

Photoreactions of β -aziridinylacrylonitrile. 1,3-Dipolar cycloadditions of photoinduced azomethine ylide

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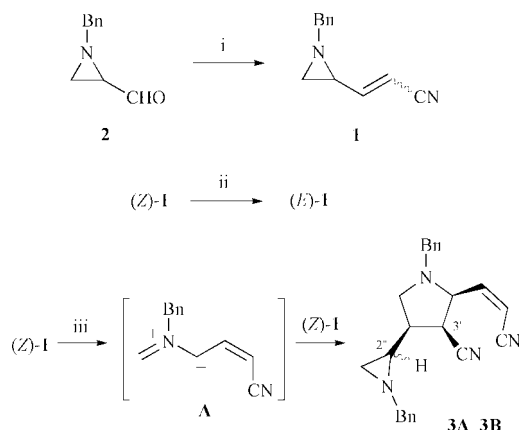
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The photoinduced azomethine ylide **A** from the 3-(1-benzylaziridin-2-yl)prop-2-enenitrile **1** undergoes 1,3-dipolar cycloaddition with electron-deficient olefins to give the head-to-head adducts selectively and efficiently.

The 1,3-dipolar cycloaddition of azomethine ylides with olefins is an important and useful strategy for the construction of the pyrrolidine system.¹ The azomethine ylides used for 1,3-dipolar cycloaddition have been generated mainly by desilylation of *N*-(silylmethyl)amine derivatives² or by heating or irradiation of the aziridines,^{3,4} most of which bear an adjacent electron withdrawing or phenyl group.

We are investigating the photochemical reactions of α,β -unsaturated γ,δ -epoxy nitriles systematically.⁵⁻⁸ These studies have revealed that the epoxy nitriles generate the carbonyl ylides more efficiently than the corresponding epoxy enones.⁵ In previous reports, we showed the usefulness of the carbonyl ylides in the syntheses of spiroacetal derivatives⁷ and in 1,3-dipolar cycloadditions with electron-rich olefins.⁸ On the basis of these studies, we became interested in extending our epoxy nitrile photochemistry to the aziridine-containing compound **1**.

The nitrile **1**[†] was prepared from the aldehyde **2**⁹ in 75% yield (*E*:*Z* = 44:31) by the Horner–Emmons reaction (Scheme 1). The nitriles (*E*)- and (*Z*)-**1** were easily separated with silica gel column chromatography.



Scheme 1 Reagents and conditions: i, $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{CN}$, NaH, THF, 0 °C; ii, $\lambda > 280$ nm, acetone, RT; iii, $\lambda = 254$ nm, acetonitrile, RT.

On triplet sensitization, the nitrile (*Z*)-**1** in acetone ($\lambda > 280$ nm) selectively undergoes (*E*/*Z*)-isomerization of the side chain leading to (*E*)-**1** (64%[†]). Direct irradiation of (*Z*)-**1** in acetonitrile ($\lambda = 254$ nm) gave two head-to-head dimers **3A**[†] (14%[†]) and **3B**[†] (32%[†]) (Scheme 1), which are probably formed by 1,3-dipolar cycloaddition of azomethine ylide **A** [generated photochemically from (*Z*)-**1**] and the ground state of (*Z*)-**1**.

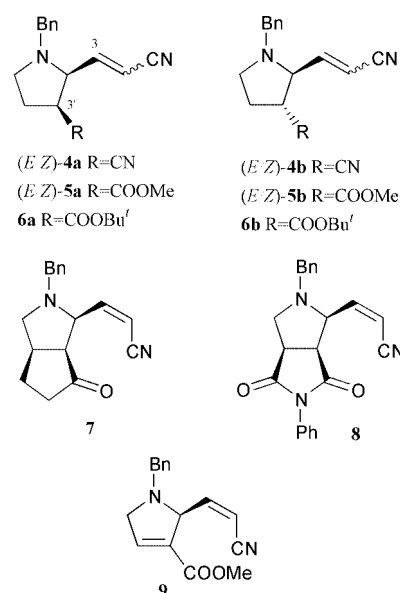
Since the photolysis of the nitrile **1** had given the cycloadducts **3** in moderate yield, the cycloadditions of **A** and electron-deficient olefins (acrylonitrile, methyl acrylate, *tert*-butyl acrylate, pent-2-enone, *N*-phenylmaleimide and methyl

