1,3-DIPOLAR CYCLOADDITION OF DIARYLNITRONES TO 1-(4-NITROPHENYL)-5H-PYRROLIN-2-ONE

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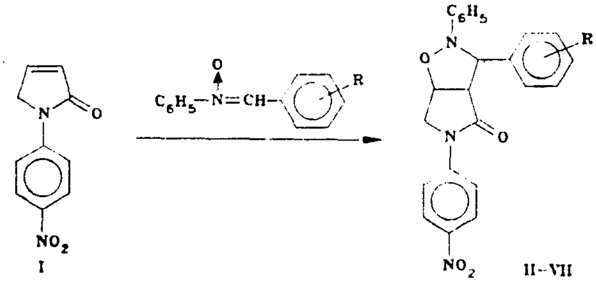
The reaction of diarylnitrones with 1-(4-nitrophenyl)-5H-pyrrolin-2-one to give 2-oxa-6-oxo-3-phenyl-4-(R-phenyl)-7-(4-nitrophenyl)-3,7-diazabicyclo(3,3,0)octanes has been examined. The structures of the products were established by NMR and IR spectroscopy, and x-ray diffraction studies. The stereoselectivity of the reaction is due to exo-approach of the reactants with cis-stereospecific addition of the trans-forms of the C,N-diarylnitrones to the pyrrolinone double bond.

The 1,3-dipolar cycloaddition of nitrones to alkenes has been used extensively for the synthesis of isoxazolidines [1-3]. We have now examined the reactions of diarylnitrones with 1-(4-nitrophenyl)-5H-pyrrolin-2-one (I), the dipolarophilic reactivity of which has not been reported. The adducts (II-VII) were obtained (Table 1).



II R=H; III R=3-NO$_2$; IV R=4-Br; V R=4-CH$_3$; VI R=4-OCH$_3$; VII R=4-N(CH$_3$)$_2$

The nitrones were prepared directly in the reaction mixture as described previously [4, 5]. In parallel, the pyrrolidone (I) was reacted with the pure nitrones. When the nitrones bore electron-acceptor groups, cycloaddition proceeded more slowly, to give high yields of the isoxazolidines (III) and (IV). When electron-donor groups were present, reaction times were shortened, but the yields of the adducts (VI) and (VII) were much lower.

It has been reported [6] that open-chain nitrones exist predominantly in the trans-form under the usual conditions. It is assumed that when nitrones react with (I), no isomerization occurs, since the rotation barrier around the C=N bond in N-phenyl-C-arylnitrones at 120°C is around 115.14 kJ [7], both the endo- and exo-approaches being possible.

The configurational composition of the bicyclic compounds (II-VII) was determined from the relationships between protons $H_{(3)}$ and $H_{(2)}$ and $H_{(4)}$ and $H_{(5)}$, in the PMR spectra (Table 2), expressed as the J_{3-5} and J_{4-5} constants, the numerical values of which for the compounds examined were greater than 6 Hz, as in cis-fused rings [8-10]. Similar J values have been reported for other bicyclo(3,3,0)octane analogs [11-13]. In this case, the $H_{(4)}$ proton will be pseudoequatorial, and the adjacent phenyl group pseudoaxial. This indicates that the trans-form of the nitrone undergoes cycloaddition, while the cis-orientation of the $H_{(4)}$ and $H_{(5)}$ protons indicates the exo-approach of the reactants.

In order to finally establish the orientation of $H_{(3)}$, $H_{(4)}$, and $H_{(5)}$, compound (II) was subjected to x-ray diffraction examination (Fig. 1; Tables 3 and 4). It was found that the pyrrolidone ring is nonplanar, having an envelope configuration in which $N_{(1)}$, $C_{(1)}$, $C_{(5)}$, and $C_{(3)}$ lie in the same plane, which incorporates $O_{(1)}$ (the departure of the atoms from this plane is no

