PSEUDOESTERS AND DERIVATIVES.XXVII[1]. THERMOLYSIS AND PHOTOLYSIS OF CYCLOADDUCTS OF DIAZOMETHANE WITH 5-METHOXY-3-PYRROLIN-2-ONES. FORMATION OF 4-ALKYL-3-PYRROLIN-2-ONES AND 3-AZABICYCLO[3.1.0]-HEXAN-2-ONES

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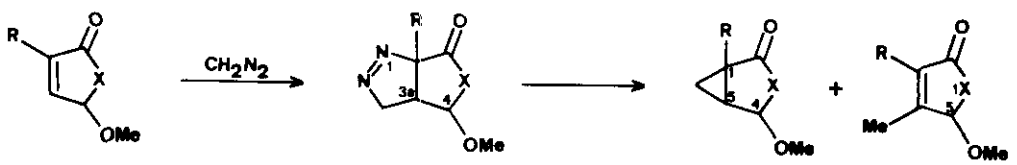
Abstract- Thermal decomposition of the cycloadducts **2a,b** and **2'a** leads to 4-methyl substituted pyrrolinones **4a,b** as the main products, along with minor amounts of the corresponding cyclopropane derivative **3a,b** and **3'a** respectively. However, by thermolysis of **2'b** and photolysis of **2a,b** and **2'a,b** the proportions of the products are reversed, the cyclopropane derivative of the type **3** being the major component. The formation of the cyclopropane derivative by both thermolysis and photolysis of the cycloadducts **2** proceeds with retention of stereochemistry.

Although thermolysis and photolysis of pyrazolines[2,3] have been widely studied and used for the synthesis of cyclopropane derivatives, there are relatively few reports[4,5,6,7] dealing with bicyclic substrates in which the ring fused to the pyrazoline nucleus is a heterocycle. In a very recent paper[8] we have described the synthesis of several pyrrolopyrazoline derivatives of the type **2** by 1,3-dipolar cycloaddition of diazomethane to 5-methoxy-3-pyrrolin-2-ones (**1**). Thus it became of interest to study their thermal and photochemical decomposition which could provide a convenient route for the synthesis of ring-fused cyclopropane derivatives of the type **3**, as well as 4-alkyl substituted pyrrolinones **4**.



1, X = NH
5, X = O

2, X = NH
6, X = O

3, X = NH
7, X = O

4, X = NH
8, X = O

We have found that pyrrolopyrazoline derivatives **2a,b** and their epimers at C-4 **2'a,b** on heating for 48 h at 130°C in chlorobenzene, lose nitrogen to afford in essentially quantitative yield a mixture of the corresponding 3-azabicyclo[3.1.0]-hexan-2-one (**3a,b** and **3'a,b**, respectively) and the 4-methyl substituted pyrrolinone (**4a,b**). The individual components can be isolated by flash chromatography on silica gel (chloroform-ethyl acetate 1:2). As indicated in Table 1, thermal decomposition of cycloadducts **2a,b** and **2'a** proceeds with predominant formation of the 4-methyl substituted pyrrolinone **4a,b**. It should be noted that the proportion of the cyclopropane derivative **3** is increased by the presence of 6a-methyl or endo-4-methoxy groups.Thus, in the case of **2'b**, in which both groups are present, the cyclopropane **3'b** becomes the major component.

Formation of cyclopropane derivatives **3** in proportions above 24% contrasts to our previous results[9] obtained by thermolysys of furopyrazolines **6**, in which the 4-methylfuranone **8** is the sole product and the corresponding cyclopropane derivative **7** is not observed.