Table 1 Photoreactions of nitrile **1** with olefins^a

1	Olefin	Conversion (%)	Products and yields (%) ^{‡b}
<i>E</i>	Acrylonitrile	100	(<i>E</i>)- 4a (52) and (<i>E</i>)- 4b (26)
<i>Z</i>	Acrylonitrile	100	(<i>Z</i>)- 4a (52) and (<i>Z</i>)- 4b (15)
<i>E</i>	Methyl acrylate	87	(<i>E</i>)- 5a (37) and (<i>E</i>)- 5b (25)
<i>Z</i>	Methyl acrylate	98	(<i>Z</i>)- 5a (38) and (<i>Z</i>)- 5b (48)
<i>Z</i>	<i>tert</i> -Butyl acrylate	90 [86] ^c	6a (23) [21] and 6b (49) [13]
<i>Z</i>	Pent-2-enone	91	7 (39)
<i>Z</i>	<i>N</i> -Phenylmaleimide	84 [81]	8 (39) [42]
<i>Z</i>	Methyl propiolate	66	9 (49)

^a A 0.060 mmol cm⁻³ solution of **1** in acetonitrile with 10 equiv. of olefin was irradiated at RT. ^b Isolated yield. ^c Values in square brackets are yields of thermal reactions in refluxing xylene.

propiolate) were studied. The results are summarized in Table 1. The photoreactions of the nitrile **1** and other electron-deficient olefins, such as dimethyl fumarate and dimethyl acetylenedicarboxylate, gave only dimethyl maleate and a complex mixture, respectively. On the other hand, the reactions of **1** and non-activated olefins (bicyclo[2.2.1]hept-2-ene and cyclohexene) or electron-rich olefins (ethyl vinyl ether) afforded no cycloadducts of these dipolarophiles, and gave only the dimer **3**.



The structures of the cycloadducts **3-9**[†] were deduced on the basis of their spectral data. The molecular ion peak in the mass spectrum (MS) indicates the 1:1 adducts of the azomethine ylide **A** and the olefin. The regio- and stereochemistries of **3A** and **3B** were determined from the H–H and C–H COSY and the phase-sensitive NOESY spectra. In particular, the cross-peaks between H-2' and H-3', H-3' and H-4', H-4' and H_a-5' and H_a-5' and H-2' in the NOESY spectra (Fig. 1) show that

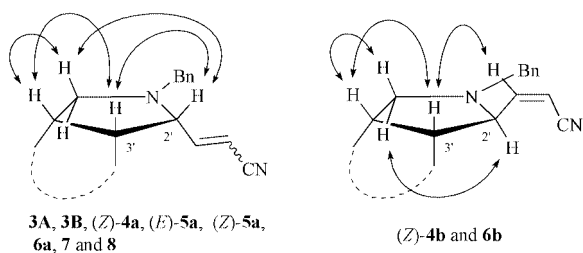


Fig. 1 Phase-sensitive NOESY.

