

Pronounced Chemo-, Regio-, and Stereoselective [2 + 2] Cycloaddition Reaction of Allenes toward Alkenes and Alkynes

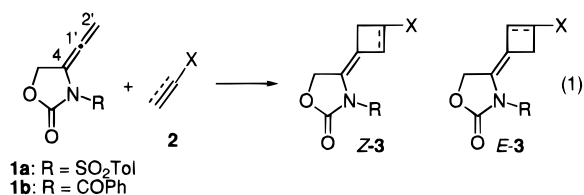
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[2 + 2] Cycloaddition reactions between allenenes and alkenes have frequently been employed for the preparation of methylenecyclobutane derivatives.^{1–4} Photochemical initiation⁵ and Lewis acid⁶ and catalytic transition-metal⁷ promotion have proved to be successful for preparative purposes. Strictly thermal reactions generally incur the drawbacks of requiring high temperatures (mostly >200 °C) and providing mixtures of chemo-, regio-, and stereoisomeric products in moderate or poor yields.

Here we disclose that 4-ethenylidene-1,3-oxazolidin-2-ones **1a–c**⁸ (eq 1) undergo an extraordinarily facile [2 + 2] addition reaction chemoselectively at the allenic C1'–C2' double bond^{9,10} with alkenes and alkynes **2** to furnish methylenecyclobutane and -cyclobutene derivatives **3** with excellent regio- and stereoselectivities. The reaction proceeded smoothly at tem-



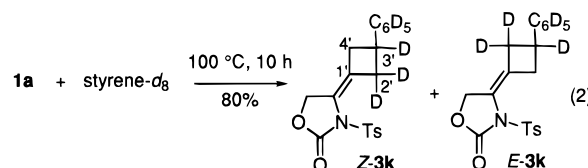
peratures as low as 70–100 °C and provided **Z-3** as single diastereomers.¹¹ The selective formation of **Z-3** indicates that **2** was apparently incorporated as the two-carbon component of

the cyclobutane and cyclobutene rings of **3** from the more congested face of the C1'–C2' double bonds *syn* to *N*-tosyl or *N*-benzoyl groups.

In Table 1 are summarized the results of the reactions of **1a,b** and **2** with substituents of a wide electronic variety. The cycloaddition of **1a,b** and electron-deficient olefins **2a–c** occurred with great facility and provided **3a–d** in good yields (runs 1–4, Table 1). To our surprise, alkenes bearing a phenyl group (runs 5 and 6) and also even alkenes directly conjugated with an electron-donating trimethylsiloxy group (run 7) reacted with similar ease. Furthermore, 2,3-dimethyl-1,3-butadiene (**2f**) served selectively as a 2π component to furnish **3h** in an excellent yield (run 8). This contrasts with the fact that dienes tend to serve as the 4π component, under both thermal^{12,13} and transition-metal activation,¹⁴ furnishing [4 + 2] adducts exclusively or preferentially over [2 + 2] adducts.¹⁵

Alkynes were also engaged in the [2 + 2] addition (runs 9 and 10). Amazingly, the products **3i,j** were isolated as single diastereomers. The structure was unequivocally elucidated to be *Z* by NOE experiments: e.g., **3i** displayed 6.4 and 4.0% NOE of the tolyl *o*-protons and C-5 protons by irradiation at C-2' and C-4' protons, respectively.

In order to clarify the stereochemical course of the reaction of **1** and alkenes, we examined the reaction of **1a** with styrene-*d*₈ (eq 2) and were gratified to find that the reaction was also highly stereoselective (**Z-3k**:**E-3k** = >45:1). The structure of



Z-3k was determined as follows. All of the cyclobutane ring protons of the parent **3e** appeared as base line separated peaks in the ¹H NMR spectrum, each of which was assigned by NOE experiments [400 MHz (CDCl₃) δ 2.76 (dm, *J* = 15.0 Hz, H4' (*cis* to Ph)), 2.99 (dm, *J* = 15.0 Hz, H4' (*trans* to Ph)), 3.24 (dm, *J* = 16.2 Hz, H2' (*cis* to Ph)), 3.49 (dm, *J* = 16.2 Hz, H2' (*trans* to Ph)), 3.65 (quint, *J* = 8.2 Hz, H3')].¹⁶ On the other hand, the ¹H NMR spectrum of **Z-3k** displayed only a pair of doublets in the cyclobutane region [400 MHz (CDCl₃) δ 2.74 (d, *J* = 15.0 Hz, H4' (*cis* to Ph)), 2.98 (d, *J* = 15.0 Hz, H4' (*trans* to Ph))]. Similar *Z*-selectivity was observed for the reactions of **1a** with both electron-deficient pentadeuterio-α-methylacrylonitrile (>97% *Z*) and electron-rich β,β-dideuterio-α-(trimethylsiloxy)styrene (>95% *Z*).

