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Synthesis of dicarboxylic acid derivatives of [60]fullerene using Diels–Alder reaction with bis(methylene)butanedioates

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Abstract

3-Sulfolene-3,4-dicarboxylates effective for generation of bis(methylene)butanedioates were applied to [4+2] cycloaddition reaction of C_{60} to give fullerocyclohexenedicarboxylates, among which a *t*-butyl ester was hydrolyzed to a dicarboxylic acid derivative, useful for further conversion into its anhydride and half-esters. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: [60]fullerene; 3-sulfolene; Diels–Alder reaction; dicarboxylic acid; anhydride.

Surface modification of fullerenes is an attractive approach in materials science and pharmaceutical applications,[1] and a wide variety of functionalized derivatives have been prepared especially using C_{60}.[2] The cycloaddition reaction is now recognized as the most promising protocol for such functionalization, because the number of addends is controlled with relative ease, and the addition site is limited to the 6,6 junction. Based on these merits, we have continuously reported [4+2] and [3+2] cycloadditions to the double bond of C_{60},[3] and our recent effort revealed that a prototypical tetrahydrothiophene-fused C_{60} could be obtained with a thiocarbonyl ylide.[4] The C_{60} derivative having two functional groups is believed to be advantageous for effective use, for example, for cyclization,[5] polymerization,[6] and the evolution of characteristic supramolecular systems.[7] In this sense, functionalization with two carboxyl groups is representative.[8] We envisaged that synthesis of a dicarboxylic acid derivative of C_{60} such as **6** can be achieved by exploiting the above thiocarbonyl ylide; a feasible four-step route includes: (1) 1,3-dipolar cycloaddition reaction of the ylide with acetylenedicarboxylates; (2) oxidation of the cycloadduct to 3-sulfolenes, (3) Diels–Alder reaction of the 3-sulfolene-3,4-dicarboxylates with C_{60}; and finally, (4) acid-catalyzed hydrolysis of the esters. Reported here are fruitful results we have achieved along this line and the further conversion into an anhydride and half-esters.

