Synthesis and [2 + 2] Cycloaddition of Dimethyleneketene Acetals. Reaction with C_{60} and Facile Hydrolysis of the C–C Bond Connected to C_{60}

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The enolate of cyclopropanecarboxylic acid and its derivatives is an important building block for organic synthesis.[1] However, the strained methylenecyclopropane structure of the enolate renders this species not only difficult to prepare[2] but also unstable, making it rather exist in its α-metallo carbonyl tautomeric form.[3] Hence, information on this enolate remains scarce and its utility unexplored. We report here that the *O*-alkylated enolates of cyclopropanecarboxylates (dimethyleneketene acetals **3**) can be prepared from readily available precursors **1**, and that they are extremely reactive, serving as useful surrogates of the elusive parent enolates (Scheme 1). Their utility is illustrated by the [2 + 2] cycloaddition to electron-deficient olefins, which, after hydrolytic workup, gives rise to the Michael addition products **8**: a type of reaction product previously unavailable. We also found that **3** reacts smoothly with C_{60} to give the [2 + 2] adduct **5** and, most remarkably, that the asterisked C–C σ bond in **5** directly connected to the fullerene core is hydrolytically unstable and can be quantitatively cleaved with aqueous acid.

Thermolysis of the readily available methylenecyclopropane **1**[4] at 150 °C for 4 h in toluene (or 1,2-dichlorobenzene) produces the ketene acetal **3** in 60–80% yield. Since mild thermolysis of **1** (40–80 °C) reversibly generates a dipolar trimethylenemethane **2**,[5] the formation of **3** at higher temperature must be due to an alternative ring closure of **2**.[6] While **3** is hydrolytically unstable, it can be characterized by its olefinic carbon signals at δ 76.83 and 148.40 ppm in the reaction carried out in C_6D_6 and by isolation of the corresponding ester **4a** (63% yield) after aqueous workup. The rearrangement of the substituted methylenecyclopropanes **1b** and **1c** (150 °C for 6–8 h) gave the corresponding ketene acetals **3b** and **3c**, which were hydrolyzed to **4b** and **4c** in 69% (66% cis) and 78% yields (87% cis), respectively.[7]

Next, we describe the thermal [2 + 2] cycloaddition of **3** with C_{60}, which proceeded with remarkable ease. Thus, upon mixing 0.4 mL of a toluene solution of **3a** (2.2 equiv) with 150 mL of a toluene solution of C_{60} (50 mg, 0.069 mmol) at room temperature for 20 h, the cyclobutane product **5** formed in 67% isolated yield and 25% of C_{60} was recovered. The sp^3 carbon signals of the C_{60} core in **5** appeared at δ 68.23 and 80.50 ppm, and the ^1H and ^{13}C NMR spectra revealed the C_s symmetry of the molecule, indicating

Scheme 1

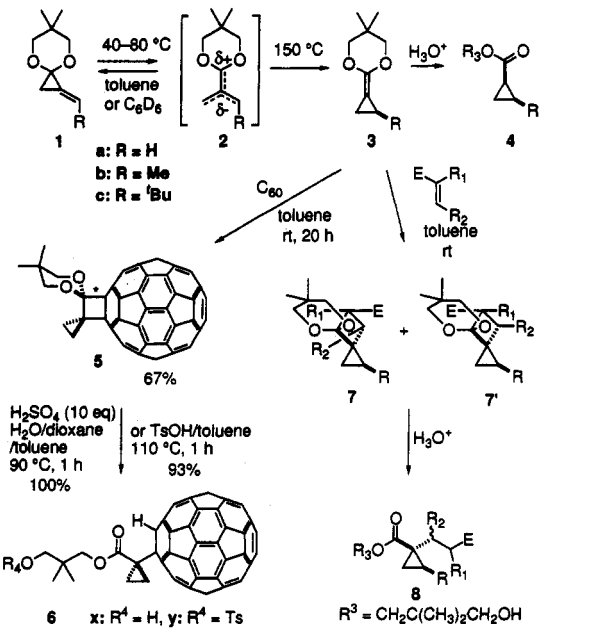
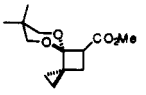
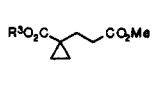
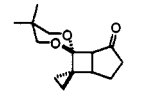
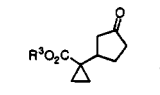
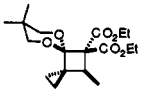
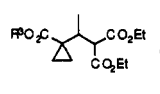
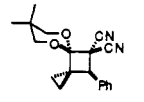
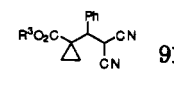
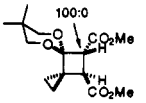
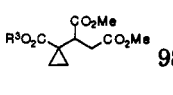
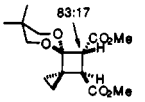
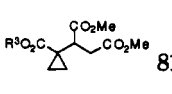
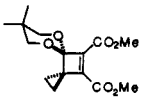
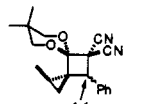
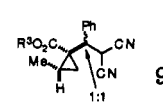


