

## 2-Carbomethoxy-1,3-butadiene: an electronically activated diene in [4 + 2] cycloadditions with electron-deficient dienophiles

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Cross Diels–Alder reactions between 2-carbomethoxy-1,3-butadiene **1** and electron-rich dienes were carried out. It was found that diene **1** had a higher reactivity than even the well-known Danishefsky diene in its Diels–Alder cycloaddition with electron-deficient dienophiles. In addition, (*Z*)-1-methylthio-3-carbomethoxy-1,3-butadiene **11** was found to have a higher reactivity than (*Z*)-1-methylthio-1,3-butadiene and (*Z*)-2-carbomethoxy-1,3-hexadiene, while both (*E*)- and (*Z*)-1,2-(bis)-carbomethoxy-1,3-butadiene **14** reacted efficiently with maleic anhydride to give the corresponding cycloadduct **15**.

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Nous avons effectué des réactions de Diels–Alder croisées entre le 2-carbomethoxy-1,3-butadiène **1** et des diènes riches en électrons. Les résultats obtenus indiquent que **1** est plus réactif que le diène de Danishefsky, dans les cycloadditions avec des diénophiles pauvres en électrons. De plus, le (*Z*)-1-méthylthio-3-carbomethoxy-1,3-butadiène **11** a montré une plus grande réactivité que le (*Z*)-1-méthylthio-1,3-butadiène et (*Z*)-2-carbomethoxy-1,3-hexadiène tandis que le (*E*)- et (*Z*)-1,2-(bis)-carbomethoxy-1,3-butadiène **14** ont réagi avec l'anhydride maléique pour donner le produit de cycloaddition **15**.

The facile dimerization of 2-carbomethoxy-1,3-butadiene **1** to give dimethyl mikanecate **4** has been known for some time (Scheme 1) (1, 2). Although the unusual ease with which this [4+2] cycloaddition takes place has been noted, a rationalization of this phenomenon has yet to be offered. A recent communication by Jung and Zimmerman provided the first kinetic data on this dimerization (3). They proposed that the high dienophilic character of the C1—C2 bond in **1** and the possibility that **1** may be more stable in its *E*-(*s-cis*) conformation could be major factors in accelerating this Diels–Alder reaction. We provide evidence herein that another electronic factor plays a significant role in the rate acceleration of this dimerization and that in fact **1** should be regarded as an electronically activated diene.

A 96% yield of dimer **4** was obtained by heating sulfolene **2** at 110°C (Scheme 1, method A) (**1a**) or by treating allylic bromide **3** with base at 25°C (Method B) (**1b**). However, in the presence of the electron-rich diene **5a** (Y = Me) (**4**) and the very reactive diene **5b** (Y = OMe) (**4b**), either method led to a mixture of dimer **4** and cross cycloadduct **6** (Table 1). In most cases, the dimerization product prevailed unless a large excess of the electron-rich diene was used. Note that the lower temperature seems to favor dimerization over cross-cycloaddition (entries 3, 4, 5, and 8). These results indicate that diene **1**, as a dienophile, cycloadds more rapidly to itself, an electron-deficient diene, than it does to the electron-rich dienes **5a** and **5b**. Note that the reactivity of diene **1** is underestimated here since diene **1** is generated slowly (3–4 h) and must be at low concentration relative to the other diene.

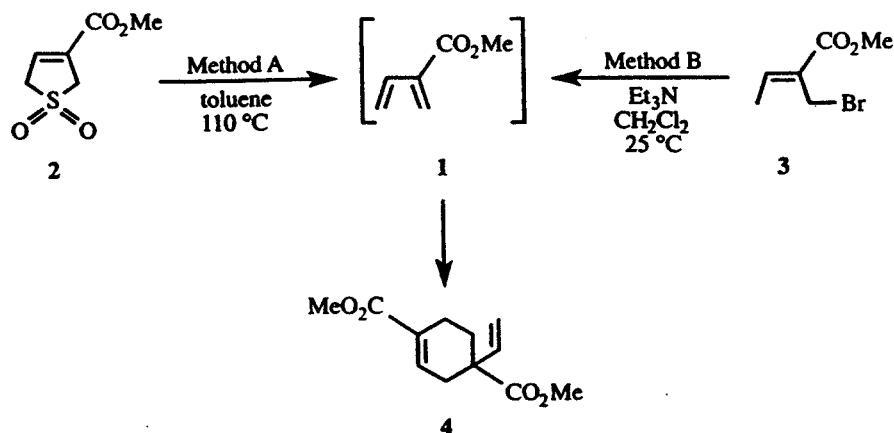
We ruled out the possibility of a local concentration effect, where molecules of diene **1** would dimerize faster because they were generated in proximity to one another, by stirring 1 equivalent each of sulfolene **2** and diene **5b** with