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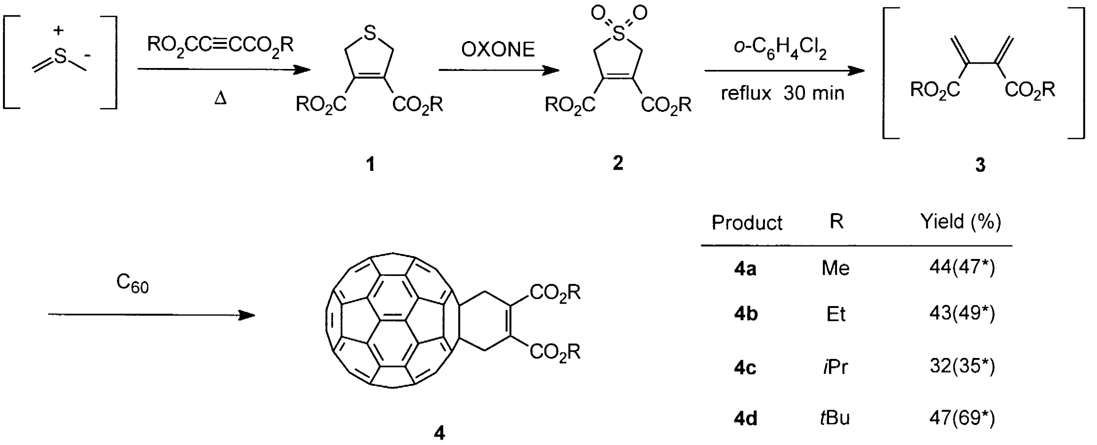
C_{60} has a low LUMO level and prefers to cycloadd with electron-rich 1,3-dienes.[3b] Yet, it was indicated to have adequate reactivity even with electron-deficient dienes, and this feature was utilized for facile introduction of a mono-functionality to C_{60}[3b] and further extension to synthesis of a free monocarboxylic acid derivative.[3c] This strategy can be applied to synthesis of the related dicarboxylic acid derivative with bis(methylene)butanedioates **3**.[9] Previously, we demonstrated that the thermal decomposition of 3-sulfolenes to 1,3-dienes gave Diels–Alder cycloadducts of C_{60} satisfactorily,[3b] and hence, it is reasonable to use this type of reagent as a reaction partner also in the present case.[10] The required 3-sulfolene-3,4-dicarboxylates **2**[11] could be obtained by 1,3-dipolar cycloaddition of the thiocarbonyl ylide with acetylenedicarboxylates[12] followed by OXONE oxidation of the cycloadduct **1** (Scheme 1). Since the model [4+2] cycloaddition reaction of **2a** with typical dienophiles showed that the yields were comparable to or even better than those reported,[11] the aimed cycloaddition reaction with C_{60} was conducted in the same manner. Thus, C_{60} was allowed to react with **2a** (5 equiv.) in *o*-dichlorobenzene at 180°C for 30 min under an argon atmosphere. The reaction occurred smoothly (the color of solution immediately changed from violet to brown), and the product was separated by silica gel chromatography (elution with hexane/toluene 1/1) to give the desired cycloadduct **4a** in 44% yield. The structure was unambiguously elucidated by spectral data; FAB-MS peaks were observed at *m/z* 890 (M^+) and 720 (base), and IR absorption indicated the presence of an ester moiety and a C_{60} core at 1721 and 527 cm^{-1}, respectively. C_{2v} symmetry was confirmed by ^{1}H NMR signals (500 MHz, $CHCl_3/CS_2$ 5/3) at δ 3.95 (s, 6 H) and 4.33 (s, 4 H) and ^{13}C NMR signals (125 MHz, $CDCl_3/CS_2$ 5/3) at δ 65.12 for fused carbons, 135.87–155.28 (17 lines[13]) for sp^2 carbons, and 166.22 for ester carbonyl groups. These facts evidence the usual addition at the 6,6 junction and the rapid flipping of a cyclohexene ring occurring at room temperature.[14] Analogous products **4b–d** were obtained with other 3-sulfolenes **2b–d** (Scheme 1).

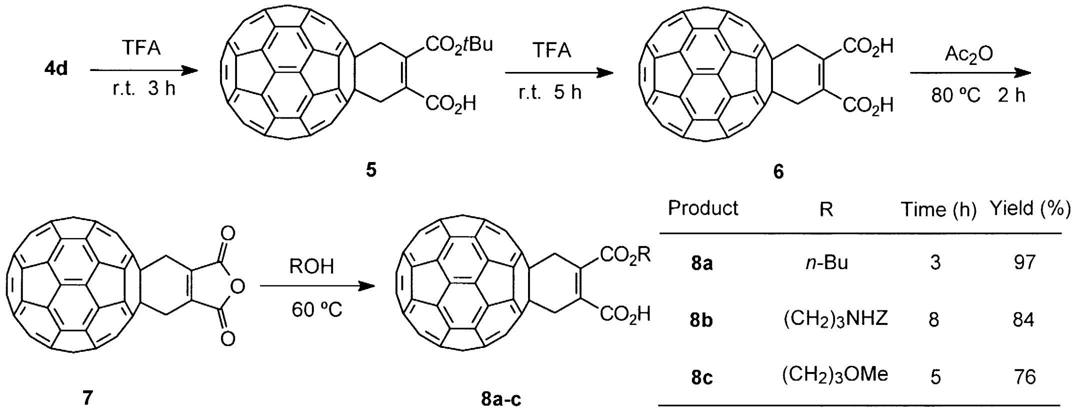


Product	R	Yield (%)
4a	Me	44(47*)
4b	Et	43(49*)
4c	*i*Pr	32(35*)
4d	*t*Bu	47(69*)

* Yield based on consumed C_{60}.

