# Single Electron Transfer Pathway in the [3 + 2] Cycloaddition of Dipolar Trimethylenemethane with Olefins

Shigeru Yamago, Satoshi Ejiri, Masaharu Nakamura, and Eiichi Nakamura*

*Department of Chemistry*
*Tokyo Institute of Technology*
*Meguro, Tokyo 152, Japan*

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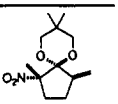
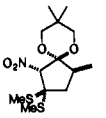
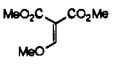
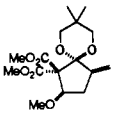
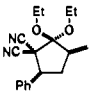
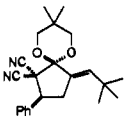
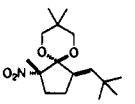
Dialkoxy trimethylenemethanes (TMM) **2** generated reversibly from methylenecyclopropanes (MCP) **1**[1] undergo [3 + 2] cycloadditions with olefins to give ketene acetal cycloadducts (KA)[2] (e.g., **8**; X = COOMe, Y = H, Z = alkyl) through a highly ordered transition state.[3,4] We report here that the same TMM reacts with highly electrophilic olefins to give predominantly an exomethylene cycloadduct (EM, e.g., **7**) via single electron transfer (SET). This reaction represents a rare example of remarkable mechanism-dependent product dichotomy in cycloaddition reactions.[5] In addition, the α-methylenecyclopentanone structure[6] and the dense functionality in the products of this reaction (cf. Table I) make the new pathway a novel and useful synthetic entry to five-membered carbocycles.

Our initial investigations were guided by the regiochemical dichotomy observed for the reaction with cycloadditions of methyl methacrylate and 2-nitro-1-propene. The former exclusively gave a KA cycloadduct,[2] while the latter mainly afforded an EM adduct, as shown in entry 1 of Table I. The new pathway was found to be general for other olefins (Table I) with a reduction potential larger than −1.8 V (SCE),[7] including $C_{60}$ fullerene (−0.42 V).[8] The reaction tolerates variation of the acetal group (**12**, entry 8) and the substituent on the TMM (**1b**, entries 9 and 10). The experimental procedure is simple: heating an equimolar mixture of an MCP and an olefin in an aprotic solvent (e.g., 1 M $CH_3CN$) under nitrogen for several hours gives the cycloadducts in high yield. Lower temperature often (but not always) improves the proportion of the EM adduct (cf. entries 4 and 7). The minor KA product **8** hydrolyzes to the corresponding hydroxyester upon workup[2] and can be easily removed by silica gel chromatography.

The mechanism of the new pathway was investigated first with stereochemical probes, benzyl methyl (*E*)- (*Z*)-methoxymethylenemalonate (**3*E*,*Z***) (Scheme I). The reaction at 80 °C in $CH_3CN$ gave a mixture of EM **7** and KA **8** as a 7:3 mixture. For both **3*E*** and **3*Z***, the EM reaction proceeded with ca. 60–80% retention of the olefin geometry.[9] The extent of the retention of the olefin geometry was 80% at the beginning of the reaction and eroded gradually (cf. entry 5 and supplementary material).

**Table I.** [3 + 2] Cycloaddition Reaction in $CH_3CN$ or $CD_3CN$[a]

| entry | olefin | *t* (°C) | time (h) | yield (%) (EM:KA) | EM |
|---|---|---|---|---|---|
| 1 |  | 70 | 1.5 | 84 (69:31) |  |
| 2 | **11** | 40 | 30 | 90 (>99:1) | **9** |
| 3 |  | 50 | 24 | 68 (83:17) |  |
| 4 |  | 80 | 12 | 84 (62:38) |  |
| | | 40 | 60 | 87 (76:24) | |
| 5 | **3E** | 60 | 0.1 | 8 (71:29) | **8**, c:t = 21:79 |
| | | 80 | 9.5 | 96 (73:27) | c:t = 38:62 |
| 6 | **3Z** | 80 | 6.5 | 97 (70:30) | c:t = 60:40 |
| 7 | **13** | 80 | 0.5 | 88 (44:56) | **14** |
| | | 40 | 8 | 87 (89:11) | |
| 8 | **13** | 40 | 14 | 94 (87:13) |  |
| 9 | **13** | 120 | 4 | 72 (85:15) |  |
| 10 |  | 120 | 2 | 42 (91:9) |  |

[a] MCP **1a** was used except in entries 8, 9, and 10. In entry 8, **12** was used, and **1b** was used in entries 9 and 10.

