Photochemical Rearrangement of 2,3-Dihydroisoxazoles. Formation of Stable Azomethine Ylides *via* Acyl Aziridines as Intermediates

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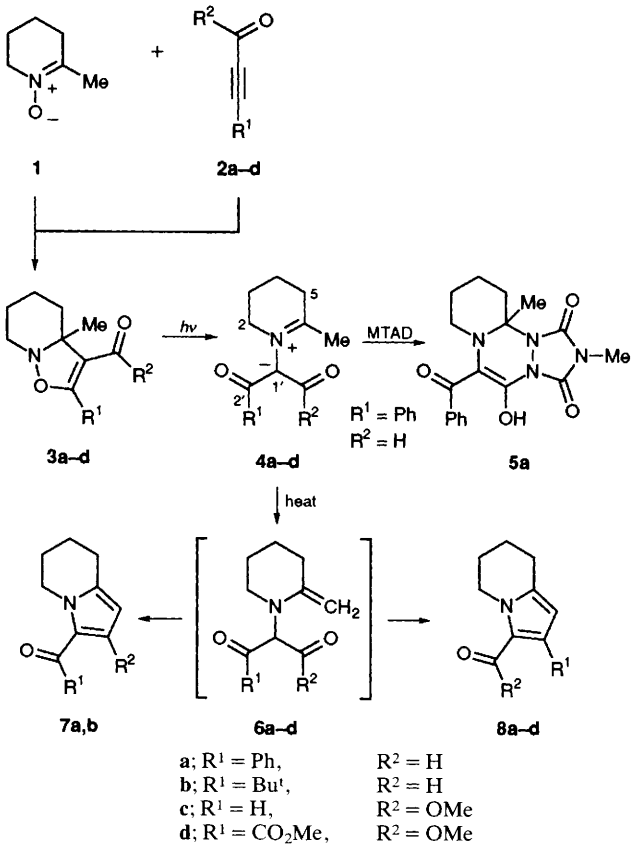
Irradiation of the 2,3-annulated 2,3-dihydroisoxazoles **3** affords azomethine ylides **4** as isolable compounds, which on heating are transformed into the tetrahydroindolizines **7** and **8**.

Although the photochemical behaviour of five-membered heteroaromatic systems as well as their dihydro analogues has been extensively studied,[1] including the excited state reactions of isoxazoles and 4,5-dihydroisoxazoles,[2,3] investigations with 2,3-dihydroisoxazoles are still lacking.[4] We now describe our results with the annulated 2,3-dihydroisoxazoles **3a–d**, which are obtained in 60–80% yield by regioselective cycloadditions of the cyclic nitrone **1** with the alkynes **2a–d**.



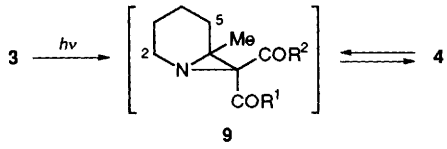
Scheme 1

Irradiation of 4×10^{-3} mol dm^{-3} solutions of **3a** in benzene with a high-pressure mercury lamp (Pyrex filter, $\lambda > 280$ nm) afforded a crystalline product in 88% yield which was identified as the azomethine ylide **4a**. Under similar conditions the *tert*-butyl derivative **3b** is likewise transformed into **4b** (Table 1). In the case of the mono- and di-ester substituted compounds **3c** and **3d**, respectively, the photolysis was performed using a Vycor filter and diethyl ether as solvent ($\lambda > 230$ nm; for UV absorptions of **3a–d** see Table 1). Again compounds with dipolar structures, **4c** and **4d**, were isolated as the main products.† The lower yield, especially of **4c**, is mainly due to product loss during the chromatographic work-up. According to ^{1}H NMR analysis prior to the purification procedure, both **4c** and **4d** are formed in about 80 and 70% yield, respectively. Furthermore, careful inspection of the spectra of the **a–c** series revealed additional signals which are compatible with the 1-azabicyclo[4.1.0]heptene structure **9** [see below and Scheme 2; the ratio **4** : **9** was 10 : 1 (**a**), 60 : 1 (**b**), 6 : 1 (**c**)]; unfortunately all attempts at isolation have failed so far.

The azomethine ylides **4** are unambiguously characterised by correct elemental analyses and/or mass spectra as well as by the spectroscopic data;† additional confirmation of the structures is based on their chemical reactivity (see below).

With the successful separation of **4a–d** the first representatives of isolable azomethine ylides are described which bear stabilizing groups only at one terminus of the 1,3-dipolar system. The few other stable systems, which have π-substituents on both sides, are derived from conjugated iminium compounds like isoquinolinium or dihydroisoquinolinium ylides[5] as well as from non-cyclic azomethine ylides.[6]

The remarkable stability of **4a–d** is reflected by their unusually low reactivity with dipolarophiles; *e.g.* cycloaddition experiments with **4a** using dimethylacetylene dicarboxylate or *N*-phenylmaleimide as 2π-components were unsuccessful; only 4-methyltriazoline-3,5-dione (MTAD) gave rise to a



Scheme 2

Table 1 Photolysis of the annulated 2,3-dihydroisoxazoles

Dihydroisoxazole	λ_{max}/nm(ε) (MeCN)	Photolysis conditions[a]	Azomethine ylide[b]
3a	302 (8800)	0.4 mmol, C_6H_6 Pyrex, 36 min	**4a** (88%, mp 133 °C)
3b	282 (7500)	0.5 mmol, C_6H_6 Pyrex, 46 min	**4b** (75%, mp 104 °C)
3c	269 (5300)	0.6 mmol, diethyl ether Vycor, 50 min	**4c** (25%, oil)
3d	268 (2900)	0.8 mmol, diethyl ether Vycor, 2.5 h	**4d** (58%, oil)

[a] Irradiations were carried out with 100 ml of degassed solutions of the dihydroisoxazoles with a 150 W high-pressure mercury lamp at 20 °C. [b] Isolated yields after chromatographic purification.