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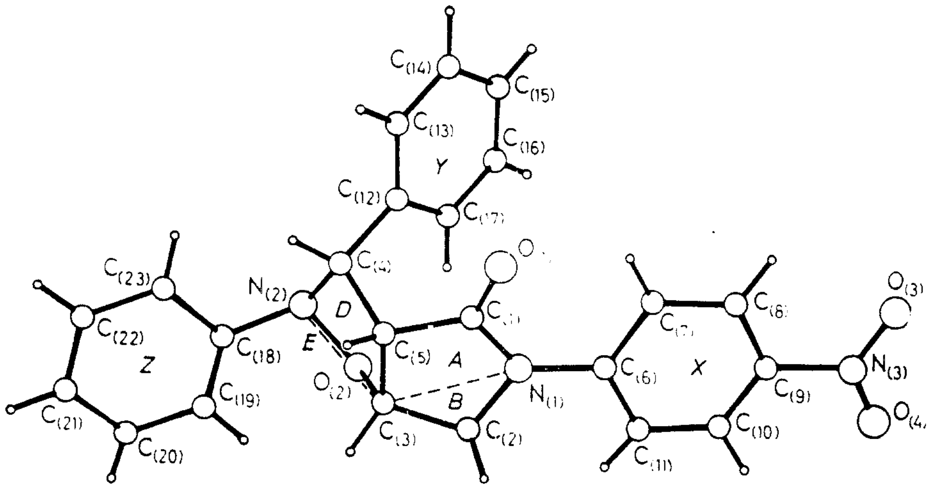

Fig. 1. Enumeràtions of atoms in (II).

TABLE 1. Properties of Compounds (II-VII)

Compound	Empirical formula	mp, °C	UV spectrum in ethanol, λ_{max}, nm (lg ε)	IR spectrum, $\nu_{C=O}$, cm^{-1}	R_f	Reaction time, h	Yield, %
II	$C_{23}H_{19}N_3O_4$	177 ... 178	322 (4,11)	1690	0,87	6	70
III	$C_{23}H_{18}N_4O_6$	203 ... 204	318 (4,24)	1715	0,86	12	82
IV	$C_{23}H_{18}BrN_3O_4$	163 ... 165	321 (4,10)	1700	0,88	10	92
V	$C_{24}H_{21}N_3O_4$	175 ... 176	321 (4,10)	1700	0,84	6	77
VI	$C_{24}H_{21}N_3O_5$	183 ... 185	324 (4,16)	1690	0,82	2	56
VII	$C_{25}H_{24}N_4O_4$	185 ... 186	321 (4,30)	1700	0,93	2	55

TABLE 2. PMR Spectra of (II-VII)

Compound	Chemical shift, ppm								Coupling constant, J, Hz				
	$H_{(2A)}$	$H_{(2B)}$	$H_{(3)}$	$H_{(4)}$	$H_{(5)}$	HCH·	$H_{(10)}$	$H_{(11)}$	$J_{2A,2B}$	$J_{2A,3}$	$J_{2B,3}$	$J_{3,5}$	$J_{4,5}$
II	4,02	4,14	5,15	5,00	3,85	—	8,07	7,39	11,00	2,50	7,00	8,25	9,50
III	4,09	4,33	5,18	5,68	4,22	—	8,18	7,62	11,50	1,50	6,00	7,25	9,50
IV	4,07	4,31	5,15	5,36	4,10	—	8,22	7,68	11,50	1,50	6,25	7,25	9,50
V	4,17	4,27	5,25	5,02	3,93	2,13	8,20	7,50	11,25	2,75	7,00	8,25	9,25
VI	4,05	4,23	5,16	5,24	4,02	3,71	8,21	7,67	11,50	2,00	6,25	8,50	9,50
VII	4,05	4,33	5,17	5,10	3,97	2,84	8,22	7,69	11,50	2,00	7,00	8,00	9,50

TABLE 3. Valence Angles in (II)

Angle	ω°	Angle	ω°	Angle	ω°
$C_{(1)}N_{(1)}C_{(6)}$	127,4(7)	$N_{(1)}C_{(2)}C_{(3)}$	104,6(7)	$N_{(2)}C_{(4)}H_{(4)}$	108(4)
$C_{(2)}N_{(1)}C_{(6)}$	120,6(7)	$O_{(2)}C_{(3)}C_{(5)}$	105,1(8)	$C_{(5)}C_{(4)}H_{(4)}$	118(4)
$C_{(1)}N_{(1)}C_{(2)}$	111,9(7)	$C_{(2)}C_{(3)}C_{(5)}$	106,6(7)	$C_{(12)}C_{(4)}H_{(4)}$	102(4)
$N_{(2)}O_{(2)}C_{(3)}$	106,5(6)	$O_{(2)}C_{(3)}H_{(3)}$	109(5)	$C_{(1)}C_{(5)}C_{(3)}$	105,5(8)
$O_{(2)}N_{(2)}C_{(4)}$	103,7(6)	$C_{(2)}C_{(3)}H_{(3)}$	112(5)	$C_{(1)}C_{(5)}C_{(4)}$	114,4(8)
$O_{(2)}N_{(2)}C_{(18)}$	111,6(7)	$C_{(5)}C_{(3)}H_{(3)}$	115(5)	$C_{(3)}C_{(5)}C_{(4)}$	104,5(7)
$C_{(4)}N_{(2)}C_{(18)}$	118,4(7)	$N_{(2)}C_{(4)}C_{(5)}$	103,5(7)	$C_{(1)}C_{(5)}H_{(5)}$	101(4)
$O_{(1)}C_{(1)}N_{(1)}$	125,5(8)	$N_{(2)}C_{(4)}C_{(12)}$	110,6(7)	$C_{(3)}C_{(5)}H_{(5)}$	114(3)
$O_{(1)}C_{(1)}C_{(5)}$	124,5(8)	$C_{(5)}C_{(4)}C_{(12)}$	115,1(8)	$C_{(4)}C_{(5)}H_{(5)}$	117(3)
$N_{(1)}C_{(1)}C_{(5)}$	109,7(8)				

