SYNTHESIS OF 3,6,7-TRIAZABICYCLO[3.3.0]OCTENES BY 1,3-CYCLOADDITION WITH N-ARYLPYRROLIDIN-2-ONES

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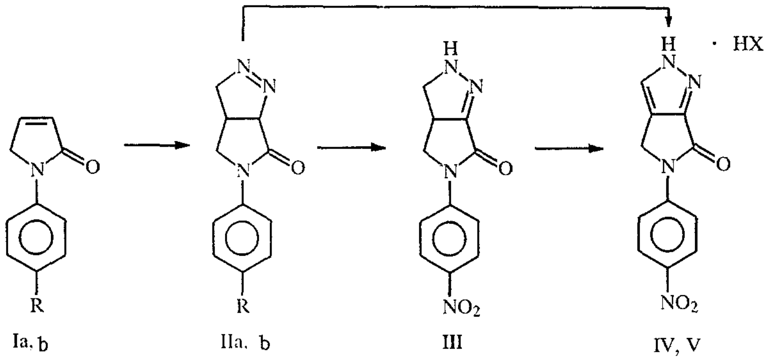
The 1,3-dipolar cycloaddition of diazomethane to 1-(4-R-phenyl)-5H-pyrrolidin-2-one was investigated. Some properties of the triazabicyclo[3.3.0]octenes, including the results of an x-ray diffraction analysis, were studied.

In a continuation of our study of 1,3-dipolar cycloaddition in the pyrrolidinone series [1] we studied the reaction of 1-(4-aryl)-5H-pyrrolidin-2-ones Ia, b with diazomethane. The cycloaddition proceeds regioselectively to give adducts IIa, b, which correspond to the "normal" relative orientation of the enone and the dipole in which the methylene groups always reacts with the most electron-deficient β-carbon atom of the dipolarophile [2, 3].



I, IIa R=NO$_2$, b R=SO$_2$NH$_2$; IV X=Cl; V X=Br

The regiospecificity corresponds to concerted 1,3-dipolar cycloaddition [4].

The reaction is distinguished by cis stereospecificity. The 5-H methylidyne proton shows up in the PMR spectrum of adduct IIa in the form of a multiplet at 5.7 ppm. The second 1-H methylidyne proton also shows up in the form of a multiplet, but it is located at stronger field (2.94 ppm, J_{15} = 9.5 Hz) with a cis orientation of the 5-H and 1-H protons.

It was established by double resonance that the 1-H proton couples with the two 2-H methylene protons (J_{12} = 9.5 Hz, J_{12} = 4.0 Hz), as well as with the 8-H proton (J_{18} = 8.5 Hz, J_{18} = 5.0 Hz). All of the methylene protons are chemically nonequivalent and resonate in different regions [2-H$_1$ at 4.12 ppm, 2-H$_2$ at 3.60 ppm (^2J = 10.5 Hz), 8-H$_3$ at 4.92 ppm, and 8-H$_4$ at 4.74 ppm (^2J = 18.5 Hz)]; this is due to the asymmetry of the molecule.

The stereochemical characteristics of the bicyclic system are controlled chiefly by two factors: repulsion of the electron shells of the covalently nonbonded atoms and the effects of n—π conjugation. Thus in the crystalline IIa molecule (Fig. 1) the pyrazoline ring has an "envelope" conformation with a deviation of 14° with respect to the $C_{(8)}$-$C_{(11)}$ axis, and the

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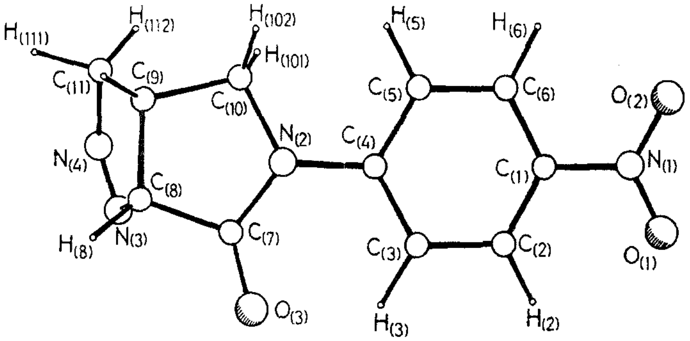

Fig. 1. X-ray diffraction pattern of crystalline IIa.

