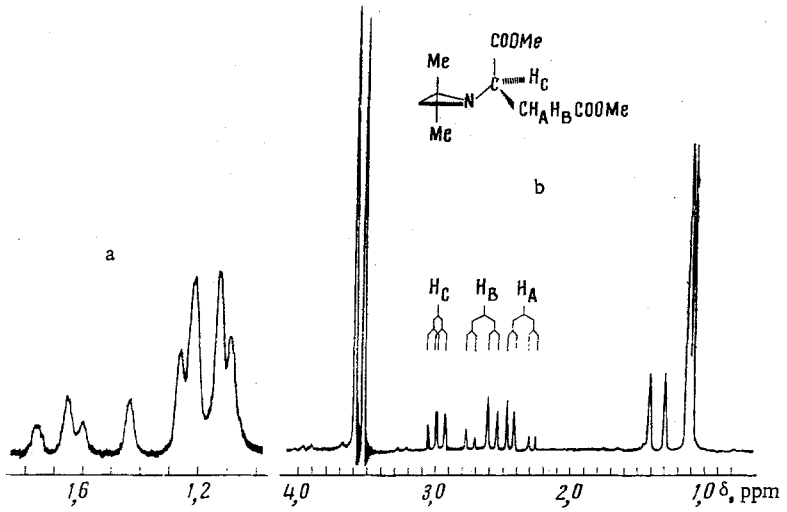
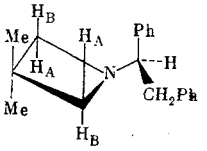


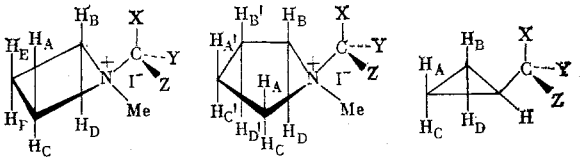
Fig. 2. PMR spectra of (I): a) at 60 MHz in CD_3OD at −40°C (ring protons and methyl groups); b) at 100 MHz in C_6F_6 at 100°C (complete spectrum); J_{AB} = 16; J_{AC} = 5; J_{BC} = 7 Hz. Under the conditions of rapid nitrogen inversion the spectra show magnetic nonequivalence of the ring protons ($\Delta\nu$ = 12 Hz) and methyl groups ($\Delta\nu$ = 2.3 Hz).

protons apparently as a result of the small values of $\Delta\nu_{AB}$. However, the expected A_2B_2 spectrum of the ring protons occurs for 1-(benzenesulfinyl)aziridine at 50°C [4]. The spectrum of dimethyl β-(2,2-dimethylaziridin-1-yl)succinate (I) with slow inversion reveals diastereomers differing in the chemical shifts of the ring CH_2, Me_2C, and COOMe groups [5] (Fig. 2). The equilibrium ratio of the diastereomers depends on the solvent. On warming these signals of the diastereomers coalesce (epimerization) [5], though under the conditions of rapid inversion the protons of the CH_2 and Me_2C groups are nonequivalent (Fig. 2) as a result of asymmetric induction (B). The related compound (II), which lacks an asymmetric substituent, with rapid nitrogen inversion shows singlet signals from the ring protons and methyl groups (Fig. 3).

An A_2B_2 spectrum has also been detected for the protons of the azetidine ring with an asymmetric nitrogen substituent [6]



In nonaziridine systems the asymmetric induction of vicinal nonequivalent of the protons has been found on derivatives of scopolamine and teloidine [7]. A rigidly oriented asymmetric center should induce magnetic nonequivalence of the protons in the following derivatives of acetidine, pyrrolidine, and cyclopropane:



To confirm this supposition we prepared derivatives of azetidine and pyrrolidine with an asymmetric center in the α position of the substituent

$$(CH_2)_nNH \xrightarrow{ROOCCH=CHCOOR} (CH_2)_nNCH(COOR)CH_2COOR$$

$n = 3$, R = Et (III);
$n = 4$, R = Me (IV)

However, we were unable to prepare the desired methiodide, since MeI caused ring opening in (III)

$$(III) \xrightarrow{MeI} I(CH_2)_3\overset{+}{N}(Me)_2CH(COOEt)CH_2COOEt \quad (V)$$
$$I^-$$

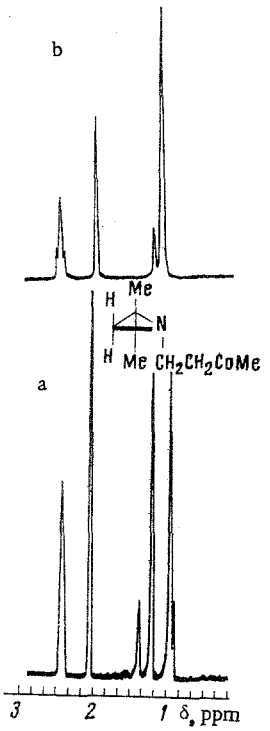


Fig. 3. PMR spectra of (II) at 60 MHz in C_6F_6: a) at −16°C under the conditions of slow nitrogen inversion; b) at 110°C under the conditions of rapid nitrogen inversion.

