Thermolysis and Photolysis of Some 5-Amino-4-methoxycarbonyl-Δ^2-1,2,3-triazolines

J. Bourgois* [a], A. Mathieu [b] and F. Texier [c]

[a] Laboratoire de Physicochimie des solutions, Ecole Nationale Supérieure des Mines, 158, cours Fauriel, 42023 Saint-Etienne Cédex, France

[b] Laboratoire de chimie analytique et organique appliquée, USTL, 34066 Montpellier Cédex, France

[c] UER Sciences et Techniques, Faculté des Sciences, Boulevard Lavoisier, 49045 Angers Cédex, France

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Thermolysis of 5-amino-4-methyl-4-methoxycarbonyl-Δ^2-1,2,3-triazolines leads to amidines and 1-methoxycarbonyl diazoethane. If the N_1 substituent is a tosyl or benzoyl group, the corresponding triazoline is not isolated, the azide addition to the olefin gives directly the thermolysis products at room temperature. Triazoline photolysis leads to amino aziridines which are azomethine ylids.

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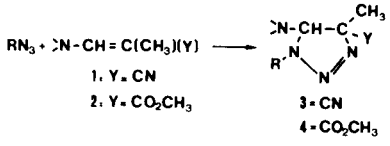
Introduction.

Most of the Δ^2-1,2,3-triazolines are unstable. The nature of the obtained compounds (aziridines, anils, ...) is controlled by the type of substituents and degradation method, either photolytic or thermolytic [1].

Arylazides react with olefins **1** and **2** to produce Δ^2-triazolines **3** and **4** respectively (Scheme 1) [2,3]. We have previously reported [4] the investigation of the thermolysis and photolysis of 5-amino-4-cyano-Δ^2-triazolines **3**. In view of the reaction's synthetic potential we have undertaken the study of the thermal and photochemical decomposition of Δ^2-triazolines **4**.

Scheme 1



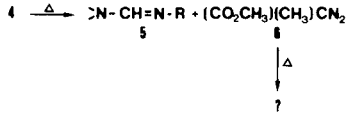
4a, R = phenyl, $>N$ = pyrrolidino; **4b**, R = phenyl, $>N$ = morpholino; **4c**, R = *p*-nitrophenyl, $>N$ = pyrrolidino; **4d**, R = *p*-nitrophenyl, $>N$ = morpholino; **4e**, R = *p*-nitrophenyl, $>N$ = piperidino; **4f**, R = *p*-nitrophenyl, $>N$ = diethylamino

Results and Discussion.

I- Thermolysis of 1-Aryl-5-amino-4-methyl-4-methoxycarbonyl-Δ^2-1,2,3-triazolines.

Thermolysis of triazolines **4** in a refluxing toluene solution or neat at 180° resulted in the formation of amidines **5** (Scheme 2). In fact, this reaction is the reversal of diazo compound-imine addition. Nevertheless, the diazo compound **6** was not characterised in the crude product because of its instability under the reaction conditions. In the case of the addition of tosyl- and benzoylazides to the same olefins **2**, the formation of the same diazo compound has been observed (see below). All the isolated amidines were characterised by ir and nmr and gave correct elemental analyses (see experimental).

Scheme 2



5a, R = *p*-nitrophenyl, $>N$ = morpholino; **5b**, R = *p*-nitrophenyl, $>N$ = piperidino; **5c** R = phenyl, $>N$ = morpholino

The amidine formation confirms orientation of the azide addition to enamines **2**. Furthermore, the regioselectivity is governed by the $LUMO_{azide}$-$HOMO_{olefin}$ interaction [2,3].

It is noted that substitution of the nitrile group by a methoxycarbonyl group at the 4-position in Δ^2-triazoline should bring about a dramatic change in the course of the thermolysis. Indeed, thermolysis of the Δ^2-triazoline **3** produced exclusively the starting materials, demonstrating the reversibility [4] of the arylazides 1,3-dipolar cycloaddition.

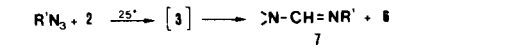
II- Tosyl- and Benzoylazides Addition to Methyl β-Aminomethyacrylate (**2**).

When the triazoline ring carries an electron-withdrawing group at the 1-position, it is very labile. Thus, the triazolines formed by the reaction of tosylazide with olefins are not readily isolated [5]. In fact, they decompose immediately after their formation *in situ* and produce aziridines and/or anils [1,5].