TABLE 1. Bond Angles in Structure IIa

Angle	ω, °	Angle	ω, °
$O_{(1)}N_{(1)}O_{(2)}$	128,8(3)	$O_{(1)}N_{(1)}C_{(1)}$	118,4(2)
$O_{(2)}N_{(1)}C_{(1)}$	118,8(2)	$C_{(4)}N_{(2)}C_{(7)}$	126,3(2)
$C_{(4)}N_{(2)}C_{(10)}$	120,3(2)	$C_{(7)}N_{(3)}C_{(10)}$	113,1(2)
$N_{(4)}N_{(3)}C_{(8)}$	111,5(2)	$N_{(3)}N_{(4)}C_{(11)}$	112,5(3)
$N_{(1)}C_{(1)}C_{(2)}$	119,5(2)	$N_{(1)}C_{(1)}C_{(6)}$	118,7(2)
$C_{(2)}C_{(1)}C_{(6)}$	121,7(2)	$C_{(1)}C_{(2)}C_{(3)}$	119,7(2)
$C_{(2)}C_{(3)}C_{(4)}$	119,3(2)	$C_{(2)}C_{(4)}C_{(3)}$	121,7(3)
$N_{(2)}C_{(4)}C_{(5)}$	118,8(2)	$C_{(3)}C_{(4)}C_{(5)}$	119,5(3)
$C_{(4)}C_{(5)}C_{(6)}$	120,8(2)	$C_{(1)}C_{(6)}C_{(5)}$	118,8(2)
$O_{(3)}C_{(7)}N_{(2)}$	126,7(3)	$O_{(3)}C_{(7)}C_{(8)}$	125,2(3)
$N_{(2)}C_{(7)}C_{(8)}$	108,1(2)	$N_{(3)}C_{(8)}C_{(7)}$	109,3(2)
$N_{(3)}C_{(8)}C_{(9)}$	105,7(2)	$C_{(7)}C_{(8)}C_{(9)}$	107,5(2)
$C_{(8)}C_{(9)}C_{(10)}$	105,2(2)	$C_{(8)}C_{(9)}C_{(11)}$	102,6(2)
$C_{(10)}C_{(9)}C_{(11)}$	115,6(2)	$N_{(2)}C_{(10)}C_{(9)}$	105,3(2)
$N_{(4)}C_{(11)}C_{(9)}$	105,6(2)		

TABLE 2. Bond Lengths in Structure IIa

Bond	d	Bond	d
$O_{(1)}—N_{(1)}$	1,217(2)	$O_{(2)}—N_{(1)}$	1,221(4)
$O_{(3)}—C_{(7)}$	1,215(3)	$N_{(1)}—C_{(1)}$	1,459(3)
$N_{(2)}—C_{(4)}$	1,411(4)	$N_{(2)}—C_{(7)}$	1,367(4)
$N_{(2)}—C_{(10)}$	1,473(3)	$N_{(3)}—N_{(4)}$	1,242(4)
$N_{(3)}—C_{(8)}$	1,500(4)	$N_{(4)}—C_{(11)}$	1,483(3)
$C_{(1)}—C_{(2)}$	1,376(4)	$C_{(1)}—C_{(6)}$	1,373(3)
$C_{(2)}—C_{(3)}$	1,389(5)	$C_{(3)}—C_{(4)}$	1,398(4)
$C_{(4)}—C_{(5)}$	1,389(4)	$C_{(5)}—C_{(6)}$	1,383(4)
$C_{(7)}—C_{(8)}$	1,508(4)	$C_{(8)}—C_{(9)}$	1,505(5)
$C_{(9)}—C_{(10)}$	1,535(4)	$C_{(9)}—C_{(11)}$	1,517(5)