while the methiodide prepared from (IV) easily underwent Hofmann degradation in acetone

$$(IV) \xrightarrow{MeI} \underset{I^-}{(CH_2)_4\overset{+}{N}(Me)CH(COOMe)CH_2COOMe} (VI) \rightarrow \xrightarrow[(CD_3)_2CO]{-MeOOCCH=CHCOOMe} (CH_2)_4NMe\cdot HI \qquad (VII)$$

The PMR spectrum of the cyclopropane (VIII) shows no distinctly observable nonequivalence of the vicinal ring protons. In an attempt to increase the asymmetry of the substituent we acylated (VIII) with bis(trifluoromethyl)ketone, but this was accompanied by rearrangement involving ring opening

$$\underline{CH_2CH_2}CHC(OH)MePh \xrightarrow{(CF_3)_2C=C=O} (CF_3)_2CHCOO(CH_2)_2CH=C(Me)Ph$$
(VIII) (IX)

We were unable to prepare suitable compounds to investigate the asymmetric induction of magnetic nonequivalence of protons and carbons in the nonaziridine systems. However, we do not doubt the generality of this phenomenon, nor that it can be used for spectral analysis and stereochemical studies of carbocycles and heterocycles.

EXPERIMENTAL

The PMR spectra were recorded with Jeol JNM-C60-HL and Varian HA-100 spectrometers; chemical shifts are referred to hexamethyldislane (internal standard) and CF_3COOH (external standard).

Dimethyl β-(2,2-Dimethylaziridin-1-yl)succinate (I). A mixture of 2,2-dimethylaziridine (1.8 g) and dimethyl maleate (3.6 g) was warmed at 50°C. Vacuum-distillation yielded dimethyl fumarate (0.3 g) followed by (I) (4.3 g, 80%), bp 86°C (1 mm), n_D^{20} 1.4467. Found: C 55.97; H 7.88; N 6.49%. $C_{10}H_{17}NO_4$. Calculated: C 55.81; H 7.90; N 6.51%.

β-(2,2-Dimethylaziridin-1-yl)ethyl Methyl Ketone (II). 2,2-Dimethylaziridine (3.6 g) and methyl vinyl ketone (3.5g) in ether (30 ml) gave (II) (6.1g, 86%), bp 30°C (1.5 mm), n_D^{20} 1.4395. Found: C68.21; H 10.54; N 10.10%. $C_8H_{15}NO$. Calculated: C 68.04; H 10.70; N 9.92%.

Diethyl Azetidin-1-ylsuccinate (III). A mixture of azetidine (1.14 g) and diethyl maleate (3.45 g) was heated for 2 h at 80°C. Distillation yielded (III) (2.3g, 50%), bp 112°C (0.5 mm), n_D^{20} 1.4492. Found: C 57.95; H 8.42; N 6.84%. $C_{11}H_{19}NO_4$. Calculated: C 57.63; H 8.30; N 6.11%. NMR spectrum (100 MHz, CCl_4, δ, ppm): 1.22 and 1.27 ($MeCH_2O$); 4.08 and 4.16 ($MeCH_2O$, $J_1 = J_2 = 7.0$ Hz); 2.2-2.66 (CH_2); 3.27 (CH–N, $J_{HCCH_A} = 8$, $J_{HCCH_B} = 6$ Hz); 1.97 M (β-CH_2); 3.27 M (α-CH_2).

In an attempt to prepare the methiodide, (III) (1 g) was treated with MeI (1.2 ml). After 24 h the mixture was dissolved in acetone; ether was added until turbidity persisted and the reaction mixture was left in a refrigerator. We isolated a yellow crystalline product (V) (0.3g, 13.6%), mp 75-76°C. Found: C 30.91; H 5.00; N 2.95%. $C_{13}H_{25}NO_4I_2$. Calculated: C 30.41; H 4.90; N 2.74%. PMR spectrum (100 MHz, acetone-d_6, δ, ppm): 1.18 and 1.27 ($MeCH_2O$); 4.1 and 4.3 ($MeCH_2O$, $J_1 = J_2 = 7$ Hz); 2.35-2.75 (CH_2I); 3.85-4.05 (CH_2N); 3.52 and 3.56 (Me_2N); 3.10-3.75 (CH_2); 4.81 (CH, $J_{HCCH_A} = 10$, $J_{HCCH_B} = 4.0$ Hz).