excess methyl acrylate (10 equiv.) in refluxing toluene (Scheme 2). After 4 h, diene **1** had reacted completely to give **7** and Danishefsky's diene **5b** had reacted to the extent of 93% to give adduct **8** (gc analysis). Also detected were **6b** (<5%) and **4** (traces). Control experiments in which each diene was reacted separately with excess methyl acrylate confirmed that diene **1** reacted more rapidly with methyl acrylate than did Danishefsky's diene **5b**. We believe that diene **1** reacted as soon as it was generated since it (or dimer **4**) was not detected in significant amount throughout the reaction (the extrusion of SO<sub>2</sub> in **2** takes ~4 h). The reaction of **3** and **5b** with methyl acrylate (10 equiv.) at 25°C following method B gave mostly dimer **4** (73%), adduct **7** (8%), and **6b** (7%) (yields based on **3**). Diene **5b** did not react at all with methyl acrylate under those conditions. The ethyl ester analog of **1** reacts as a dienophile with cyclopentadiene (excess) at 25°C in quantitative yield (**5**). As a diene, **1** is more reactive than **5b** toward both methyl acrylate and itself. It also appears to be less reactive than cyclopentadiene. As a dienophile, **1** is more reactive than methyl acrylate towards both itself and **5b**. We believe that this increased dienophilicity is due to a strong polarization of the C1—C2 double bond in **1**, as suggested by Jung and Zimmerman (3).

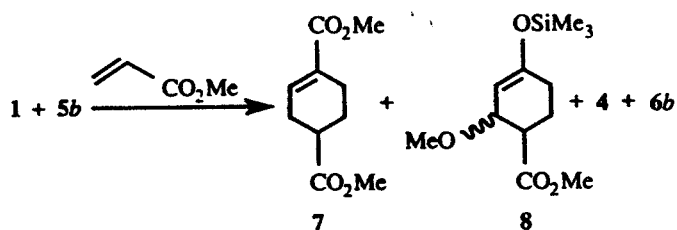
The regiochemistry of the dimer **4** (>97%) cannot be accounted for by any reasonable ionic pathway. Also, we repeated the dimerization of **1** from **2** or **3** and its cycloaddition with methyl acrylate in the absence of light and in the presence of 2,6-di-*tert*-butylphenol or hydroquinone with no effect on the rate of reaction. The above reactions thus appear to be proceeding via a normal thermal [4+2] cycloaddition mechanism.

We then prepared compounds **11** and **14** to examine the effect of an electron-donating or -withdrawing group at an end position on the reactivity of diene **1** (Schemes 3 and 4). Dihydrothiophene **9** was prepared from methyl acrylate following the method of Belleau and co-workers (**6a**). After

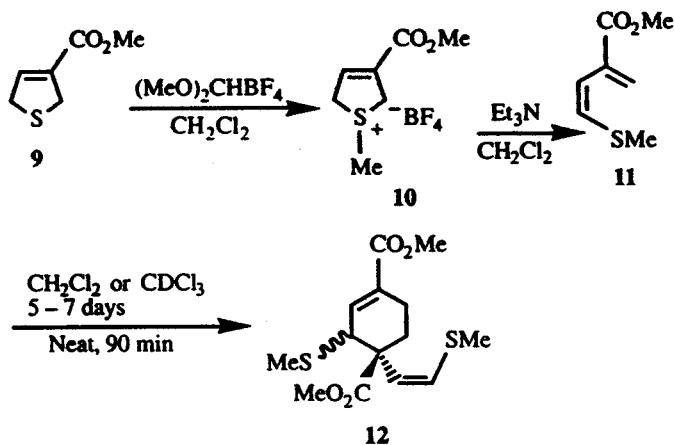
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SCHEME 1



SCHEME 2



SCHEME 3

methylation with Borch's salt (7), the resulting sulfonium salt **10** underwent an elimination reaction with triethylamine at 25°C to yield the (*Z*)-enethiol ether **11**. Upon standing at 25°C in solvent, **11** dimerized to give a 9:1 mixture of stereoisomeric **12** in 5–7 days. However, when concentrated, **11** dimerized in 90 min in 89% yield. The <sup>1</sup>H nmr spectra of both isomers of **12** were consistent with (*Z*)-enethiol ether structures, indicative of a concerted cycloaddition mechanism. The slower dimerization of **11** compared to **1** is probably due to the severe steric interactions in the former when it adopts a *cisoid* conformation. Clearly the 2-carbomethoxy group activates **11** toward dimerization since the known (*Z*)-1-methylthio-1,3-butadiene does not undergo Diels–Alder reactions (8). However, the sulfur also plays an activating role since the carbon analog of **11**, (*Z*)-1-ethyl-2-carbomethoxy-1,3-butadiene, does not dimerize readily (9).