pyrrolidone ring deviates 9.1° with respect to the $C_{(8)}$-$C_{(10)}$ axis. The angle between the flaps of the envelopes with a base along the $C_{(8)}$-$C_{(9)}$ bond is 58.7°. The benzene ring is situated in the plane of the base of the "envelope" of the pyrrolidone ring — torsion angle $C_{(7)}N_{(2)}C_{(4)}C_{(5)}$ is equal to 179.4°. The nitro group, in turn, deviates to a small degree from the plane of the benzene ring — torsion angle $C_{(2)}C_{(1)}N_{(1)}O_{(2)}$ is equal to 178.3°. The principal bond distances and some of the bond angles of structure IIa are presented in Tables 1 and 2. The C—H distances range from 0.93 to 1.02 Å. There are no intramolecular interactions, and the intermolecular interactions are limited to van der Waals interactions.

We carried out a number of transformations with the pyrazolines obtained. It is known [5] that Δ^1-pyrazolines are unstable: Under the influence of acids and bases they are readily converted to Δ^2-pyrazolines. This possibility was checked in the case of IIa. Triethanolamine was used as the base, and 4-oxo-3-(4-nitrophenyl)-3,6,7-triazabicyclo[3.3.0]oct-5-ene (III)

TABLE 3. Characteristics of the Synthesized Compounds

Compound	mp, °C	TLC, R_f	UV spectrum (in ethanol), λ_{max}, nm (log ε)	IR spectrum, cm^{-1}			
				C=O	C=N	N=H	N=N
IIa	181...183	0,80	206(4,16); 312(4,32)	1700	—	—	1590
IIb	156...158	0,49	211(4,07); 270(4,03)	1685	—	3300, 3420	1590
III	163...165	0,74	208(4,22); 316(4,80)	1700	1675	3390	—
IV	161...163	0,58	225(4,89); 321(4,95)	1705	1632	3345 br	—
V	168...169	0,54	225(4,74); 319(4,83)	1705	1638	3350 br	—

TABLE 4. Coordinates of the Nonhydrogen Atoms (×10^4) in Structure IIa

Atom	x	y	z	Atom	x	y	z
$O_{(1)}$	3861(2)	72(1)	4442(3)	$C_{(3)}$	3397(3)	1689(1)	6469(4)
$O_{(2)}$	5270(3)	698(1)	3134(4)	$C_{(4)}$	4066(3)	2324(1)	5927(4)
$O_{(3)}$	2441(1)	2463(1)	8192(2)	$C_{(5)}$	4912(2)	2389(1)	4851(2)
$N_{(1)}$	4516(2)	621(1)	4076(2)	$C_{(6)}$	5083(2)	1832(1)	4277(3)
$N_{(2)}$	3888(2)	2905(1)	6417(3)	C(7)	3090(2)	2929(1)	7453(3)
$N_{(3)}$	2128(2)	3677(1)	6693(4)	C(8)	3134(2)	3640(1)	7506(3)
$N_{(4)}$	2387(2)	4097(1)	5606(3)	C(9)	4109(2)	4058(1)	6516(3)
$C_{(1)}$	4394(2)	1210(1)	4781(3)	C(10)	4514(2)	3556(1)	5678(3)
$C_{(2)}$	3566(3)	1131(1)	5876(4)	C(11)	3605(2)	4439(1)	5442(4)

was obtained in good yield. In addition, the hydrochloride (IV) and hydrobromide (V) salts of the pyrazole were obtained by oxidation of IIa. The oxidation proceeds through the formation of Δ^2-pyrazoline III; this was observed by TLC.

EXPERIMENTAL

The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The ^1H NMR spectra of solutions in $CDCl_3$ and d_6-DMSO were recorded with a Bruker WM-250 spectrometer (250 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol-254 plates with acetone—CCl_4—petroleum ether (4:2:1) as the eluent and development with 2,4-dinitrophenylhydrazine hydrochloride.

