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# Photoreactions of $\beta$ -aziridinylacrylonitrile. 1,3-Dipolar cycloadditions of photoinduced azomethine ylide

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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.<sup>1</sup> The azomethine ylides used for 1,3-dipolar cycloaddition have been generated mainly by desilylation of N-(silylmethyl)amine derivatives<sup>2</sup> or by heating or irradiation of the aziridines,<sup>3,4</sup> most of which bear an adjacent electron withdrawing or phenyl group.

We are investigating the photochemical reactions of  $\alpha$ , $\beta$ unsaturated  $\gamma$ , $\delta$ -epoxy nitriles systematically.<sup>5-8</sup> These studies have revealed that the epoxy nitriles generate the carbonyl ylides more efficiently than the corresponding epoxy enones.<sup>5</sup> In previous reports, we showed the usefulness of the carbonyl ylides in the syntheses of spiroacetal derivatives<sup>7</sup> and in 1,3dipolar cycloadditions with electron-rich olefins.<sup>8</sup> 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,  $(EtO)_2P(O)CH_2CN$ , 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

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 Table 1
 Photoreactions of nitrile 1 with olefins<sup>a</sup>

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

<sup>*a*</sup> A 0.060 mmol cm<sup>-3</sup> solution of **1** in acetonitrile with 10 equiv. of olefin was irradiated at RT. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> 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 nonactivated 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  $3-9^{\dagger}$  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<sub>a</sub>-5' and H<sub>a</sub>-5' and H-2' in the NOESY spectra (Fig. 1) show that

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Fig. 1 Phase-sensitive NOESY.



Fig. 2

Table 2 Chemical shift of H-C(3') in the <sup>1</sup>H NMR spectrum for 3-6

Adduct	δ	Adduct	δ
$3A^{a}$ (E)-4a (Z)-4a <sup>a</sup> (E)-5a <sup>a</sup> (Z)-5a <sup>a</sup>	3.46 dd 3.18–3.25 m 3.29 ddd 3.20–3.28 m 3.29–3.37 m	3Ba     (E)-4b     (Z)-4ba     (E)-5b     (Z)-5b     (Z)-5b	3.36 dd 2.82 ddd 2.85 ddd 2.81 ddd 2.83 ddd
6a <sup>a</sup>	3.18–3.24 m	6b <sup><i>a</i></sup>	2.74 ddd

<sup>a</sup> 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§ (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') (<sup>3</sup>J), between H-2' and C-C(3') (<sup>3</sup>J) and between H-2' and C(3') (<sup>2</sup>J) 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  $H_2$ -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.<sup>4</sup> 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%<sup>‡</sup>) as yielded by the photoreactions, 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.<sup>10</sup> 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 cm<sup>3</sup>) 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 hexaneethyl acetate, 7:3) of the residue yielded (Z)-4a<sup>+</sup> (33.3 mg, 52% ‡) and (Z)-4b † (9.7 mg, 15% ‡).

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### Notes and references

<sup>†</sup> All new compounds were isolated and exhibited IR, <sup>1</sup>H NMR, <sup>13</sup>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 CDCl<sub>3</sub> for 3A, 3B, (Z)-4a, (Z)-4b and 9 are representative (J values in Hz). 3A:  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  33.4 (t), 38.8 (d), 40.0 (d), 43.1 (d), 54.4 (t) and 65.3 (d). **3B**:  $\delta_{\rm H}$  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, dd, *J* 8.5 and 7.0), 3.72 (1H, dd, dd, dd) and a statement of the statement of 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);  $\delta_{\rm C}$  33.9 (t), 37.5 (d), 40.5 (d), 42.5 (d), 56.0 (t) and 65.0 (d). (Z)-4a: δ<sub>H</sub> 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);  $\delta_{\rm c}$  28.5 (t), 33.3 (d), 51.8 (t) and 64.9 (d). (Z)-**4b**:  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  27.8 (t), 33.6 (d), 52.1 (t) and 68.3 (d). 9:  $\delta_{\rm H}$  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);  $\delta_{\rm C}$  59.0 (t), 68.8 (d), 133.5 (s) and 141.8 (d).

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

§ Crystal data:  $C_{24}H_{24}N_4$ , M = 368.48, monoclinic, a = 18.906(2), b = 5.616(6), c = 20.119(2) Å, V = 2115(2) Å<sup>3</sup>, T = 298 K, space group  $P2_1/n$ , Z = 4,  $\mu$ (Cu-K $\alpha$ ) = 5.42 cm<sup>-1</sup>, 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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