

# 1,3-Dipolar Cycloadditions of Photoinduced Carbonyl Ylides from $\alpha,\beta$ -Unsaturated $\gamma,\delta$ -Epoxy Dinitriles

Masashi Kotera, Keitaro Ishii,\* Osamu Tamura and Masanori Sakamoto  
Meiji College of Pharmacy, 1-35-23 Nozawa, Setagaya-ku, Tokyo 154, Japan

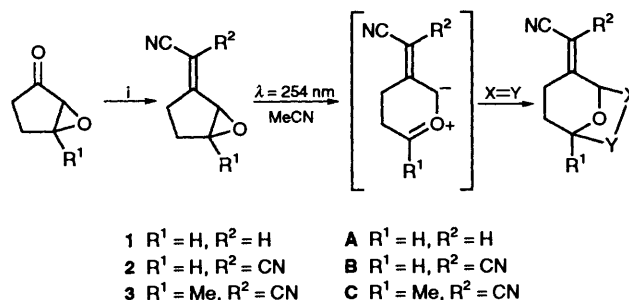
The photoinduced carbonyl ylides **B** and **C** from the  $\alpha,\beta$ -unsaturated  $\gamma,\delta$ -epoxy dinitriles **2** and **3** undergo 1,3-dipolar cycloaddition with enol ethers, leading regioselectively to the 8-oxabicyclo[3.2.1]octane system.

1,3-Dipolar cycloadditions have been widely investigated,<sup>1</sup> and many organic chemists have been attracted by the regioselectivity, stereoselectivity and reactivity of these reactions. The cycloaddition of a carbonyl ylide with olefins is an important and useful strategy for the construction of the tetrahydrofuran system,<sup>2</sup> which is a component of many natural products.<sup>3</sup> Carbonyl ylides have been generated by heating of oxiranes bearing an adjacent electron withdrawing group<sup>4</sup> or by treatment of an  $\alpha$ -diazo ketone and a carbonyl compound with rhodium(II) acetate.<sup>5</sup> However, relatively few reports have dealt with intermolecular 1,3-dipolar cycloadditions of photoinduced carbonyl ylides, most of which have been generated from oxiranes possessing adjacent phenyl groups.<sup>6</sup>

We are investigating the photochemistry of  $\alpha,\beta$ -unsaturated  $\gamma,\delta$ -epoxy nitriles,<sup>7,8</sup> and are interested in the reactivity of the carbonyl ylides obtained from epoxy nitriles and the possibility of using these reactions in synthesis. In a previous report,<sup>7</sup> we showed that the direct irradiation of  $\delta$ -hydroxybutyl  $\alpha,\beta$ -unsaturated  $\gamma,\delta$ -epoxy nitriles gives spiroketals *via* carbonyl ylide intermediates. On the basis of these studies, we report here intermolecular 1,3-dipolar cycloadditions of the carbonyl ylides **A–C** generated photochemically from  $\alpha,\beta$ -unsaturated  $\gamma,\delta$ -epoxy nitrile systems.

The mononitrile **1**† was prepared from the corresponding epoxy ketone in 84% yield (*E*:*Z* = 2:1) by the Horner–Emmons reaction,<sup>7</sup> and the dinitriles **2**† and **3**† in 76 and 79% yields, respectively, by Knoevenagel condensation.<sup>9</sup>

Preparative irradiation of **1** and 10 equiv. of ethyl vinyl ether (EVE) in acetonitrile with a low-pressure mercury lamp through a quartz filter ( $\lambda = 254$  nm) at 0 °C gave no cycloadduct. However, when the dinitrile **2** was irradiated under the same conditions the *exo*-adduct **4a**† (36%) and the *endo*-adduct **4b**† (8%) were produced regioselectively.‡ The structures of **4a**