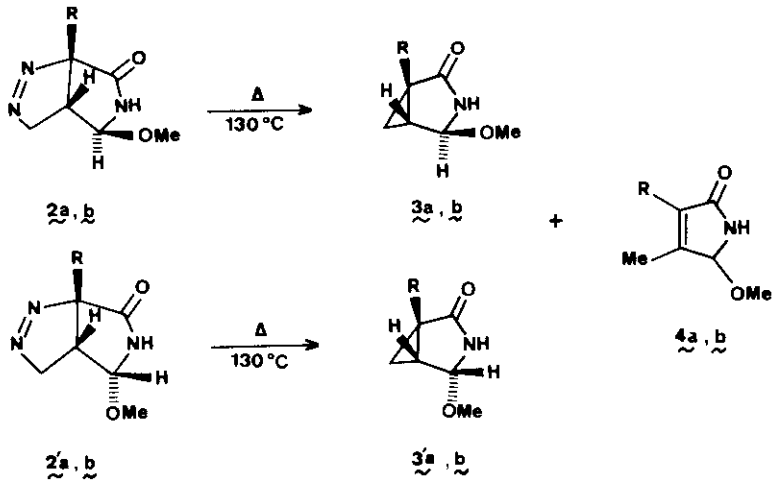


Table 1. Products[a] from decomposition of cycloadducts **2** and **2'**.

Substrate	R	Thermolysis		Photolysis		
2a	H	**3a** (24)	**4a** (76)	**3a** (66)	**4a** (19)	**1a** (15)
2'a	H	**3'a** (37)	**4a** (63)	**3'a** (53)	**4a** (23)	**1a** (24)
2b	Me	**3b** (40)	**4b** (60)	**3b** (50)	**4b** (26)	**1b** (24)
2'b	Me	**3'b** (56)	**4b** (44)	**3'b** (42)	**4b** (29)	**1b** (29)

[a] Relative product distribution (%) determined by ^{1}H-nmr.

Photolysis of the cycloadducts **2** has been carried out by irradiation in a pyrex vessel, in acetonitrile solution, with a medium pressure mercury lamp. In all cases we have obtained the corresponding cyclopropanes **3** as the major components,

along with substantial amounts of the 4-methyl substituted pyrrolinones **4** and pyrrolinones **1**. The components can be separated by chromatography on silica gel (chloroform-ethyl acetate 1:2). As deduced from the results summarized in Table 1, the proportion of the cyclopropane derivative **3** depends upon the substitution on the cycloadduct **2**, being higher for the exo epimers **2a,b** and when R=H.

The structure of the 3-azabicyclo[3.1.0]hexan-2-ones **3** and **3'** is supported by the spectral data, in particular the ^{1}H-nmr. The assignment of the stereochemistry is based mainly on the value of the coupling constant $J_{4,5}$ (Table 2). Thus the presence of a coupling constant $J_{4,5} \simeq 5$ Hz indicates that H-4 and H-5 must be cis to each other (endo- MeO group, **3'**), whereas a coupling constant $J_{4,5} \simeq 1$ Hz suggests a trans relationship (exo MeO group,**3**).