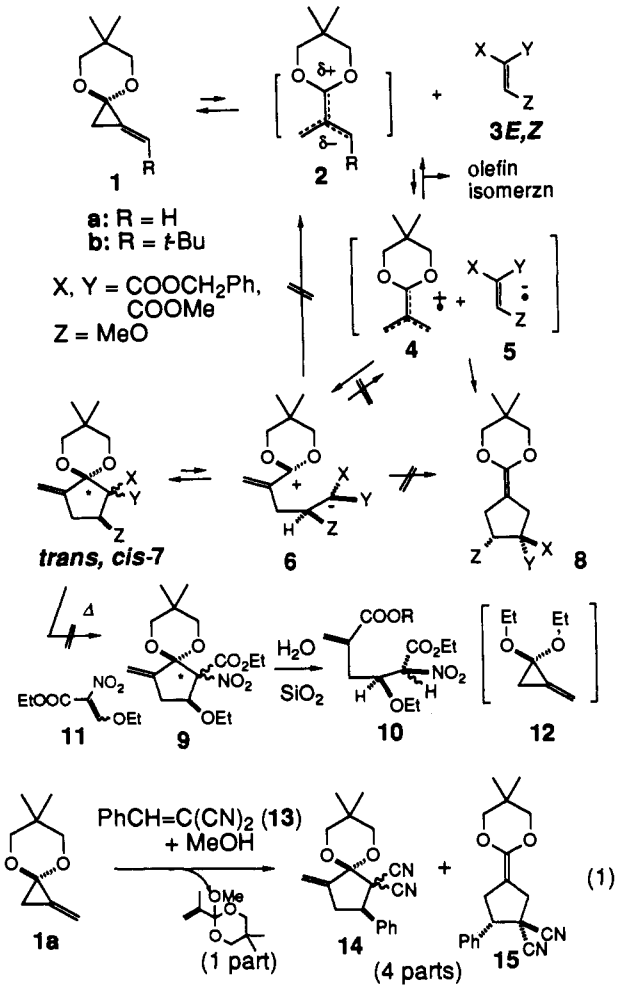
The products, *trans*- and *cis*-**7**, slowly isomerize at 80 °C (final trans/cis ratio = 6:4) via the zwitterion **6** formed by heterolysis of the asterisked C-C bond. The heterolytic lability of this bond is indicated by the fact that the cycloadduct **9** undergoes *hydrolysis of the C-C bond* on wet silica gel at room temperature to give **10**. The reversible formation of **6** does not lead further to global cycloreversion, as shown by the fact that thermolysis of a mixture of **7** and an extremely electrophilic olefin **11** does not produce the cross-over product **9**. Interestingly, thermolysis of **7** did not produce any trace of the KA **8**,[10] indicating that **6** is not an intermediate to **8**.

We have observed that the starting olefins **3*E*** and **3*Z***, which are thermally stable by themselves, isomerize slowly in the course of cycloaddition (cf. supplementary material). This result, combined with the fact that the global cycloreversion did not take place, indicates that an SET process is involved as the initial step of the EM-forming pathway leading first to **6**. In addition, some additional results discount other alternative mechanisms (vide infra). First, we found that, through competition[11] between benzylidenemalononitrile **13** and a proton source (MeOH or AcOH), the cycloaddition is faster than protonation of **2a** (eq 1).