Dimethyl Pyrrolidin-1-ylsuccinate (IV). Reaction of pyrrolidine (1.4 g) and dimethyl maleate (2.9 g) followed by vacuum-distillation at 50-70°C (2 mm) yielded (IV) (3.6 g, 83.7%), mp. 42-43°C. Found: C 55.68; H 7.93; N 6.57%. $C_{10}H_{17}NO_4$. Calculated: C 55.81; H 7.91; N 6.51%. NMR spectrum (100 MHz, CCl_4, δ, ppm): 1.65 M (β-CH_2); 2.68 M (α-CH_2); 3.2-3.9 M (CH, CH_2); 3.57 and 3.62 (MeO).

Dimethyl Pyrrolidin-1-ylsuccinate Methiodide (VI). A mixture of (IV) (1.8 g) and MeI (3.9 g, threefold excess) in ether (15 ml) was allowed to stand for two days at 20°C. The precipitate was removed and recrystallized from acetone–ether. We obtained (VI) (1.5 g, 50%), mp 86-88°C. Found: C 36.92; H 5.77; N 3.82%. $C_{11}H_{20}NO_4$. Calculated: C 36.97; H 5.60; N 3.92%. On dissolution in acetone-d_6 (VI) decomposed forming dimethyl fumarate (δ, ppm): 3.71 (MeO); 6.7 (CH) (acetone-d_6), and N-methylpyrrolidine hydroiodide (VII), mp 107°C, (δ, ppm): 2.08 and β-CH_2); 3.37 m (α-CH_2); 2.86 (MeN) (acetone-d_6).

Methylphenylcyclopropylmethanol (VIII) was prepared from methyl cyclopropyl ketone and phenylmagnesium bromide following [8], bp 130°C (22 mm), n_D^{20} 1.5345, and also from phenyl cyclopropyl ketone and methylmagnesium iodide in 54.5% yield, bp 119-120°C (14 mm), n_D^{20} 1.5352 [8].

3-Buten-1-yl Bis-2-(trifluoromethyl)acetate (IX). Reaction of bis(trifluoromethyl)ketene (2.2 g) and (VIII) (2 g) at –70°C followed by distillation yielded (IX) (0.9 g, 21%), bp 95-97°C (1 mm), n_D^{20} 1.4612. PMR spectrum (100 MHz, acetone-d_6, δ, ppm): 2.0 (Me); 2.52 (CH_2–CH=, $J_{CH_2CH_2} = J_{CH_2CH} = 7.0$ Hz); 3.85 (CH, $J_{HCCF} = 7.5$ Hz); 4.27 (CH_2O); 5.58 (CH=, $J_{HC=CCH_3} = -1.4$ Hz); 7.22 (Ph). ^{19}F NMR spectrum: $\delta_{CF_3} - 0.5$ ppm. The cis orientation of the proton and the CH_3 group follows from the value of $J_{HC=CCH_3}$, since $J^{cis}_{HC=CCH_3} = -1.5$ Hz and $J^{trans}_{HC=CCH_3} = -0.8$ Hz for α-methylstyrene [9].

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CONCLUSIONS

1. The PMR spectra of 1-(α-phenylethyl)aziridine under conditions of slow nitrogen inversion show vicinal nonequivalence of the ring protons, which is greater for the protons trans to the N substituent.

2. The PMR spectra of dimethyl β-(2,2-dimethylaziridin-1-yl)succinate under the conditions of rapid nitrogen inversion show magnetic nonequivalence of the ring protons and methyl groups.

3. Acylation of methylphenylcyclopropylmethanol with bis(trifluoromethyl)ketene results in anionotropic rearrangement involving ring opening.

LITERATURE CITED

1. R. G. Kostyanovskii, A. A. Fomichev, G. K. Kadorkina, and Z. E. Samoilova, Dokl. Akad. Nauk SSSR, 195, 406 (1970); R. G. Kostyanovskii, A. A. Fomichev, L. M. Zagurskaya, G. K. Kadorkina, and Kh. Khafizov, Izv. Akad. Nauk SSSR, Ser. Khim., 2154 (1970).
2. E. P. Tyurina, Dissertation, Moscow (1975).
3. Yu. K. Grishin, N. M. Sergeyev, O. A. Subbotin, and Yu. A. Ustynyuk, Mol. Phys., 25, 297 (1973).
4. F. A. Anet, R. D. Trepka, and D. J. Cram, J. Am. Chem. Soc., 89, 357 (1967).
5. R. G. Kostyanovskii, A. E. Polyakov, M. D. Isabaev, G. K. Kadorkina, and V. I. Markov, Izv. Akad. Nauk SSSR, Ser. Khim., 1444 (1974).
6. A. G. Anderson, Jr., and M. T. Wills, J. Org. Chem., 33, 2123 (1968).
7. S. R. Johns and J. A. Lamberton, Chem. Commun., 458 (1965).
8. T. A. Favorskaya and Sh. A. Fridman, Zh. Obshch. Khim., 20, 586 (1950).
9. M. Barfield, Chem. Rev., 69, 757 (1969); J. Am. Chem. Soc., 92, 1066 (1971).