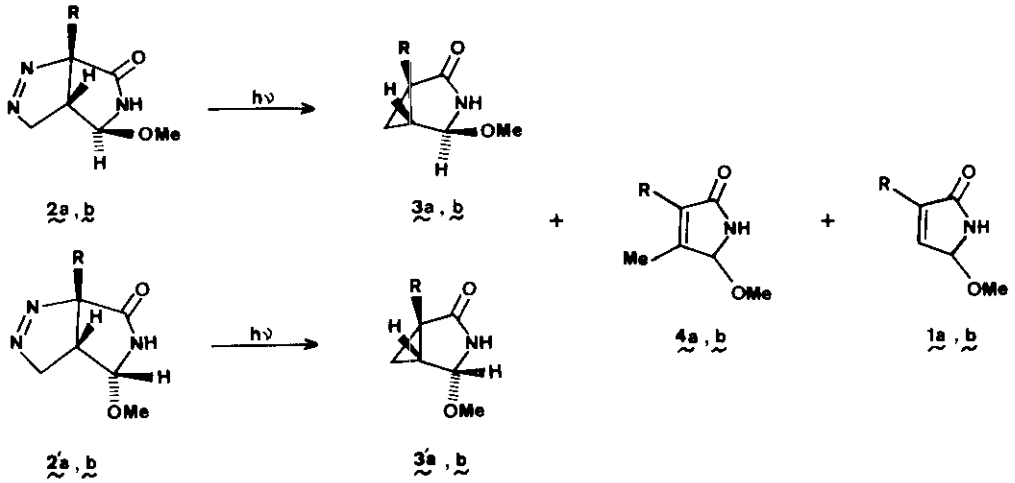


Table 2. Ir and ^{1}H-nmr spectral data of compounds **3** and **3'**.

	Ir[a]		^{1}H-Nmr[b]					
Compound	C=O	NH	H-1	H-4	H-5	H-6	OMe	$J_{4,5}$
3a	1700 1680	3200 3100	1.99[c]	4.77	1.96[c]	1.13 0.67	3.36	1.3
3'a	1700	3210 3080	2.12[c]	5.05	1.90[c]	1.22 1.04	3.38	5.2
3b	1700	3280 3110	(1.36)[d]	4.73	1.84	0.94 0.73	3.32	1.2
3'b	1700	3210 3100	(1.32)[d]	5.02	1.91	1.28 0.83	3.36	5.1

[a]Nujol. [b]$CDCl_3$. [c]Signals may be interchanged. [d]Me signals.

The formation of cyclopropane derivatives by both thermolysis and photolysis proceeds with retention of the stereochemistry of the initial cycloadduct.

The formation of the pyrrolinones **1a,b** suggests the presence of a competing cycloreversion of the adducts **2a,b** or **2'a,b**. The presence of cycloreversion products has previously been reported in the photodecomposition of pyrazolines and bicyclic pyrazolines[2,3,4] and has recently been observed by us[10] in the photolysis of furopyrazolines of the type **6**.

Evidence has previously been presented[11] in favour of the formation of carbene species in the photolysis of pyrazolines. It was therefore suggested that a considerable fraction of the cyclopropane formation might result from cycloaddition of the carbene to the olefin originated by cycloreversion. The clear stereospecificity observed by us in the photolysis of the cycloadducts **2a,b** and **2'a,b** seems to rule out the carbene pathway in the present case.

EXPERIMENTAL

Mps are uncorrected. Ir spectra were recorded on a Perkin-Elmer model 681 grating spectrometer, ν values in cm^{-1}. ^{1}H-Nmr spectra were obtained on a Varian EM-390 or on a Bruker WM-200-SY spectrometer for $CDCl_3$ solutions (unless otherwise stated) and the chemical shifts are reported in δ (ppm from internal TMS). Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 60 (70-230 mesh), 60 (230-400 mesh) and DC-Alufolien 60 F_{254} were used for conventional, flash column chromatography and analytical tlc, respectively.

Thermal Decomposition of the Cycloadducts 2 or 2'. General Procedure.

A solution of the adduct (10 mmol) in chlorobenzene (20 ml) was heated under reflux for 48 h. The solvent was removed in vacuo and the residue was analyzed by ^{1}H-nmr (Table 1). The crude mixture was chromatographed on silica gel under pressure (chloroform-ethyl acetate 1:2).

Thermolysis of 2a. Chromatography of the residue afforded **4-exo-methoxy-3-azabicyclo-[3.1.0]hexan-2-one** (**3a**) in 15% yield and **4-methyl-5-methoxy-3-pyrrolin-2-one** (**4a**) (mp 83°C, lit.[12] 83°C) in 65% yield.

3a. Mp 82-83°C (from chloroform-hexane). (Found: C, 56.40; H, 7.29; N, 10.70. $C_6H_9O_2N$ requires, C, 56.69; H, 7.09; N, 11.02). Ms, m/z: 127 (M^+), 96 (100%), 84, 78, 68.