Scheme 1 Reagents and conditions: i,  $(EtO)_2P(O)CH_2CN$ , NaH, DMF,  $-50$  °C for **1**, malononitrile,  $AcONH_4$ , AcOH, room temp. for **2** and **3**

and **4b** were determined from a comparison of the 1-H coupling constants in the <sup>1</sup>H NMR spectra with the dihedral angle between 1-H and 7-H obtained from MM2 force field calculations using the CAChe system.§ The carbonyl ylide **B** reacted with the other enol ethers (ethyl prop-1-enyl ether, 2,3-dihydrofuran or 3,4-dihydro-2H-pyran) under the same conditions yielding the corresponding cycloadducts **5–7**.† The results are summarized in Table 1. Although the ethyl prop-1-enyl ether was *trans* rich (*E*/*Z* = 3:1), the *cis* cycloadducts **5a** and **5b** were predominantly obtained. This may be due to the difference of the reaction rate between *E* and *Z*. The dinitrile **3** also reacted with EVE under the same conditions, affording the cycloadducts **8a**† (25%) and **8b**† (7%).‡ All these cycloadditions of carbonyl ylides and enol ethers presumably involved a thermal process, and gave predominantly *exo*-adducts, because of steric hindrance in the *endo* transition state.

In order to compare the reactivity between **1** and **2**, semiempirical AM 1 calculations<sup>10</sup>¶ were performed. The additional cyano group in **B** lowers the LUMO energy, and hence the LUMO (**B**) – HOMO (EVE) energy difference ( $\Delta E = 7.56$  eV) is smaller than the LUMO (**A**) – HOMO (EVE) ( $\Delta E = 8.23$  eV). Consequently, the 1,3-dipolar cycloadditions of the dinitriles **2** and **3** with enol ethers are more favourable than that of mononitrile **1**. Furthermore, AM 1 calculations showed that the secondary orbital interactions between the LUMO (**B**) and the HOMO (enol ethers) were unfavourable for the cycloaddition. Thus, the *exo*-adducts were formed preferably.

We examined also the reaction of **2** with other dipolarophiles (dimethyl acetylenedicarboxylate, cyclohexene or vinyl acetate) under the same conditions, however, no cycloadducts were produced. The carbonyl ylides **B** and **C** have a tendency to react with electron-rich olefins because they have two cyano groups.


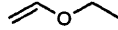
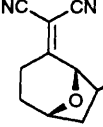
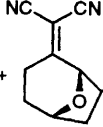












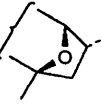
† All new compounds were isolated and exhibited IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and mass spectra which were consistent with the assigned structures, and gave satisfactory elemental analyses and/or high-resolution mass spectra. Selected NMR data for **4a**, **4b**, **5a**, **5b** and **5c** are representative (*J* Values in Hz). **4a**:  $\delta_H(CDCl_3)$  3.47 and 3.57 (2 H, each dq, *J* 8.9 and 6.9), 3.93–3.97 (1 H, m), 4.74 (1 H, br s) and 5.03 (1 H, s);  $\delta_C$  65.8 (t), 75.0 (d), 80.9 (d), 82.7 (d), 83.4 (s), 110.2 (s), 110.7 (s) and 176.5 (s). **4b**:  $\delta_H$  3.46 and 3.55 (2 H, each dq, *J* 9.2 and 6.9), 4.37 (1 H, ddd, *J* 10.2, 6.6 and 4.0), 4.46–4.50 (1 H, m) and 5.08 (1 H, d, *J* 6.6);  $\delta_C$  67.1 (t), 74.7 (d), 77.5 (d), 80.4 (d), 84.8 (s), 110.9 (s), 110.0 (s) and 178.0 (s). **5a**:  $\delta_H$  3.43 and 3.64 (2 H, each dq, *J* 9.0 and 7.1), 3.79 (1 H, d, *J* 7.6), 4.20 (1 H, br d, *J* 3.4) and 5.01 (1 H, s);  $\delta_C$  66.9 (t), 82.4 (d), 82.9 (d), 83.9 (d), 83.2 (s), 110.3 (s), 110.7 (s) and 177.4 (s). **5b**:  $\delta_H$  2.62 (1 H, d quintet, *J* 10.0 and 7.0), 3.46 and 3.56 (2 H, each dq, *J* 9.3 and 7.1), 4.24–4.29 (2 H, m) and 5.16 (1 H, d, *J* 6.8);  $\delta_C$  67.8 (t), 78.0 (d), 78.6 (d), 80.4 (d), 84.1 (s), 110.0 (s), 110.0 (s) and 179.2 (s). **5c**:  $\delta_H$  2.55 (1 H, quintet d, *J* 7.3 and 4.4), 3.44–3.52 (2 H, m), 3.56 (1 H, dq, *J* 9.0 and 7.1), 4.44–4.47 (1 H, m) and 4.94 (1 H, s);  $\delta_C$  66.2 (t), 78.4 (d), 81.4 (d), 89.9 (d), 83.0 (s), 110.3 (s), 110.7 (s) and 177.0 (s).