Table 1. [2 + 2] Cycloaddition of Dimethyleneketene Acetal with Olefins[a]

entry	3[b]	olefin	time (h)	7	8	%yield[c]
1	**3a**		12			54
2	**3a**		23			56
3	**3a**		7			94
4	**3a**		2			91
5	**3a**		1			98
6	**3a**		3			81
7	**3a**		4			54
8	**3b**		4			91

[a] The reaction was carried out at room temperature in toluene or C_6D_6 except for entries 2 and 5–7, where it was carried out at 40 °C. The cycloadducts **7** were fully characterized only for entry 7. [b] The ketene acetal **3** was prepared from 2 equiv of **1**, which generates approximately 1.2 equiv of **3** for the acceptor. [c] Isolated yield of **8**, which is based on olefin.

that the reaction took place on the 6,6-juncture.[8,9] The success of the cycloaddition crucially depends on the strain in **3**, since a

(1) For reviews, see: Paquette, L. A. *Chem. Rev.* **1986**, *86*, 733. Reissig, H.-U. In *The Chemistry of Cyclopropane Group*; Rappoport, Z., Ed.; John Wiley & Sons: Chichester, 1987; Vol. 1, pp 375–443.

(2) (a) Reissig, H.-U.; Böhm, I. *J. Am. Chem. Soc.* **1982**, *104*, 1735. (b) Paquette, L. A.; Blankenship, C.; Wells, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 6442. (c) Häner, R.; Maetzke, T.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1655 and references therein.

(3) Boche, G.; Harms, K.; Marsch, M. *J. Am. Chem. Soc.* **1988**, *110*, 6925.

(4) The two-step sequence proceeds in >70% yield on a 50-g scale: Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1989**, *111*, 7285. Yamago, S.; Nakamura, E. *Org. Synth.*, submitted for publication.

(5) Nakamura, E.; Yamago, S.; Ejiri, S.; Dorigo, A. E.; Morokuma, K. *J. Am. Chem. Soc.* **1991**, *113*, 3183.

(6) While the extremely high reactivity of **2** so far precluded detailed investigations, the formation of **3** appears to be irreversible (see supplementary material).

(7) Difference NOE experiments for **4c** indicated the cis stereochemistry between the ^{t}Bu and the ester groups. The stereochemistry of **4b** was determined by analogy.

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nonstrained equivalent of **3**, the *O*-trimethylsilyl ketene acetal of methyl isobutyrate, did not react at all with C_{60} even under a pressure of 9 kbar.