The addition of tosyl- and benzoylazides to enamines **2** is similar to that observed with the ethylenic compounds **1** [4]. No triazoline could be detected. The isolated products were amidines **7** and the diazo compound **6** which were

produced by decomposition of the unstable Δ^2-triazoline (Scheme 3). The characteristics of amidines **7** are given in the experimental.

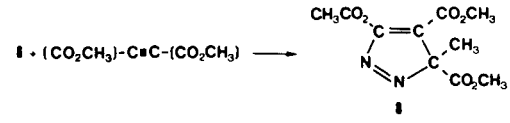
Scheme 3



7a, R' = tosyl, $\geq N$ = piperidino; **7b**, R' = tosyl, $\geq N$ = morpholino; **7c**, R' = tosyl, $\geq N$ = pyrrolidino; **7d**, R' = tosyl, $\geq N$ = cyclohexylamino; **7e**, R' = *p*-nitrobenzoyl, $\geq N$ = pyrrolidino

Compound **6** was characterised by ir (ν C=N$_2$ = 2150 cm^{-1}) and nmr (see experimental) and its addition product with dimethyl acetylenedicarboxylate (DMAD) (Scheme 4).

Scheme 4

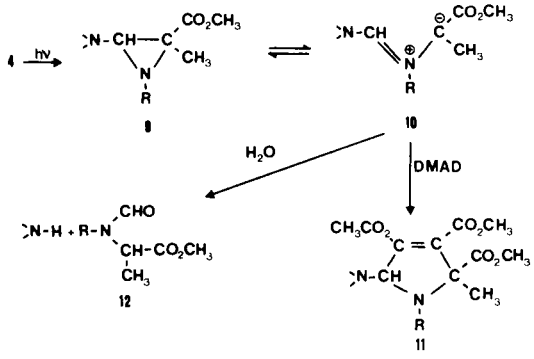


III- Photolysis of 1-Aryl-5-amino-4-methyl-4-methoxycarbonyl-Δ^2-triazolines.

Photochemical decomposition of Δ^2-1,2,3-triazolines has been shown to be a more efficient method than thermolysis for obtaining aziridines [1]. This fact has been further substantiated by the present experimental work.

Photolysis of triazolines **4** in benzene solution resulted in loss of nitrogen and formation of the 2-aminoaziridines **9**. These heterocycles must be in equilibrium with the corresponding azomethine ylid **10** (Scheme 5).

Scheme 5



Trapping of ylid **10**, a reactive intermediate, with DMAD to give cycloaddition products illustrates its formation. The photolysis was carried out in benzene solution containing DMAD under a nitrogen atmosphere. Under these experimental conditions, two epimeric Δ^3-pyrrolidines **11** were obtained [6]. Aminoaziridines **9** could not be isolated because they readily hydrolysed under the experimental conditions to amides **12**. In fact, we believe that these compounds resulted from the hydrolysis of azomethine ylid 10. This is so because of the ease with which **9** can ring open at room temperature. A possible explanation of this was given recently with the use of the relaxation method [7]. The amino and ester groups are -I in inductive effect and consequently they lower the $\sigma^*_{C_2C_3}$ orbital energy of the bond which is cleaved during the ring opening. Thus, these substituents enhanced the charge transfer $P_N \rightarrow \sigma^*_{C_2C_3}$, the driving force for this electrocyclic reaction [7,8]. Formation of the azomethine ylid **10** explains the reactivity difference between the aminoaziridines **9** and the aminoaziridines described by De Poortere and De Schryner [9] which undergo C-N cleavage.

EXPERIMENTAL

Melting points were not corrected. Infrared spectra were recorded on a Perkin Elmer 225 and 257 spectrophotometer. The nmr spectra were determined on a Jeol JNM MH100 spectrometer using TMS as an internal standard. Analyses were performed by Service Central de Microanalyses, CNRS.

The Δ^2-triazolines [3], the olefins [10,11] and the azides [12-14] used in this work were prepared by the procedures described in previous publications.

N^2-*p*-Nitrophenyl-*N*^{1},*N*^{1}-cyclo(ethyleneoxyethylene)formamide (**5a**).

A solution of 0,5 g of Δ^2-triazoline **4d** (*R* = *p*-nitrophenyl, $\geq N$- = morpholino) in 30 ml of toluene was heated to reflux temperature for 48 hours. After removing the solvent *in vacuo*, the residue was dissolved in a small amount of methanol. After cooling, a solid was precipitated. The product was obtained in 62% yield (0,20 g), mp 132° after recrystallization from ethanol; nmr (deuteriochloroform): δ = 7.43 (s, CH=N), 6.90 to 8.02 (m, phenyl group), 3.72 (m, morpholino group), ir (nujol): 1660 cm^{-1} (C=N).