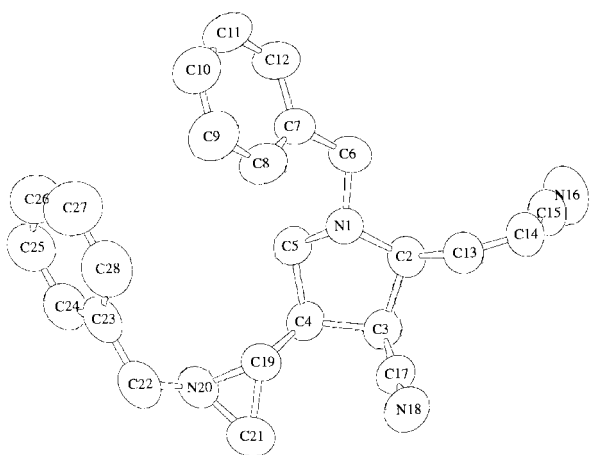


Fig. 2

Table 2 Chemical shift of H-C(3') in the ^1H NMR spectrum for 3–6

Adduct	δ	Adduct	δ
3A ^a	3.46 dd	3B ^a	3.36 dd
(E)-4a	3.18–3.25 m	(E)-4b	2.82 ddd
(Z)-4a ^a	3.29 ddd	(Z)-4b ^a	2.85 ddd
(E)-5a ^a	3.20–3.28 m	(E)-5b	2.81 ddd
(Z)-5a ^a	3.29–3.37 m	(Z)-5b	2.83 ddd
6a ^a	3.18–3.24 m	6b ^a	2.74 ddd

^a The stereochemistry was also determined from the phase-sensitive NOESY spectrum.

the configurations at C(2'), C(3') and C(4') in the pyrrolidine ring are all *cis*. Therefore the dimers **3A** and **3B** are epimeric at C(2'). Further evidence for the structure of **3B** was provided by an X-ray structure analysis \S (Fig. 2).

The regio- and stereochemistries of (Z)-**4a** were determined from its H–H and C–H COSY, phase-sensitive NOESY (Fig. 1) and HMBC spectra. In the HMBC spectrum of (Z)-**4a**, the crosspeaks between H-3 and C(3') (3J), between H-2' and C-C(3') (3J) and between H-2' and C(3') (2J) are observed.

The structures of (Z)-**4b**, (E)-**5a**, (Z)-**5a**, **6a**, **6b**, **7** and **8** were determined from their phase-sensitive NOESY (Fig. 1) spectra. The structures of the other adducts (E)-**4a**, (E)-**4b**, (E)-**5b** and (Z)-**5b** were deduced from a comparison of the chemical shift of H-C(3') with that for **3A**, **3B**, (Z)-**4a**, (Z)-**4b**, (E)-**5a**, (Z)-**5a**, **6a** and **6b**, which are summarized in Table 2. The regiochemistry of **9** was deduced from the crosspeaks between H-C(4') and H₂-C(5') in its phase-sensitive NOESY spectrum.

The 1,3-dipolar cycloaddition of an azomethine ylide (derived from an aziridine bearing an ester function) and electron-deficient olefins normally affords products in which the electron-withdrawing group is located at the C(4') position in the pyrrolidine.⁴ We observed the opposite regiochemistry [C(3') instead C(4')] in the cycloaddition of electron-deficient olefins and the azomethine ylide **A**, and then assumed initially that the cycloadditions may occur *via* the excited state of **A** or the electron-deficient olefin.

Consequently, we studied the thermal reactions of **1** and electron-deficient olefins. A mixture of (Z)-**1** and *tert*-butyl acrylate or *N*-phenylmaleimide was heated in refluxing xylene

and gave the same adducts **6a** (21% \ddagger) and **6b** (13% \ddagger) and **8** (42% \ddagger) as yielded by the photochemical reactions, respectively. The results may suggest that the ring cleavage of the aziridine **1** proceeds photochemically or thermally and the cycloaddition occurs thermally.

The regiochemistry of the adducts could not be clearly explained by frontier-MO theory.¹⁰ In order to clarify the reaction mechanism, further work with unsymmetrically substituted dipolarophiles and 3'-alkyl substituted aziridine is currently in progress.