As summarized in eq 3, even **1c**, the C-5 *gem*-dimethyl derivative of **1a**, displayed a reactivity and diastereoselectivity similar to **1a**: **1c** reacted with styrene (20 equiv, 100 °C, 5 h, neat) to furnish **3l** in 79% isolated yield. The reaction with styrene-*d*₈ (50 equiv., 80 °C, 10 h, neat) provided **Z-3m** exclusively in 80% yield. Furthermore, **1c** reacted with *cis*-β-monodeuteriostyrene¹⁷ (96 atom % D; 20 equiv, 100 °C, 28 h, neat) to give a mixture of *Z,cis*-**3n** and *Z,trans*-**3n** in a ratio of ca. 97:3 in 90% isolated yield. This clearly indicates that the *cis*-geometry of the starting alkenes was retained almost com-

(12) Yeo, S.-K.; Shiro, M.; Kanematsu, K. *J. Org. Chem.* **1994**, *59*, 1621–1632. Padwa, A.; Meske, M.; Murphree, S. S.; Watterson, S. H.; Ni, Z. *J. Am. Chem. Soc.* **1995**, *117*, 7071–7080.

(13) Dolbier, W. R., Jr. *Acc. Chem. Res.* **1991**, *24*, 63–69.

(14) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49–92.

(15) Some strained 1,2-cycloalkadienes react with dienes to provide mixtures of [2 + 2] and [4 + 2] products: Johnson, R. P. *Chem. Rev.* **1989**, *89*, 1111–1124.

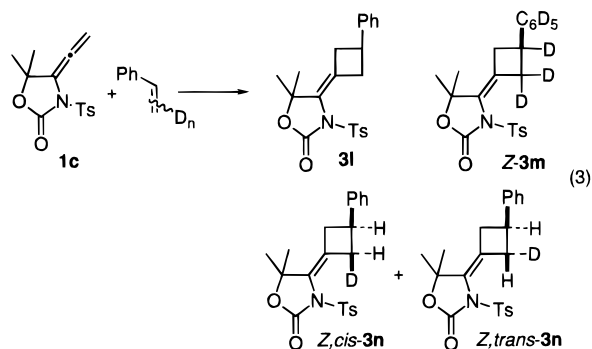
(16) For NOE data of **3e**, **3l–n** and 400 MHz ¹H NMR spectra (cyclobutane region) of **3l–n**, see the Supporting Information.

(17) Preparation of *cis*-β-monodeuteriostyrene: Brown, H. C.; Gupta, S. K. *J. Am. Chem. Soc.* **1975**, *97*, 5249–5255.

Table 1. Thermal [2 + 2] Cycloaddition of **1a,b** with Alkenes and Alkynes **2**

run	2	conditions ^a temp (°C)/time (h)	products (% isolated yield) ^b
1	2a : W = CO ₂ Me	80/22	3a (R = Ts, W = CO ₂ Me, 73) 4a (20)
2	2a : W = CO ₂ Me	80/22	3b (R = Bz, W = CO ₂ Me, 71)
3	2b : W = CONMe ₂	80/22	3c (R = Ts, W = CONMe ₂ , 69)
4	2c : W = CN	80/17 ^c	3d (R = Ts, W = CN, 88)
5	2d : R' = H	100/22 ^d	3e (R = Ts, R' = H, 63)
6	2d : R' = H	80/48 ^e	3f (R = Bz, R' = H, 66)
7	2e : R' = OSiMe ₃	100/46 ^e	3g (R = Ts, R' = OSiMe ₃ , 45) ^f
8		70/47 ^c	
9		80/11 ^c	3i (R = Ts, 60)
10	2g	80/23 ^c	3j (R = Bz, 55)

^a Unless otherwise noted, **1** (0.5 mmol) and **2** (4.0 mL, 40–60 mmol) were heated under N₂. ^b All products were characterized by ¹H (400 MHz), ¹³C (100 MHz) NMR, IR, MS, and/or elemental analyses. The structure of **3a** was determined by X-ray crystallographic analysis. ^c Mixture of **1** and **2** was diluted with dioxane (1 mL). ^d Compounds **1a** (0.5 mmol) and **2d** (20 mmol) were reacted. ^e Compounds **1a** (0.5 mmol) and **2e** (10 mmol) were reacted. ^f An unidentified product (10% based on a 1:1 adduct) was isolated.



pletely in the product.¹⁸ The structures of **Z-3m** and **Z,cis-3n** were elucidated in a manner similar to that for **Z-3k**.¹⁶

The mechanistic details associated with the thermal [2 + 2] reactions constitute a topic of much study and debate (either concerted or stepwise).^{1–4,13,15,18,19} Most studies, evidenced by the regio- and stereochemical outcome and hydrogen–deuterium isotope effects,²⁰ seem to strongly favor the stepwise biradical mechanism. All of the results obtained from the [2 + 2] addition reactions of **1a–c**, on the other hand, seem to point to a concerted mechanism involving a six-electron Hückel [$\pi_{2s} + (\pi_{2s} + \pi_{2s})$] transition state, proposed by Pasto (Figure 1).²¹

(18) Complete loss of stereochemical integrity of *cis*- β -monodeuteriostyrene for the [2 + 2] addition with 1,2-cyclohexadiene: Harnos, S.; Tivakompannarai, S.; Waali, E. E. *Tetrahedron Lett.* **1986**, 27, 3701–3704.