The compositions of the compounds obtained were confirmed by the results of elementary analysis with respect to C, H, and N. The physicochemical constants of the synthesized compounds are presented in Table 3.

Colorless, transparent, monoclinic crystals with the dimensions 0.35 by 0.30 by 0.10 mm ($C_{11}H_{10}N_4O_3$) were obtained by crystallization of the compound from ethyl acetate—ethanol (2:1). The cell parameters were as follows: a = 12.957(2) Å, b = 21.496(3) Å, c = 8.407(1) Å, γ = 111.54(1) Å, V = 2177.9(5) Å^3, space group P2/a, and Z = 8. The experimental data were obtained with a Syntex P-1 automatic diffractometer (Mo K_α emission, β filter, $\theta/2\theta$ scanning up to $2\theta_{max}$ = 48°). A total of 977 independent reflections with $J \geq 3\sigma(J)$ were obtained. The structure was decoded by the direct method by means of a complex of SHELXTL programs [6] with a NOVA-3 computer and was refined within the anisotropic (isotropic for the hydrogen atoms) approximation up to divergence factors R = 0.029 and R_W = 0.032. The coordinates of the nonhydrogen atoms are presented in Table 4.

4-Oxo-3-(4-nitrophenyl)-3,6,7-triazabicyclo[3.3.0]oct-6-ene (IIa, $C_{11}H_{10}N_4O_3$). An ether solution (100 ml) of diazomethane, obtained from 0.1 mole of N-nitrosomethylurea [7], was added dropwise with constant stirring at room temperature in the course of 30 min to a solution of 2.5 g (12.5 mmole) of 1-(4-nitrophenyl)-5H-pyrroline-2-one (Ia) in 200 ml of DMF, after which the mixture was allowed to stand overnight. At the end of the reaction, the solvent was removed by distillation in vacuo, and the precipitated crystals were removed by filtration and washed with diethyl ether. The yield was 2.9 g (96%).

4-Oxo-3-(4-aminosulfonylphenyl)-3,6,7-triazabicyclo[3.3.0]oct-6-ene (IIb, $C_{11}H_{12}N_4O_3S$). The process was carried out in the same way as the synthesis of IIa using 2.5 g (10.5 mmole) of 1-(4-aminosulfonylphenyl)-5H-pyrrolin-2-one in 100 ml of DMF and 100 ml of an ether solution of diazomethane. The yield was 2 g (67%).

4-Oxo-3-(4-nitrophenyl)-3,6,7-triazabicyclo[3.3.0]oct-5-ene (III, $C_{11}H_{10}N_4O_3$). Triethanolamine (0.2 ml) was added with constant temperature at room temperature to a solution of 0.5 g (2 mmole) of IIa in 50 ml of DMF. After 5 h, the solvent was removed by distillation in vacuo, and the crystals were isolated and washed with ether. The yield was 0.45 g (71%).

4-Oxo-3-(4-nitrophenyl)-3,6,7-triazabicyclo[3.3.0]octa-5,8-diene Hydrochloride (IV, $C_{11}H_9N_4O_3Cl$). Concentrated HCl (0.2 ml) was added dropwise with constant stirring to a solution of 0.5 g (2 mmole) of IIa in 50 ml of ethanol, and the mixture was refluxed for 10 min. The solvent was then removed by distillation, and the precipitated crystals were removed by filtration and washed with ether. The yield was 0.48 g (86%).

4-Oxo-3-(4-nitrophenyl)-3,6,7-triazabicyclo[3.3.0]octa-5,8-diene Hydrobromide ($C_{11}H_9N_4O_3Br$). A solution of 0.16 g (1 mmole) of bromine in 3 ml of chloroform was added dropwise with stirring at room temperature to a solution of 0.5 g (2 mmole) of IIa in 80 ml of chloroform. At the end of the reaction, a precipitate formed immediately. It was removed by filtration and washed initially with chloroform and then with ether. The yield was 0.55 g (85%).

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