X-RAY STRUCTURAL INVESTIGATION OF NOVEL AZABICYCLIC SYSTEMS CONTAINING AZIRIDINE RINGS

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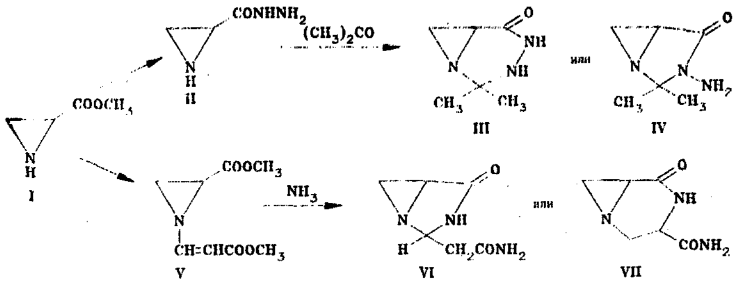
Successive conversion reactions of methyl aziridine-2-carboxylate have been used to prepare novel azabicyclic derivatives, namely, 2-carbamoylmethyl-1,3-diazabicyclo[3.1.0]hexan-4-one and 2,2-dimethyl-1,3,4-triazabicyclo[4.1.0]heptan-5-one, whose structures were established unequivocally by x-ray structure analysis.

Derivatives of aziridine-2-carboyxlic acid are of interest both from a biological [1-3] and chemical point of view [4, 5], since they may be regarded as analogs of naturally occurring α-amino acids. The presence of two reactive sites in these molecules opens up a wide range of synthetic possibilities, among them the synthesis of novel bicyclic systems containing an aziridine ring and a bridging nitrogen atom. Only a few reports have appeared concerning the preparation of these types of structures [6, 7], and only one report has dealt with x-ray structure analysis for structure proof of a diazabicyclic derivative [8].

We have examined [5, 9] the feasibility of synthesizing novel heterocyclic systems containing an aziridine fragment in two ways, by the reaction of the hydrazide of aziridine-2-carboxylic acid with acetone, and by successive reactions of the methyl ester of aziridine-2-carboxylic acid with methyl propiolate and ammonia:



According to a published report [10], the imine group in hydrazides is the most reactive site in hydrazide derivatives of acyclic amino acids; we have come to the opposite conclusion on the basis of NMR spectral analysis, which showed that, for the reaction of hydrazide II with acetone, only structure III, and not IV, is obtained [9]. In this reaction, then, the carbonyl component reacts with the amine nitrogen atom of the hydrazide derivative. An x-ray structural analysis was carried out on compound III in order to verify this conclusion. A three-dimensional representation of a molecule of III, with atomic designations, bond length values (Å), and bond angles (degrees), is shown in Fig. 1. The six-membered ring in III occupies a half-chair conformation. The deviations of atoms $C_{(2)}$ and $N_{(3)}$ from the average plane of the remaining four atoms are 0.276 and 0.342 Å, in opposite directions, respectively. $N_{(3)}$ is bent away in the direction of $C_{(7)}$ in the aziridine ring. The dihedral angle between the three-membered ring and the average plane of the six-membered ring is 83.7°. The endocyclic bond angles around atoms $N_{(1)}$ and $C_{(6)}$ in the six-membered ring are similar in value to the corresponding bond angles in non-condensed aziridine derivatives [11, 12]. $N_{(3)}$ adopts a pyramidal configuration, with the pyramid height equal to 0.673 A. The $C_{(2)}$–$N_{(1)}$ bond is bent away from the plane of the aziridine ring (φ') by 59.0°. The sum of the bond angles around $N_{(1)}$ is 293.2°. The geometric parameters of the cis-amide group in III overlap those

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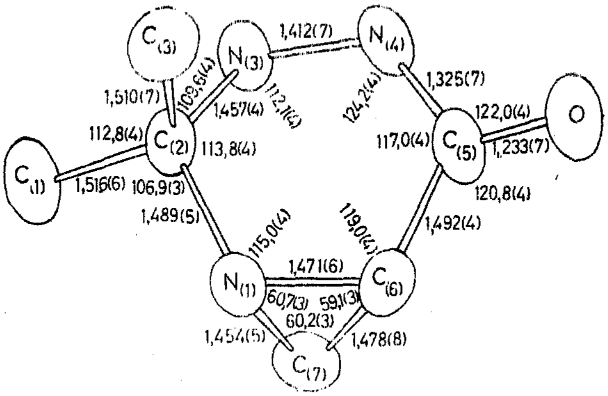

Fig. 1. Geometric parameters of a molecule of III.