(19) Pasto, D. J.; Warren, S. E.; Weyenberg, T. J. *J. Org. Chem.* **1986**, 51, 2106–2110. Pasto, D. J.; Sugi, K. D. *J. Org. Chem.* **1991**, 56, 3795–3801.

(20) Dai, S.-H.; Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1972**, 94, 3946–3952.

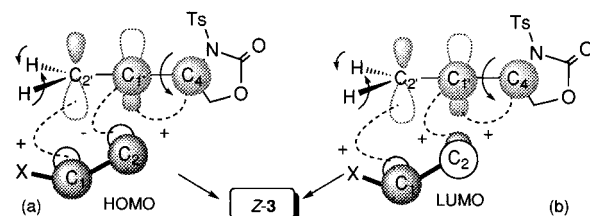


Figure 1. Orbital interactions for (a) electron-rich and (b) electron-deficient alkenes. In both a and b, the p orbitals of C-1' and C-2' overlap coaxially and those of C-2' and C-1 perpendicularly.

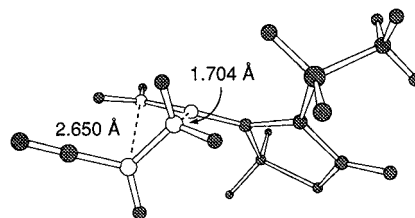


Figure 2. RHF/3-21G* transition structure for the reaction of **1a** (SO₂Me in place of SO₂Tol) and **2c**.

The unique reactivity associated with **1a–c** (and the related allene compounds)¹⁰ might be primarily attributed to a strong $\sigma^*_{N-S}-\pi^*_{C1'-C2'}$ interaction of **1a,c** (or $\sigma^*_{N-C}-\pi^*_{C1'-C2'}$ interaction for **1b**), which causes (1) the lowering of the $\pi^*_{C1'-C2'}$ energy level (and hence, lowering of the activation energy for the [2 + 2] addition) and (2) the rehybridization of the $\pi^*_{C1'-C2'}$ orbitals [sp³-like, and hence, better overlap between the p orbitals of C-1 and C-2' in the opposite face to *N*-tosyl]. Three-system interaction²² [HOMO_{C1'-C4}, LUMO_{C1'-C2'}, and HOMO_{electron-rich 2} (Figure 1a) or LUMO_{electron-deficient 2} (Figure 1b)], with a coaxial overlap of the p orbitals of C-1' and C-2 and a perpendicular overlap of the p orbitals of C-2' and C-1, necessitates a 90° counter-clockwise rotation of the oxazolidinone ring (i.e., the rotation of the *N*-tosyl toward C-2) to furnish **Z-3**. The mechanism proposed here was supported by the RHF/3-21G* concerted transition state structure (Figure 2) and the geometrical transformation along the intrinsic reaction coordinate for the reaction of **1a** (SO₂Me in place of SO₂Tol) and **2c**.²³ An alternative coaxial approach of the p orbitals of C-2' and C-1, accompanied by a perpendicular interaction between the p orbitals of C-1' and C-2,²¹ could hardly be reconciled with the selective formation of **Z-3m** and **Z,cis-3n** (eq 3), since the C-5 dimethyl groups of **1c** would sterically prohibit this mode of approach.

In summary, the allenes **1a–c** readily undergo thermal [2 + 2] additions with alkenes and alkynes with pronounced chemo, regio-, and stereoselectivities. The alkenes encompass ethylenes bearing not only electron-attracting and conjugating groups but also electron-donating groups. Even 1,3-dienes are engaged in exclusive [2 + 2] addition reactions.

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Supporting Information Available: Physical and spectral data for the products and data for Cartesian coordinate (Figure 2) and IRC calculation (11 pages). See any current masthead page for ordering and Internet access instructions.

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(21) Pasto, D. J. *J. Am. Chem. Soc.* **1979**, 101, 37–46.

(22) Inagaki, S.; Fujimoto, H.; Fukui, K. *J. Am. Chem. Soc.* **1976**, 98, 4693–4701.

(23) Gaussian 94, Revision D.3; Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc.: Pittsburgh, PA, 1995.