Table 2 Thermal transformation of **4** into **7** and **8**

4	Reaction time[a,c]	7[b,c] (%)	8[b,c] (%)
4a	6 h [42 h]	71 [48]	18 [18]
4b	3.5 h [5 days]	62 [56]	11
4c	1.5 h [64 h]		65 [55]
4d	3 h [20 h]		69 [59]

[a] Reflux in toluene. [b] % Yield after chromatographic purification. [c] Values in square brackets refer to the thermolysis of **3a–d** under simultaneous irradiation with a 500 W lamp.

product, namely **5a**, formed in 78% yield (CH_2Cl_2, room temp., 10 min) by a Diels–Alder reaction and subsequent H-shift.

On heating **4a–d** in refluxing toluene, a rearrangement took place leading to the tetrahydroindolizines **7a, b** and **8a–d**, respectively (see Table 2). The possible reaction pathway includes a 6π-suprafacial 1,4-H-migration to the enamines **6a–d** followed by cyclodehydration (Scheme 1).

Intermediates like **6** have already been suggested for the formation of the corresponding pyrrole derivatives upon thermolysis of simple 2,3-dihydroisoxazoles.[4,7] In contrast with these results, direct heating of **3a–d** in boiling toluene gave only decomposition products. However, a one-pot transformation of **3** into **7–8** can be accomplished by heating a toluene solution of **3a–d** with simultaneous irradiation with a 500 W lamp (Table 2).

According to these observations, but in disagreement with results from other 2,3-dihydroisoxazoles,[4,8] a photochemical step has to be involved during the rearrangement **3** → **4**. Thus a mechanism is proposed which is initiated by a light-induced dihydroisoxazole → acyl-aziridine isomerisation as the first, symmetry-allowed step (**3** → **9**)‡ followed by ring opening to the iminium ylide **4** (Scheme 2).

Further evidence for this explanation has been obtained from independent photolysis experiments with **4a**; after illumination of 0.08 mmol of **4a** in 100 ml of benzene (Pyrex filter, 10 min) the ^1H NMR spectrum of the crude reaction mixture indicated the presence of a 10 : 1 mixture of starting material **4a** and a minor compound; the new signals are fully consistent with the bicyclic aziridine structure **9a** [250 MHz, in $CDCl_3$: δ 2.58 (s, CH_3), 3.55 (m, 2H, 5-H), 3.79 (m, 2H, 2-H), 9.29 (s, CHO)] and have already been observed after the preparative irradiation of **3a** (see above).§ It is interesting that the 10 : 1 ratio of **4a** : **9a** corresponds remarkably well with the result obtained by photolysis of **3a** implying a photochemical equilibrium between **4** and **9**.

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Footnotes

† Selected spectroscopic data, **4a**: δ_H ($CDCl_3$) 1.93, (m, 2 H, 3-H), 2.09 (m, 2 H, 4-H), 2.34 (s, Me), 2.91 (m, 2 H, 5-H), 3.90 (m, 2 H, 2-H), 8.91 (s, CHO); δ_C ($CDCl_3$) 186.6 (C-2'), 176.7 (CHO), 140.3 (C-6), 123.0, (C-1'), 53.7 (C-2), 33.4 (C-5), 23.8 (Me), 21.5 (C-3), 17.6 (C-4); λ_{max}/nm (MeCN) 333 (ε 3500), 280 (ε 13500). **4b**: δ_H ($CDCl_3$) 1.31 (CMe_3), 1.89 (m, 2 H, 3-H), 2.00 (m, 2 H, 4-H), 2.18 (s, Me), 2.81 (m, 2 H, 5-H), 3.67 (m, 2 H, 2-H), 9.41 (s, CHO). **4c**: δ_H ($CDCl_3$) 1.88 (m, 2 H, 3-H), 2.02 (m, 2 H, 4-H), 2.32 (s, Me), 2.80 (m, 1 H, 5-H), 2.89 (m, 1 H, 5-H), 3.70 (s, OMe), 3.73 (m, 2 H, 2-H), 9.00 (s, CHO). **4d**: δ_H ($CDCl_3$) 1.90 (m, 2 H, 3-H), 2.03 (m, 2 H, 4-H), 2.36 (s, Me), 2.87 (m, 2 H, 5-H), 3.67 (s, OMe), 3.81 (m, 2 H, 2-H), 3.84 (s, OMe).

‡ According to preliminary results with **3a**, the transformation into **4a** takes place with equal efficiency using acetone as solvent, hence supporting a reaction from the triplet excited state of **3**.

§ Relevant ^1H NMR absorptions (250 MHz, $CDCl_3$) of **9b**: δ 2.41 (Me), 9.70 (CHO); **9c**: δ 2.47 (s, Me), 3.57 (m, 2 H, 5-H), 3.90 (m, 2 H, 2-H), 3.73 (CO_2Me), 9.53 (CHO)

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