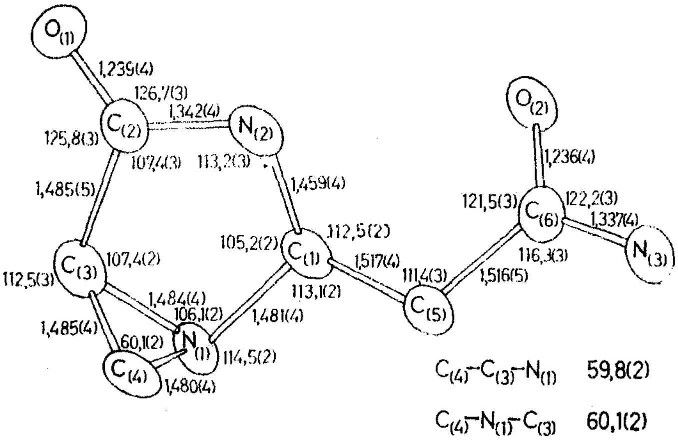

Fig. 2. Geometric parameters of a molecule of VI.

TABLE 1. X–H•••Y Hydrogen Bond Parameters in Structures III and VI

Structure	Atom X	Atom Y	X···Y, Å	H···Y, Å	∠X–H···Y, deg
III	$N_{(3)}$ $N_{(4)}$	O $N_{(1)}$	3,00 2,91	2,12 1,95	167,8 167,7
VI	$N_{(3)}$ $N_{(3)}$ $N_{(2)}$	$O_{(1)}$ $O_{(2)}$ $N_{(1)}$	2,90 2,93 2,95	2,14 2,05 2,12	159,2 173,2 154,2

found in the cis-peptide bond in cyclic dipeptides [13]. The $N_{(4)}$–$C_{(5)}$ bond [1.325(7) Å] has one and one-half bond character, whereas the other C–N bond is a single bond. In the crystalline state molecules of III are associated via a system of intermolecular hydrogen bonds, the parameters of which are given in Table 1.

The product of the reaction of aziridine-2-carboxylic acid hydrazide with acetone has thus been shown to be 2,2-dimethyl-1,3,4-triazabicyclo[4.1.0]heptan-5-one.

We have also previously demonstrated that ammonia reacts readily with diester V [5]. NMR structure analysis of this reaction led to the conclusion that compound VI was formed as the reaction product. X-ray structural analysis of this reaction product was carried out in order to select unequivocally between the two structural possibilities, VI and VII. A three-dimensional representation, with atom designations, bond lengths (Å), and bond angles (degrees) is shown in Fig. 2. The five-membered ring present in molecule VI adopts an envelope conformation. The deviation of $N_{(2)}$ away from the strict planarity (±0.01 Å) of the $C_{(1)}C_{(2)}C_{(3)}N_{(1)}$ fragment is 0.110 Å in the direction of $C_{(4)}$ of the aziridine ring. The substituent attached to $C_{(1)}$ occupies a pseudoequatorial orientation. The angle between the planar (±0.03 Å) $C_{(1)}$-

TABLE 2. Atomic Coordinates of Nonhydrogen Atoms in Structures III and VI ($\times 10^4$)

Structure III				Structure VI			
atom	x	y	z	atom	x	y	z
$C_{(1)}$	4229 (7)	1872 (0)	1562 (7)	$O_{(1)}$	9454 (5)	1695 (1)	7094 (2)
$C_{(2)}$	3780 (4)	3206 (6)	2674 (5)	$O_{(2)}$	7100 (5)	0154 (1)	1915 (2)
$C_{(3)}$	5615 (6)	4120 (8)	3184 (7)	$N_{(1)}$	13864 (5)	1254 (2)	4328 (3)
$C_{(5)}$	1150 (5)	4984 (6)	4538 (6)	$N_{(2)}$	9525 (6)	1100 (2)	4623 (3)
$C_{(6)}$	0903 (5)	4850 (6)	1911 (5)	$N_{(3)}$	7401 (7)	0780 (2)	-0429 (3)
$C_{(7)}$	0130 (5)	3564 (6)	0777 (6)	$C_{(1)}$	11415 (6)	0863 (2)	3600 (3)
$N_{(1)}$	2255 (4)	3927 (6)	0902 (4)	$C_{(2)}$	10585 (7)	1474 (2)	5978 (3)
$N_{(3)}$	3067 (4)	2895 (6)	4876 (4)	$C_{(3)}$	13353 (7)	1616 (2)	5864 (3)
$N_{(4)}$	2235 (4)	4041 (6)	5820 (4)	$C_{(4)}$	13723 (8)	2157 (2)	4500 (4)
O	0452 (4)	5971 (6)	5445 (5)	$C_{(5)}$	10593 (7)	1109 (2)	1867 (3)
				$C_{(6)}$	8226 (6)	0634 (2)	1120 (3)