(1) Nakamura, E.; Yamago, S.; Ejiri, S.; Dorigo, A. E.; Morokuma, K. *J. Am. Chem. Soc.* **1991**, *113*, 3183.
(2) Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1989**, *111*, 7285. Cf.: Yamago, S.; Nakamura, E. *J. Org. Chem.* **1990**, *55*, 5553.
(3) Ejiri, S.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 8707. See also: Berson, J. A. *Acc. Chem. Res.* **1978**, *11*, 446.
(4) Reviews on 1,3-dipolar addition: Huisgen, R. In *Advances in Cycloaddition*, Curran, D. P., Ed.; JAI Press: Greenwich, CT, 1988; Vol. 1, p 1. Padwa, A. *1,3-Dipolar Cycloaddition Chemistry*; John Wiley & Sons: New York, 1984; Vols. 1 and 2. Little, R. D. *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 239–270.
(5) Discussions on the possibility of intervention of electron transfer in the following cycloadditions (a) Diels–Alder reaction: Kiselev, V. D.; Miller, J. G. *J. Am. Chem. Soc.* **1975**, *97*, 4036. Fukuzumi, S.; Kochi, J. K. *Tetrahedron* **1982**, *38*, 1035. Sustmann, R.; Korth, H.-G.; Nüchter, U.; Siangouri-Feulner, I.; Sicking, W. *Chem. Ber.* **124**, *1991*, 2811 and references therein. (b) [3 + 2] cycloaddition: Boger, D. L.; Brotherton, C. E. In *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI Press: Greenwich, CT 1990; Vol. 2, p 147.
(6) Cf. Scarborough, R. M., Jr.; Toder, B. H.; Smith, A. B., III *J. Am. Chem. Soc.* **1980**, *102*, 3904 and references therein.
(7) (a) The reduction potential of methyl crotonate is −2.33 V (vs. SCE), cf.: House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59. (b) We thank Prof. T. Fuchigami for assistance in the measurement of reduction potentials.
(8) Prato, M.; Suzuki, T.; Foroudian, H.; Li, Q.; Khemani, K.; Wudl, F.; Leonetti, J.; Little, R. D.; White, T.; Rickborn, B.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 1594.
(9) The KA formation was 100% stereospecific.
(10) The closure to **8** is a 5-endo-trig cyclization.
(11) Cf.: Little, R. D.; Brown, L. M.; Masjedizadeh, M. R. *J. Am. Chem. Soc.* **1992**, *114*, 3071.

0002-7863/93/1515-5344$04.00/0 

**Scheme I**




It may be noted that excess methanol or acetic acid rapidly protonates the TMM **2a** much faster than the ring closure from **2a** to **1a**.[1] Thus, the reaction of **1a** with a mixture of 1 equiv each of **13** and MeOH in $CD_3CN$ at 40 °C gave **14** and **15** in 58% and 8% yield, respectively, with recovery of MeOH (by $^1H$ NMR). The relative rate of the cycloaddition and the protonation was about 4:1. Notably, the cycloaddition pathway also predominated over protonation by acetic acid (1 equiv).

Second, the cycloaddition reaction was not much affected by the presence of molecular oxygen. Thus, **1a** reacted with **13** in oxygen-saturated $CD_3CN$ to give **14** (67%) and **15** (23%), and no products due to oxygen trapping[1] of **2a** formed. Finally, the presence of a radical trap (TEMPO, 1 equiv) did not affect the reaction.

The mechanistic proposal for the EM pathway shown in Scheme I is fully consistent with the above experimental results. The partial loss of the olefin geometry rules out the possibility of [4π + 2π] concerted cycloaddition. The oxygen and TEMPO probes indicate that free radicals are not involved along the reaction pathway. The cycloaddition/protonation competition rules out a two-electron Michael addition mechanism at a route to **6**, and, instead, gives full support to the SET mechanism.[12] In this mechanism, the radical ion pair **4**/**5** undergoes rapid coupling without diffusion of the radical ions (lack of oxygen effects),[13a] and back electron transfer within the solvent cage causes isomerization of the olefins **3**. Steric congestion allows **6** to undergo bond rotation before ring closure to **7**.

In summary, the singlet TMM **2** undergoes [3 + 2] cycloaddition with highly electron-deficient olefins through a SET process, showing very little character of zwitterionic or biradical species.[14]

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**Supplementary Material Available:** Experimental details for the cycloaddition and time-dependent analysis of the reaction of **3*E*,*Z*** (14 pages). Ordering information is given on any current masthead page.

(12) A single electron transfer reaction is generally much more facile than a reaction involving two-electron orbital interactions that necessitates the change of atomic geometry.

(13) (a) Miyashi, T.; Kamata, M.; Mukai, T. *J. Am. Chem. Soc.* **1987**, *109*, 2780. (b) We thank a referee for suggesting the oxygen probe.

(14) Financial support from Tokuyama Science Foundation is gratefully acknowledged.