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.17; N, 17.87; O, 20.43. Found: C, 55.94; N, 18.02; O, 20.9.

N^2-*p*-Nitrophenyl-*N*^{1},*N*^{1}-cyclopentylformamide (**5b**).

Compound **5b** was prepared in a similar way as shown above from 0.5 g of Δ^2-triazoline **4b** (*R* = *p*-nitrophenyl, $\geq N$- = piperidino group) in 54% yield (0.18 g), mp 124° (from ethanol); nmr (deuteriochloroform): δ = 7.28 (s, CH=N), 6.87 to 7.95 (m, phenyl group), 3.48, 1.80 (m, piperidino group); ir (nujol): 1640 cm^{-1} (C=N).

Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.80; N, 18.03; O, 13.73. Found: C, 62.04; N, 17.95; O, 13.51.

N^2-Nitrophenyl-*N*^{1},*N*^{1}-cyclo(ethyleneoxyethylene)formamide (**5c**).

It was prepared as the above compound, from Δ^2-triazoline **4c** (*R* = phenyl, $\geq N$- = morpholino group), in 73% yield (0.25 g), mp 112° (from ethanol); nmr (deuteriochloroform): δ = 7.42 (s, CH=N), 3.70 (m, morpholino group), 7.52 (m, phenyl group); ir (nujol): 1680 cm^{-1} (C=N).

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.47; N, 14.74; O, 8.42. Found: C, 70.01; N, 15.01; O, 8.59.

General Procedure for the Addition of Tosyl- and Benzoylazides to Methyl β-Aminomethacrylate (**2**).

The tosyl or benzoylazide (1 g) was added to a stoichiometric amount of olefin **2**. When the two reactants were solids, a moderate heating gave two liquid phases. With a vigourous shaking, an exothermic reaction started immediately. At the end of the reaction, the mixture was cooled and added with cold diethyl ether. The separated product **7** was filtered off, washed with cold ether and purified by recrystallization from ethanol. The ethereal solution contained the soluble diazo compound **6**.

N^2-Tosyl-N^1,N^1-cyclopentyl formamide (**7a**).

This compound was prepared in 92% yield (from tosylazide and methyl β-piperidinomethacrylate), mp 150° (from ethanol); nmr (deuteriochloroform): δ = 8.16 (s, CH=N), 7.28 to 7.80 (m, phenyl group), 3.52, 1.82 (m, piperidino group), 2.40 (s, CH_3-SO_2); ir (nujol): 1600 cm^{-1} (C=N).

Anal. Calcd. for $C_{13}H_{18}N_2SO_2$: C, 58.65; H, 6.77; N, 10.52; O, 12.03. Found: C, 58.94; H, 6.59; N, 10.54; O, 12.01.

N^2-Tosyl-N^1,N^1-cyclo(ethyleneoxyethylene)formamide (**7b**).

It was prepared in a similar way from tosylazide (1 g) and methyl β-morpholino methacrylate (1 g) in 88% yield (1.3 g), mp 164° (fom ethanol); nmr (deuteriochloroform): δ = 8.26 (s, CH=N), 7.28 to 7.80 (m, phenyl group), 3.63 (m, morpholino group), 2.40 (s, CH_3-SO_2); ir (nujol): 1620 cm^{-1} (C=N).

Anal. Calcd. for $C_{12}H_{16}N_2SO_3$: C, 53.73; H, 5.97; N, 10.45; O, 17.91. Found: C, 54.01; H, 5.92; N, 10.32; O, 17.79.

N^2-Tosyl-N^1,N^1-cyclobutylformamide (**7c**).

It was obtained as the above compound from tosylazide and methyl β-pyrrolidinomethacrylate in 87% yield, mp 139° (from ethanol); nmr (deuteriochloroform): δ = 8.26 (s, CH=N), 7.26 to 7.80 (m, phenyl group), 3.52, 1.92 (m, pyrrolidino group), 2.40 (s, CH_3-SO_2); ir (nujol): 1610 cm^{-1} (C=N).

Anal. Calcd. for $C_{12}H_{16}N_2SO_2$: C, 57.14; H, 6.35; N, 11.11; O, 12.70. Found: C, 57.37; H, 6.37; N, 11.32; O, 12.82.

N^2-Tosyl-N^1-cyclohexylformamide (**7d**).