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

§ Tektronix Corp., version 3.0 (Beaverton, Oregon, USA).

¶ CAChe MOPAC version 94. All orbital energies were obtained from AM1 optimized geometries.

**Table 1** Results of 1,3-dipolar cycloadditions of 1–3

Compound	Dipolarophile	Conv'n	Adducts
1		35	No adduct
2		95	  <b>4a (36%)</b> <b>4b (8%)</b>
	 <i>E:Z</i> = 3:1	94	    <b>5a (19%)</b> <b>5b (10%)</b> <b>5c (3%)</b> <b>5d (trace)</b>
		97	  <b>6a (21%)</b> <b>6b (5%)</b>
		98	 <b>7a (7%)</b>
3		79	  <b>8a (25%)</b> <b>8b (7%)</b>

## Experimental

**Typical Procedure for the Photochemical Reaction of 2 and EVE.**—A solution of **2** (265 mg, 1.81 mmol) in acetonitrile (35 cm<sup>3</sup>) and EVE (13.1 g, 181 mmol) was irradiated with a low-pressure mercury lamp (60 W) through a quartz filter (95% conversion) under argon for 6 h at 0 °C. After removal of the solvent, chromatography (eluting with methylene chloride–hexane, 5:1) of the residue yielded **4a** (133 mg, 36%<sup>‡</sup>) and **4b** (29 mg, 8%<sup>‡</sup>).

## References

- R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, 1963, **2**, 565; R. Huisgen, *J. Org. Chem.*, 1976, **41**, 403; *1,3-Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley, New York, 1984, vols. I and II.
- T. L. B. Boivin, *Tetrahedron*, 1987, **43**, 3309; J. E. Semple and M. M. Joullie, *Heterocycles*, 1980, **14**, 1825.
- Chemical and Biological Perspectives*, ed. P. J. Scheuer, New York, 1978, vol. I.
- R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, 1977, **16**, 572 and references cited therein.
- A. Padwa, *Acc. Chem. Res.*, 1991, **24**, 22 and references cited therein; A. Padwa and S. F. Hornbuckle, *Chem. Rev.*, 1991, 263 and references cited therein; A. Padwa and D. L. Hertzog, *Tetrahedron*, 1993, **49**, 2589; W. G. Dauben, J. Dinges and T. C. Smith, *J. Org. Chem.*, 1993, **58**, 7635.
- E. F. Ullman and J. E. Milks, *J. Am. Chem. Soc.*, 1964, **86**, 3814; D. R. Arnold and L. A. Karnischky, *J. Am. Chem. Soc.*, 1970, **92**, 1404; A. G. Schultz and R. D. Lucci, *J. Org. Chem.*, 1975, **40**, 1371.
- K. Ishii, T. Nakano, T. Zenko, M. Kotera and M. Sakamoto, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2057.
- K. Ishii, M. Abe and M. Sakamoto, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1937; K. Ishii, D. Gong, R. Asai and M. Sakamoto, *J. Chem. Soc., Perkin Trans. 1*, 1990, 855.
- V. Bardakos and C. Sandris, *Org. Magn. Reson.*, 1981, **15**, 339.
- M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.

Paper 4/03879G

Received 27th June 1994

Accepted 11th July 1994