Thermolysis of 2'a. Chromatography of the residue afforded **4-endo-methoxy-3-aza-bicyclo[3.1.0]hexan-2-one** (**3'a**) in 25% yield and pyrrolinone **4a** in 55% yield.

3'a. Mp 78-81°C (from chloroform-hexane). (Found: C, 56.52; H, 7.26; N, 10.86. $C_6H_9O_2N$ requires, C, 56.69; H, 7.09; N, 11.02). Ms, m/z: 127 (M^+), 96 (100%), 78, 68.

Thermolysis of 2b. Chromatography of the residue afforded **1-methyl-4-exo-methoxy-3-azabicyclo[3.1.0]hexan-2-one** (**3b**) in 30% yield and **3,4-dimethyl-5-methoxy-3-pyrrolin-2-one** (**4b**) in 50% yield.

3b. Mp 82-83°C (from cyclohexane). (Found: C, 59.64; H, 7.68; N, 10.27. $C_7H_{11}O_2N$ requires, C, 59.57; H, 7.80; N, 9.92). Ms, m/z: 141 (M^+), 127, 110 (100%), 92, 82, 67.

4b. Mp 141°C (from hexane). (Found: C, 59.29; H, 7.66; N, 9.57. $C_7H_{11}O_2N$ requires, C, 59.57; H, 7.80; N, 9.92. Ir (nujol): 3260 NH, 1700 C=O. ^{1}H-Nmr ($CDCl_3$): 6.5 (br, 1H, HN); 5.15 (s, 1H, H-5); 3.12 (s, 3H, OCH_3); 1.82 (s, 3H, CH_3); 1.78 (s, 3H, CH_3). Ms, m/z: 141 (M^+), 126, 110 (100%), 94, 82, 67.

Pyrrolinone **4b** was also obtained by ammonolysis of 3,4-dimethyl-5-methoxyfuran-2(5H)-one (**8**, R=Me), followed by acid catalyzed treatment with methanol according to the method previously described by us[13].

Thermolysis of 2'b. Chromatography of the residue afforded **1-methyl-4-endo-methoxy-3-azabicyclo[3.1.0]hexan-2-one** (**3'b**) in 45% yield and the pyrrolinone **4b** in 35% yield.

3'b. Mp 104-105°C (from cyclohexane). (Found: C, 59.50; H, 8.10; N, 9.86. $C_7H_{11}O_2N$ requires, C, 59.57; H, 7.80; N, 9.92). Ms, m/z: 141 (M^+), 127, 110 (100%), 82, 67.

Photolysis of the Cycloadducts 2 or 2'b. General Procedure.

A solution of the adduct (10 mmol) in acetonitrile (300 ml) was irradiated with a Osram HQL 125 W lamp, in a pyrex immersion well reactor, until the starting adduct was consumed (monitored by tlc; 48-72 h). The solvent was removed in vacuo and the residue was analyzed by ^{1}H-nmr (Table 1). The crude mixture was chromatographed on silica gel under pressure (chloroform-ethyl acetate 1:2).

Photolysis of 2a. Chromatography of the residue afforded cyclopropane **3a** in 55% yield, pyrrolinone **4a** in 10% yield and **5-methoxy-3-pyrrolin-2-one** (**1a**) (mp 38° C, lit.[13] 38°C) in 8% yield.

Photolysis of 2'a. Chromatography of the residue afforded cyclopropane **3'a** in 42% yield and the pyrrolinones **4a** in 15% yield and **1a** in 15% yield.

Photolysis of 2b. Chromatography of the residue afforded cyclopropane **3b** in 40% yield and the pyrrolinones **4b** in 16% yield and **3-methyl-5-methoxy-3-pyrrolin-2-one** (**1b**) (mp 50°C, lit.[13] 50°C) in 14% yield.

Photolysis of 2'b. Chromatography of the residue afforded cyclopropane **3'b** in 34% yield and the pyrrolinones **4b** in 17% yield and **1b** in 17% yield.

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