The cycloadduct was thermally stable and showed no sign of cycloreversion upon heating at 100 °C in the presence of dimethyl fumarate as a trapping agent of **3** (vide infra). In contrast, under acidic conditions, *hydrolysis of the asterisked C–C σ bond* of the cyclobutane ring took place instead of the expected acetal hydrolysis. Thus, heating of **5d** with 10 equiv of H_2SO_4 and 100 equiv of H_2O in a 1:1 1,4-dioxane/toluene mixture at 90 °C for 1 h afforded **6x** in quantitative yield.[10] We also obtained the *p*-toluenesulfonate ester **6y** (93%) upon heating **5d** with 10 equiv of *p*-toluenesulfonic acid in refluxing toluene for 1 h. While the mechanism of this intriguing reaction awaits further studies, it can be envisaged that the cleavage is caused either by direct protonation of the C–C σ bond or by that of an adjacent C_{60} π bond. In view of chemical modifications of fullerene-containing molecules[11] as well as their chemical and biochemical use,[12,13] the novel fullerene-substituted cyclopropanes **6** would prove to be interesting molecules for future studies.

The ketene acetal **3** also reacts smoothly with electron-deficient olefins to give the Michael adducts **8**. Thus, a mixture of **3a** and methyl acrylate in C_6D_6 at room temperature for 12 h gave initially the cyclobutane **7a**, which then afforded the cyclopropanecarboxylic ester **8a** in 54% yield upon aqueous workup (Table 1, entry 1). The cycloadducts **7a** were hydrolytically unstable and could only be characterized by NMR, except in the case of the **3a**/acetylene adduct in entry 7, which was stable and fully characterizable. The Michael addition reaction was found to be quite general for various electron-deficient olefins as shown in Table 1. Unlike the protonation (vide supra), the cycloaddition of **3b** took place stereoselectively from the less hindered face to give **7b** and **7'b** (entry 8).[14]

The reaction of **3a** and dimethyl fumarate and maleate indicated that the [2 + 2] cycloaddition proceeds in a stepwise manner.[15] Thus, while the former reaction took place stereospecifically (entry 5), the latter gave a 63:37 cis/trans mixture of adduct (15 min, 40 °C, 19% yield). Upon further heating (entry 6), the isomeric ratio changed further (17:83 cis/trans mixture after heating at 40 °C for 3 h, 81%), suggesting that there is also a reversible opening of the cyclobutane ring upon thermolysis.

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Supplementary Material Available: Experimental data for the reactions in Scheme 1 and in Table 1 (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(8) Hoke, S. H., II; Molstad, J.; Dilettato, D.; Jay, M. J.; Carlson, D.; Kahr, B.; Cooks, R. G. *J. Org. Chem.* **1992**, *57*, 5069. Prato, M.; Lucchini, V. *J. Org. Chem.* **1993**, *58*, 3613. Wilson, S. R.; Kaprinidis, N.; Wu, Y.; Schuster, D. I. *J. Am. Chem. Soc.* **1993**, *115*, 8495.

(9) The cycloaddition could have proceeded in a [4 + 2] manner which would, however, gave a highly strained adduct (see supplementary material).

(10) The ^{13}C NMR resonances of protonated and alkylated C_{60} carbons appeared at δ 61.26 ($^1J_{CH}$ = 138.3) and 65.41 ($^2J_{CH}$ = 7.6 Hz) ppm, respectively.

(11) (a) Yamago, S.; Tokuyama, H.; Nakamura, E.; Prato, M.; Wudl, F. *J. Org. Chem.* **1993**, *58*, 4796. (b) An, Y.-Z.; Anderson, J. L.; Rubin, Y. *J. Org. Chem.* **1993**, *58*, 4799.

(12) Sijbesma, R.; Srdanov, G.; Wudl, F.; Castoro, J. A.; Wilkins, C.; Friedman, S. H.; DeCamp, D. L.; Kenyon, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 6505. Schinazi, R. F.; Sijbesma, R.; Srdanov, G.; Hill, C. L.; Wudl, F. *Antimicrob. Agents Chemother.* **1993**, *37*, 1707.

(13) Tokuyama, H.; Yamago, S.; Nakamura, E.; Shiraki, T.; Sugiura, Y. *J. Am. Chem. Soc.* **1993**, *115*, 7918.

(14) NOE experiments for **8** indicated the cis stereochemistry between the methyl and the ester groups.

(15) Baldwin, J. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon Press: Oxford, 1991; Vol. 5, pp 63–84.