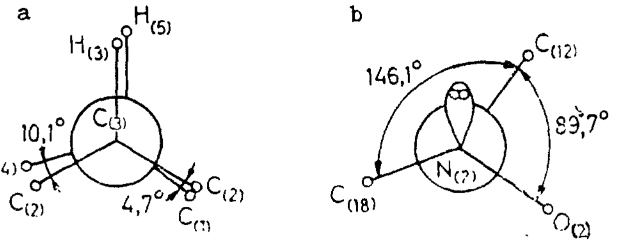

Fig. 2. Newman projection along bonds: a) $C_{(3)}$–$C_{(5)}$; b) $N_{(2)}$–$N_{(4)}$.

TABLE 4. Bond Lengths in (II)

Bond	d, Å	Bond	d, Å	Bond	d, Å
$O_{(1)}-C_{(1)}$	1,223(11)	$N_{(2)}-C_{(4)}$	1,483(12)	$C_{(4)}-C_{(12)}$	1,504(13)
$O_{(2)}-N_{(2)}$	1,440(10)	$N_{(2)}-C_{(18)}$	1,426(11)	$C_{(2)}-H_{(2A)}$	0,90(7)
$O_{(2)}-C_{(3)}$	1,448(12)	$C_{(1)}-C_{(5)}$	1,511(13)	$C_{(2)}-H_{(2B)}$	1,01(6)
$N_{(1)}-C_{(1)}$	1,371(12)	$C_{(2)}-C_{(3)}$	1,539(13)	$C_{(3)}-H_{(3)}$	1,00(9)
$N_{(1)}-C_{(2)}$	1,474(11)	$C_{(3)}-C_{(5)}$	1,513(13)	$C_{(4)}-H_{(4)}$	1,08(7)
$N_{(1)}-C_{(6)}$	1,379(11)	$C_{(4)}-C_{(5)}$	1,559(14)	$C_{(5)}-H_{(5)}$	1,01(6)

TABLE 5. Coordinates of Atoms (× 10^4) and Hydrogen Atoms (× 10^3) in (II)

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
$O_{(1)}$	3265(1)	5000(0)	2076(3)	$C_{(11)}$	9301(3)	3682(6)	1421(3)
$O_{(2)}$	9118(9)	5535(3)	3262(5)	$C_{(12)}$	5594(2)	6640(0)	2556(6)
$O_{(3)}$	7828(8)	3869(7)	−674(3)	$C_{(13)}$	3763(4)	7168(1)	2414(9)
$O_{(4)}$	10962(4)	3245(9)	−372(2)	$C_{(14)}$	3727(8)	7677(9)	1882(7)
$N_{(1)}$	6921(0)	4425(0)	2156(6)	$C_{(15)}$	5552(8)	7645(1)	1493(5)
$N_{(2)}$	7629(5)	6213(1)	3490(5)	$C_{(16)}$	7416(1)	7125(5)	1625(4)
$N_{(3)}$	9120(9)	3609(6)	−277(0)	$C_{(17)}$	7442(5)	6628(5)	2162(8)
$C_{(1)}$	4976(9)	4822(7)	2375(7)	$C_{(18)}$	7470(3)	6190(8)	4138(1)
$C_{(2)}$	8580(3)	4230(6)	2645(8)	$C_{(19)}$	9146(2)	5834(4)	4490(0)
$C_{(3)}$	7712(9)	4759(1)	3196(2)	$C_{(20)}$	9088(4)	5893(7)	5119(8)
$C_{(4)}$	5493(6)	6102(6)	3129(9)	$C_{(21)}$	7321(1)	6287(6)	5403(6)
$C_{(5)}$	5347(4)	5093(8)	3029(9)	$C_{(22)}$	5587(0)	6659(2)	5065(6)
$C_{(6)}$	7369(4)	4180(2)	1564(0)	$C_{(23)}$	5711(0)	6617(5)	4415(8)
$C_{(7)}$	5959(4)	4424(1)	1076(1)	$H_{(2A)}$	868(7)	365(6)	272(7)
$C_{(8)}$	6491(0)	4228(5)	478(1)	$H_{(2B)}$	1019(7)	440(8)	253(6)
$C_{(9)}$	8440(9)	3770(5)	368(5)	$H_{(3)}$	777(3)	441(2)	358(2)
$C_{(10)}$	9822(5)	3479(8)	801(6)	$H_{(4)}$	411(1)	641(1)	337(8)
				$H_{(5)}$	404(8)	477(5)	323(8)