This compound was prepared, using the general procedure, in 94% yield (from tosylazide and methyl β-cyclohexylaminomethacrylate), mp 180° (from ethanol); nmr (deuteriochloroform): δ = 8.17 (d, CH=N), J = 7.3 Hz, 7.25 to 7.75 (m, phenyl group), 2.38 (CH_3-SO_2), 5.05 (d, NH), 1.50 (m, cyclohexyl group); ir (nujol): 1605 cm^{-1} (C=N).

Anal. Calcd. for $C_{14}H_{20}N_2SO_2$: C, 60.00; H, 7.14; N, 10.00; O, 11.42. Found: C, 60.11; H, 7.09; N, 10.23; O, 11.29.

N^2-*p*-Nitrobenzoyl-N^1,N^1-cyclobutylformamide (**7e**).

It was prepared in the same way in 69% yield. Its melting point, after 3 recrystallizations from ethanol, was 123°; nmr (DMSO-d_6): 8.24 (s, CH=N), 7.60 to 8.30 (m, phenyl group), 3.50, 1.75 (pyrrolidino group); ir (nujol): 1620 cm^{-1} (C=N).

Anal. Calcd. for $C_{13}H_{15}N_3O_3$: C, 59.77; N, 16.09; O, 18.39. Found: C, 59.89; N, 16.13; O, 18.31.

2-Diazopropionate (**6**).

The ethereal solution obtained above contained almost exclusively the diazo compound **6**. The solvent was distilled *in vacuo*, and the removing oil was characterised: nmr (deuteriochloroform): δ = 1.96 (s, CH_3-C=N_2), 3.78 (s, CO_2CH_3); ir (film): 2150 cm^{-1} (CN_2), 1700 to 1750 (C=O). The product was used without another purification.

3,4,5-Trimethoxycarbonyl-5-methyl-1,2-pyrázolenine (**8**).

The ethereal solution of **6** was added to DMAD (stoichiometric conditions). The mixture was kept at room temperature for a week. After removing the solvent, the remaining solid was recrystallized twice from ethanol to give **8** in 52% yield, mp 92°; nmr (deuteriochloroform): δ = 2.84 (s, CH_3), 3.90 (s, OCH_3), 3.98 (s,OCH_3), 4.12 (s, OCH_3); ir (nujol): 1728 to 1760 (C=O).

Anal. Calcd. for $C_{10}H_{12}N_2O_6$: C, 46.88; N, 10.94; O, 37.50. Found: C, 47.03; N, 10.82; O, 37.65.

Photolysis of the 1-*p*-Nitrophenyl-4-methoxycarbonyl-4-methyl-5-diethylamino-Δ^2-1,2,3-triazoline (**4f**).

N,*p*-Nitrophenyl-*N*-(α-methylpropionate)formamide (**12**).

Compound **4f** (0.5 g, 1.5 × 10^{-3} mole) in 100 ml of benzene was irradiated (Hanau type Q81 HP 70W, high pressure mercury arc, pyrex filter) at 40° for two hours. After cooling, benzene was removed under vacuum and a yellow oily product was left. The nmr spectrum of the residue showed quantitative formation of amide **12**. The nmr and ir spectra of **12** are analogous to those of *N*-phenyl-*N*-1-cyanoethylformamide which was obtained from the photolysis of Δ^2-1,2,3-triazoline **3** [2,4]; nmr (deuteriochloroform): δ = 1.48 (d, CH_3-CH), 5.55 (q, CH-CH_3), J = 7 Hz, 8.10 (s, CH=O), 3.76 (s, CH_3-O); ir (film): 1660 cm^{-1} (CH=O), 1730 cm^{-1} (CO_2CH_3).

1-*p*-Nitrophenyl-2-methyl-2,3,4-trimethoxycarbonyl-4-dimethylamino-Δ^3-pyrrolines (**11**).

A solution of Δ^2-triazoline **4f** (0.5 g) in 100 ml of benzene containing 0.3 g of DMAD was irradiated under nitrogen atmosphere for two hours using the same uv source. The solvent was removed under vacuum and the remaining oil product was analyzed. Analysis (nmr) of this oily product indicated that it is a mixture of two epimers of **11** in 50:50 ratio (65% overall yield). We were unable to separate the two epimers but the nmr spectra of their mixture is analogous to that of Δ^3-pyrrolines obtained by photolysis of 5-amino-4-methyl-4-cyano-Δ^2-triazolines in solution containing DMAD [6]; nmr (deuteriochloroform): δ = 5.60 and 5.96 (s, H-5), 1.68 and 1.92 (s, CH_3-C 2), 3.95, 3.99 and 3.45 (3 s, OCH_3), 7.25, 8.05 (m, phenyl group).

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