Finally, the dianion of sulfolene **2** was acylated with methyl chloroformate to give a 78% yield of **13** (10). Upon heating in toluene for 12 h, **13** underwent a sigmatropic elimination of SO<sub>2</sub> to afford the stable, but volatile, diene **14** as a 1:1 mixture of *E* and *Z* isomers. Heating **13** for 12 h in toluene containing maleic anhydride gave 87% of two isomeric cycloadducts **15** in a near 1:1 ratio, along with a small amount of unreacted (*E*)-**14**. Compound **15** undergoes a retro-Diels–Alder reaction upon chromatography on silica gel, to give back **14** and maleic anhydride. The ease of cycloaddition of **14**, especially the *E* isomer, with maleic anhydride is noteworthy. Studies to better assess the reactivities of **11** and **14** are underway and will be reported in a more detailed article in due course.

The above results cannot be reconciled with Frontier Molecular Orbital (FMO) theory arguments (11). Indeed, the HOMO of dienes like **1** have been shown to be of lower energy than that of 1,3-butadiene itself by approximately 0.2 eV (12). The results from the cross-cycloaddition experiments between **1** and Danishefsky's diene indicate that the high dienophilic character of **1** is not the sole factor in accelerating its dimerization and therefore the high eneophilic character of **1** must also play a role. Butadienes with other electron-withdrawing groups at C2 have also been shown to dimerize readily (6, 13) and it is likely that they, and dienes **11** and **14**, are all activated in a similar way. Importantly, studies on the dimerization of 2-cyano-1,3-butadiene and its cycloaddition reactions with electron-deficient dienophiles indicate that it has a comparable reactivity to **1** (13). 2-Cyano-1,3-butadiene is more stable in its (*Z*)-(*s-trans*) conformation relative to less eneophilic dienes such as 2,3-dimethyl-1,3-butadiene.<sup>2</sup> This suggests that it, and diene **1**, owe their eneophilicity to a factor other than an enhanced population of the *s-cis* conformation.

We therefore conclude that an electronic factor is activating diene **1** with respect to thermal [4 + 2] cycloadditions

<sup>2</sup>The ethyl ester analog of **1** dimerizes (90% yield) when generated in the presence of an excess of 2,3-dimethyl-1,3-butadiene (see ref. 5). Molecular Mechanics calculations using CSC Chem 3D plus™ software showed that while diene **1** was found to have a preferred (*E*)-(*s-cis*) conformation approximately 1.5 kcal/mol lowest in energy, 2-cyano-1,3-butadiene and 2,3-dimethyl-1,3-butadiene were more stable in their (*s-trans*) conformation by about 1 kcal/mol and 0.4 kcal/mol, respectively.

TABLE 1. Cross Diels–Alder reaction between diene 1 and electron-rich dienes



Entry	Y	Diene (Equiv.) <sup>a</sup>	Method <sup>b</sup>	Ratio 4:6 <sup>c</sup>	Combined yield of adducts (%) <sup>d</sup>
1	Me	5a (1)	A	2:1 <sup>e</sup>	95
2	Me	5a (5)	A	1:4 <sup>e</sup>	95
3	Me	5a (1)	B	9:1 <sup>f</sup>	94
4	Me	5a (5)	B	3:1 <sup>f</sup>	93
5	Me	5a (>5)	B <sup>g</sup>	2:1 <sup>f</sup>	98
6	OMe	5b (1)	A	1:2 <sup>e</sup>	89
7	OMe	5b (5)	A	1:9 <sup>f</sup>	80
8	OMe	5b (1)	B	3:1 <sup>f</sup>	80

<sup>a</sup>Molar equivalents with respect to 2 or 3.

<sup>b</sup>Method A: toluene, reflux; method B: Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, r.t.

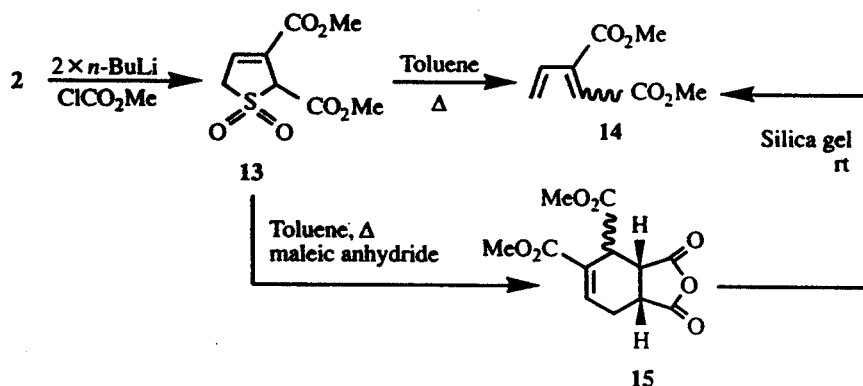
<sup>c</sup>Adducts 6a and 6b were isolated as the hydrolyzed product after chromatography on silica gel.