Experimental

Typical procedure for the photochemical reaction of (Z)-**1** and acrylonitrile

A solution of (Z)-**1** (50.6 mg, 0.271 mmol) and acrylonitrile (144 mg, 2.71 mmol) in acetonitrile (4.5 cm³) was irradiated with a low-pressure mercury lamp (60 W) through a quartz filter (100% conversion) under argon for 7 h at RT. After removal of the solvent, chromatography (eluting with hexane–ethyl acetate, 7:3) of the residue yielded (Z)-**4a** \dagger (33.3 mg, 52% \ddagger) and (Z)-**4b** \dagger (9.7 mg, 15% \ddagger).

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Notes and references

\dagger All new compounds were isolated and exhibited IR, ^1H NMR, ^{13}C NMR and mass spectra that were consistent with the assigned structures, and gave satisfactory elemental analyses and/or high-resolution mass spectra. Selected NMR data in CDCl₃ for **3A**, **3B**, (Z)-**4a**, (Z)-**4b** and **9** are representative (*J* values in Hz). **3A**: δ_{H} 1.48 (1H, d, *J* 6.1), 1.68 (1H, d, *J* 3.4), 1.85–1.89 (1H, m), 2.11–2.18 (1H, m), 3.46 (1H, dd, *J* 8 and 6.1), 3.75 (1H, dd, *J* 9.2 and 6.1), 5.59 (1H, dd, *J* 11.0 and 0.6) and 6.65 (1H, dd, *J* 11.0 and 9.2); δ_{C} 33.4 (t), 38.8 (d), 40.0 (d), 43.1 (d), 54.4 (t) and 65.3 (d). **3B**: δ_{H} 1.65 (1H, d, *J* 6.1), 1.75 (1H, d, *J* 3.4), 1.84–1.89 (1H, m), 1.96–2.02 (1H, m), 3.36 (1H, dd, *J* 8.5 and 7.0), 3.72 (1H, dd, *J* 9 and 7.0), 5.53 (1H, dd, *J* 11.0 and 0.6) and 6.59 (1H, dd, *J* 11.0 and 9.2); δ_{C} 33.9 (t), 37.5 (d), 40.5 (d), 42.5 (d), 56.0 (t) and 65.0 (d). (Z)-**4a**: δ_{H} 3.29 (1H, ddd, *J* 8.8, 7.3 and 5.5), 3.68 (1H, dd, *J* 9.2 and 7.3), 5.59 (1H, dd, *J* 11.0 and 0.6) and 6.61 (1H, dd, *J* 11.0 and 9.2); δ_{C} 28.5 (t), 33.3 (d), 51.8 (t) and 64.9 (d). (Z)-**4b**: δ_{H} 2.85 (1H, ddd, *J* 10.1, 8.9 and 6.7), 3.75 (1H, dd, *J* 9.5 and 8.9), 5.56 (1H, d, *J* 11.0) and 6.28 (1H, dd, *J* 11.0 and 9.5); δ_{C} 27.8 (t), 33.6 (d), 52.1 (t) and 68.3 (d). **9**: δ_{H} 4.82–4.87 (1H, m), 5.39 (1H, dd, *J* 10.7 and 0.6), 6.37 (1H, dd, *J* 10.7 and 9.2) and 6.89 (1H, q, *J* 2.1); δ_{C} 59.0 (t), 68.8 (d), 133.5 (s) and 141.8 (d).

\ddagger Yields for compounds throughout the rest of the paper are based on converted starting material.

\S Crystal data: C₂₄H₂₄N₄, *M* = 368.48, monoclinic, *a* = 18.906(2), *b* = 5.616(6), *c* = 20.119(2) Å, *V* = 2115(2) Å³, *T* = 298 K, space group *P2₁/n*, *Z* = 4, $\mu(\text{Cu-K}\alpha)$ = 5.42 cm⁻¹, 4418 reflections measured, 4284 unique (*R*_{int} = 0.039), the final *wR* was 0.066 (observed data). CCDC reference number 207/462. See <http://www.rsc.org/suppdata/p1/b0/b004850j/> for crystallographic files in .cif format.

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