greater than 0.02 Å). Atom $C_{(2)}$ departs from the plane of the pyrrolidone ring by 0.2 Å, with the result that the angle between the planes of the envelope (planes A and B) is 11.8°. The isoxazolidine ring is also nonplanar, having the envelope conformation in which $C_{(3)}$, $C_{(5)}$, $C_{(4)}$, and $N_{(2)}$ are disposed in one plane D (the departure of the atoms is no greater than 0.09 Å). Atom $O_{(2)}$ departs from this plane by 0.5 Å, with the result that the angle between planes D and E (plane $C_{(3)}O_{(2)}N_{(2)}$) is 37.6°. The angle between planes A and D, forming the bicyclic structure, is 126.8°. The Newman projection along the annelated bond $C_{(3)}$–$C_{(5)}$ is shown in Fig. 2a. The hydrogen atoms $H_{(3)}$, $H_{(4)}$, and $H_{(5)}$ are cis-oriented. The benzene ring $C_{(6)}$...$C_{(11)}$ is rotated relative to plane A by 14.7° toward plane B, and the NO_2 group is rotated relative to plane X in the opposite direction by 5.3°. The Newman projection along bond $N_{(2)}$–$C_{(4)}$ (Fig. 2b) shows the combination of the benzene rings $C_{(12)}$...$C_{(17)}$ (plane Y) and $C_{18)}$...$C_{(23)}$ (plane Z) with the isoxazolidine ring. The angles between plane D and planes Z and Y are 65 and 95.5°, respectively. No intramolecular bonds were identified, but the intermolecular bonds in the crystal had the van der Waals values.

EXPERIMENTAL

UV spectra were recorded on a Specord UV-VIS spectrophotometer in ethanol, and IR spectra on a UR-20 spectrometer. PMR spectra were recorded on a Bruker WM-250 (250 MHz) in $CDCl_3$ or DMSO-D_6, internal standard HMDS. TLC was carried out in Silufol UV-254 plates, eluent acetone–CCl_4–petroleum ether (2:1:0.5). The developer was 2,4-dinitrophenylhydrazine hydrochloride.

The elemental analyses of the products for C, H, and N were in agreement with the calculated values. The x-ray diffraction examination of (II) was carried out on a Nikolet P3/R3 automatic diffractometer (MoK_α-irradiation, β-filter, θ/2θ scanning to $2\theta_{max}$ 48°). Using transparent rhombic crystals $C_{23}H_{19}N_3O_4$, grown from the solvent mixture heptane–ethyl acetate (1:2), 764 reflections were obtained with $I \geq 2\sigma_I$. The cell parameters were a = 5.816(2), b = 15.275(5), c = 21.965(7) Å; V = 1951(1) $Å^3$, space group P_c2_1b, Z = 4. The structure was solved directly using the SHELXTL suite of programs [14] on a NOVA-3 computer, and refined in anisotropic (isotropic for hydrogen atoms) approximation to divergence factors R = 0.058, R_w = 0.064. The atom coordinates are given in Table 5. The values of the anisotropic temperature factors for the nonhydrogen atoms may be obtained from the authors.

2-Oxa-6-oxo-3,7-diazabicyclo(3,3,0)octanes (II-VII). Compound (I) (0.5 g, 2.5 mmoles) was boiled with 0.68 g (6.25 mmoles) of phenylhydroxylamine and 6.25 mmoles of the appropriate benzaldehyde in 60 ml of benzene until all the (I) had reacted. The solution was evaporated to 1/3 of its initial volume, the residue diluted with ether, and the solid which separated filtered off. Compounds (II-VII) were recrystallized from ethanol.

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