<sup>d</sup>Isolated yields based on 2 or 3 after chromatography.

<sup>e</sup>Ratios of isolated adducts.

<sup>f</sup>Ratios determined by <sup>1</sup>H nmr integrations of crude mixture.

<sup>g</sup>Slow addition of 3 over 12 h.



SCHEME 4

with electron-deficient dienophiles. Although we cannot draw conclusions, from our present studies, about the nature of this electronic effect, one possibility is that the cycloadditions of 1 with dienophiles proceed via a transition state (TS) having a high double-bond character between C2 and C3, such as was calculated for the reaction of butadiene with ethylene by Hehre and co-workers (14a) and Bach *et al.* (14b). Such a transition state could be stabilized due to conjugation with the ester group at C2. It is conceivable that the activation energy of such cycloadditions (from a cross-conjugated six-atom  $\pi$ -system in the starting diene to a conjugated four-atom  $\pi$ -system in the TS) may be lower than that of other cycloadditions involving dienes without a C2-conjugating group or other stabilizing effects (from a conjugated four-atom  $\pi$ -system in the starting diene to a non-conjugated two-atom  $\pi$ -system in the TS).

In any case, we have provided evidence that an elec-

tronic factor, at present unknown, is responsible for the activation of 2-carbomethoxy-1,3-butadiene. We believe that the above results could have far-reaching consequences for the theoretical aspect of the Diels–Alder reaction. We are initiating ab initio calculations of dienes like 1, as well as extending the present studies to include other dienes, to gain a better understanding of the fundamental principles underlying their reactivity.

#### Acknowledgements

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- (a) J.M. McIntosh and R.A. Sieler. *J. Org. Chem.* **43**, 4431 (1978); (b) H.M.R. Hoffmann and J. Rabe. *Angew. Chem. Int. Ed. Engl.* **22**, 795 (1983).

2. W. Poly, D. Schomburg, and H.M.R. Hoffmann. *J. Org. Chem.* **53**, 3701 (1987); L.K. Sydnos, L. Skattebøl, C.B. Chapleo, D.G. Leppard, K.L. Svanholt, and A.S. Dreiding. *Helv. Chim. Acta*, **58**, 2061 (1975); O. Goldberg and A.S. Dreiding. *Helv. Chim. Acta*, **59**, 1904 (1976); A.I.D. Alanine, C.W.G. Fishwick, A.D. Jones, and M.B. Mitchell. *Tetrahedron Lett.* **30**, 5653 (1989).
3. M.E. Jung and C.N. Zimmerman. *J. Am. Chem. Soc.* **113**, 7813 (1991).
4. (a) H.-J. Liu, T.K. Ngooi, and E.N.C. Browne. *Can. J. Chem.* **66**, 3143 (1988); (b) S. Danishefsky and T. Kitahara. *J. Am. Chem. Soc.* **96**, 7807 (1974).
5. D. Martina and F. Brion. *Tetrahedron Lett.* **23**, 865 (1982).
6. (a) J.F. Honek, M.L. Mancini, and B. Belleau. *Synth. Commun.* **14**, 483 (1984); (b) M. Franck-Neumann, D. Martina, and M.-P. Heitz. *J. Organomet. Chem.* **301**, 61 (1986); T.-s. Chou and S.-C. Hung. *J. Org. Chem.* **53**, 3020 (1988); (c) M. Franck-Neumann, D. Martina, and F. Brion. *Angew. Chem. Int. Ed. Engl.* **20**, 864 (1981).
7. R.F. Borch. *J. Org. Chem.* **34**, 627 (1969).
8. R.L. Crumbie and D.D. Ridley. *Aust. J. Chem.* **34**, 1017 (1981).
9. H. Düttmann and P. Weyertahl. *Chem. Ber.* **112**, 3480 (1979).
10. T.-s. Chou, C.-Y. Tsai, and L.-J. Huang. *J. Org. Chem.* **55**, 5410 (1990).
11. I. Fleming. *In Frontier orbitals and organic chemical reactions*. Wiley & Sons, New York, 1976. p. 110 and references therein.
12. K.N. Houk. *J. Am. Chem. Soc.* **95**, 4092 (1973).
13. P.G. Baraldi, A. Barco, S. Benetti, S. Manfredini, G.P. Pollini, D. Simoni, and V. Zanirato. *Tetrahedron*, **44**, 6451 (1988).
14. (a) R.E. Townshend, G. Ramunni, G. Segal, W.J. Hehre, and L. Salem. *J. Am. Chem. Soc.* **98**, 2190 (1976); (b) R.D. Bach, J.J.W. McDouall, H.B. Schlegel, and G.J. Wolber. *J. Org. Chem.* **54**, 2931 (1989).