$C_{(5)}C_{(6)}O_{(2)}N_{(3)}$ fragment and the average plane of the five-membered ring is 52.2°. The crystal structure of 2-p-bromphenyl-1,3-diazabicyclo[3.1.0]hexane has been studied [8]; in analogy with compound VI, this molecule possesses condensed aziridine and imidazoline rings. The deviation of the aziridine ring from the average planarity of the five-membered ring is identical in the two structures, close to 75°. The endocyclic bond angles around atoms $N_{(1)}$ and $C_{(3)}$ in the five-membered ring are similar in values to those in corresponding bicyclic derivatives, and are 7-12° less than those in noncondensed aziridine derivatives [11, 12]. $N_{(1)}$ adopts a pyramidal configuration with a pyramid height of 0.747 Å. The $C_{(1)}-N_{(1)}$ bond forms an angle of 65.0° with the plane of the aziridine ring (φ'). The crystal packing of molecules of III is stabilized by a system of three hydrogen bonds, whose parameters are given in Table 1. The other intermolecular contacts are within the sum of van der Waals radii of the respective atoms in contact [14]. An interesting characteristic of these structures is the involvement of the aziridine ring nitrogen atom in intermolecular hydrogen bond formation.

EXPERIMENTAL

2,2-Dimethyl-1,3,4-triazabicyclo[4.1.0]heptan-5-one (III) was prepared according to [10], and 2-carbamoylmethyl-1,3-diazabicyclo[3.1.0]hexan-4-one (VI) according to [5].

X-Ray Structural Analysis. Crystals of 2,2-dimethyl-1,3,4-triazabicyclo[4.1.0]heptan-5-one (III) of composition $C_6H_{11}N_3O$ were monoclinic: a = 6.681(1), b = 9.874(2), c = 5.731(1) Å, β = 100.04°, V = 372.3(1) Å^3, M = 141.17, d_{calc} = 1.26 g/cm^3, Z = 2, space group $P2_1$, F_{000} = 152.

Crystals of 2-carbamoylmethyl-1,3-diazabicyclo[3.1.0]hexan-4-one (VI) of composition $C_6H_9N_3O_2$ were monoclinic: a = 5.235(1), b = 16.266(3), c = 8.448(1) Å, β = 98.50(2)° V = 711.5 (2) Å^3, M = 155.16, d_{calc} = 1.45 g/cm^3, Z = 4, space group $P2_1/c$, F_{000} = 328.

The intensities of 561 independent reflections for compound III and 1111 independent reflection for compound VI were measured on a Syntax $P2_1$ diffractometer (CuK_α irradiation, graphite monochromator) using θ/2θ scan method up to $2\theta_{max}$ = 150°. The structures were solved by direct methods using a MULTAN system XTL program and were refined by the method of least squares using full matrix anisotropic approximations for the nonhydrogen atoms and isotropic parameters for the hydrogen atoms; the positions of the hydrogen atoms were obtained by difference (Fourier) synthesis. The final R factors were 0.034 for III and 0.047 for VI. The atomic coordinates of the nonhydrogen atoms in compounds III and VI are given in Table 2.

LITERATURE CITED

1. I. Kalvins and E. B. Astapenok, Patent 860 239 (Belgium); Chem. Abst., 90, 30439 (1979).
2. U. Bicker and U. Hebold, IRCS Med. Sci.; Libr. Compend., 5, 428 (1977).
3. U. Bicker, Cancer Treatment Reports, 62, 1987 (1978).
4. P. T. Trapentsier, I. Ya. Kalvin'sh, E. E. Liepin'sh, and E. Ya. Lukevits, Khim. Geterotsikl. Soedin., No. 4, 481 (1983).
5. P. T. Trapentsier, I. Ya. Kalvin'sh, E. E. Liepin'sh, and E. Ya. Lukevits, Khim. Geterotsikl. Soedin., No. 3, 350 (1983).
6. S. A. Giller, A. V. Eremeev, I. Yu. Lidak, and V. A. Kholodnikov, Khim. Geterotsikl. Soedin., No. 5, 607 (1971).

7. H. Moureau, P. Chovin, and L. Petit, C. r., 243, 910 (1956).
8. S. A. Giller, Ya. Ya. Bleidelis, A. A. Kemme, A. V. Eremeev, and V. A. Kholodnikov, Khim. Geterotsikl. Soedin., No. 16, 411 (1975).
9. P. T. Trapentsier, I. Ya. Kalvin'sh, E. E. Liepin'sh, E. Ya. Lukevits, G. A. Bremanis, and A. V. Eremeev, Khim. Geterotsikl. Soedin., No. 6, 774 (1985).
10. P. S. Lobanov, A. N. Poltorak, and A. A. Potekhin, Zh. Org. Khim., 14, 1086 (1978).
11. A. F. Mishniev, Ya. Ya. Bleidelis, A. V. Eremeev, F. D. Polyak, and B. S. Kataev, Zh. Struk. Khim., 23, 86 (1982).
12. A. V. Eremeev, F. D. Polyak, A. F. Mishniev, Ya. Ya. Bleidelis, E. E. Liepiñ'sh, Sh. S. Nasibov, I. I. Chervin, and R. G. Kostyanovskii, Khim. Geterotsikl. Soedin., No. 11, 1495 (1982).
13. G. N. Tishchenko in: Itogi Nauku: Kristallokhimiya, Moscow (1979), Vol. 13, p. 189.
14. Yu. V. Zefirov and P. M. Zorkii, Zh. Strukt. Khim., 17, 994 (1976).

NEW EXAMPLES OF THE VINYLATION OF NH-HETEROCYCLES WITH ACETYLENE AT ATMOSPHERIC PRESSURE IN THE KOH—DMSO SYSTEM

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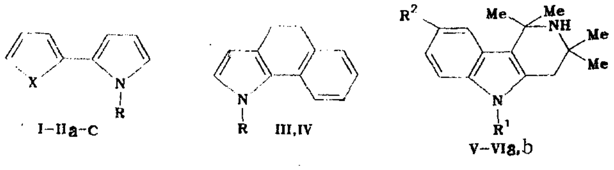
Vinylation of 2-hetarylpyrroles, 4,5-dihydrobenzo[g]indole, and 1,2,3,4-tetrahydro-γ-carbinols at atmospheric pressure in the superbasic system KOH—DMSO at 100-120°C has given the corresponding N-vinyl derivatives in yields of 92-99%.

Until recently, the N-vinylation of heterocycles with acetylene was carried out under a pressure of 20-40 atm at 160-200°C. In view of the explosive hazards of this reaction, its preparative use was extremely limited, and this has substantially retarded the development of the chemistry of N-vinylheterocycles.

It has recently been shown that the superbasic KOH—DMSO catalytic system enables the vinylation of alkyl- and arylpyrroles to be carried out at atmospheric pressure and temperatures as low as 100-120° (see [1] and the citations therein).

The object of this investigation was to assess to what extent this novel method was suitable for the synthesis of N-vinyl derivatives of other heterocycles.

The subjects chosen for study were the 2-hetarylpyrroles Ia, b, 4,5-dihydrobenzo[g]indole (III), and the 1,2,3,4-tetrahydro-γ-carbinols Va,b, 2-phenylpyrrole (Ic) being taken for comparison with the corresponding 2-furyl- (Ia) and 2-thienyl- (Ib) pyrroles.



I–IIa–c
III,IV
V–VIa,b

Ia–c, III $R=H$, IIa–c, IV $R=CH{=}CH_2$; I, II a $X=O$, b $X=S$, e $X=CH{=}CH$; Va,b $R^1=H$, VIa, b $R^1=CH{=}CH_2$; V, VI a $R^2=H$, b $R^2=Me$

The reaction was carried out in a glass flask with a stirrer. Acetylene was passed into the reaction mixture at atmospheric pressure. When vinylating the 2-hetarylpyrroles Ia,b and 2-phenylpyrrole Ic, a fivefold exceys of KOH was employed. The progress of the reaction was followed by GC. Chromatographically pure N-vinylpyrroles IIa,b were obtained by a single

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