Scheme 1.

Among the cycloadducts obtained here, the *t*-butyl ester is a good candidate for conversion into a free dicarboxylic acid derivative, because its hydrolysis, which occurs quite readily under mild acidic conditions, is desirable particularly in C_{60} chemistry.[3c] In fact, treatment of the ester **4d** (30 mg) with excess trifluoroacetic acid (2 ml) in toluene (20 ml) at room temperature for 3 h afforded half-hydrolyzed product **5** (27 mg) in 96% yield. The expected dicarboxylic acid **6** was successfully obtained in 75% yield by further hydrolysis for another 5 h and purification with chromatography [silica gel, elution with $CHCl_3$/EtOH (5/1)]. The structure was supported by FAB-MS which had the expected M^+ peak at *m/z* 862 together with IR absorptions at 3387, 1701 (COOH) and 527 (C_{60}) cm^{-1}. Although the dicarboxylic acid **6** is slightly soluble in aq. K_2CO_3 as documented in the case of methanofullerenedicarboxylic acid by Hirsch,[8] its extremely low solubility in organic solvents did not allow NMR measurement. Nevertheless, this drawback could be cleared by further transformation of **6** to a soluble anhydride **7** by dehydration with acetic anhydride using a large amount of the reagent (20 equiv.) in dry toluene at 80°C for 2 h (quantitative yield). Again, the structure was shown to have C_{2v} symmetry by NMR patterns similar to those of **4** [^{1}H NMR (500 MHz, $CDCl_3/CS_2$ 4/1) δ 4.55 (s, 4 H); ^{13}C NMR (125 MHz, $CDCl_3/CS_2$ 4/1) δ 65.45 (fused carbons), 135.85–155.44 (17 lines,[15] sp^2 carbons), and 163.02 (C=O)]. Until now, this functionality has not been utilized for surface modification of C_{60}. Thus, the reaction of **7** with alcohol can lead to a functionalized fullerenecarboxylic acid. The anhydride **7** was treated with several alcohols (10 equiv.) in dry toluene at 60°C for 3–8 h and chromatographic separation [silica gel, elution with $CHCl_3$/EtOH (5/1)] gave half-esters **8a–c** in good yields. Particularly, a protected amino acid derivative of C_{60} such as **8b** was obtainable in this way (Scheme 2).



Product	R	Time (h)	Yield (%)
8a	*n*-Bu	3	97
8b	$(CH_2)_3NHZ$	8	84
8c	$(CH_2)_3OMe$	5	76

Z = $PhCH_2OCO$-

Scheme 2.

In summary, the Diels–Alder reaction of C_{60} with bis(methylene)butanedioate **3** generated by thermal decomposition of 3-sulfolene-3,4-dicarboxylates **2** afforded functionalized C_{60} having double ester groups. Among them, the *t*-butyl ester **4d** was easily hydrolyzed to a dicarboxylic acid derivative of C_{60}, which is useful for a variety of applications. An example is its conversion into an anhydride and half-esters, and our further work with the dicarboxylic acid itself is aimed at realizing some sandwich-type interaction with clays.

Acknowledgements

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9. We have previously prepared a bicyclic diester derivative of C_{60}, but the less simple structure and low yield of this compound prompted us to develop prototypical **4** and **6** (see Ref. 3b).
10. Bis(methylene)butanedioates are reported to be produced by the methods of: (a) retro Diels–Alder reaction of anthracene cycloadduct; (b) pyrolysis of diacetate; (c) ring-opening reaction of cyclobutene; (d) debromination of bis(bromomethyl)maleate; (e) Horner–Emmons condensation of succinate, and (f), (g) metal-promoted coupling and insertion reactions. However, most of these methods do not fully meet the purpose of the present reaction with C_{60}: (a) Tarnchompoo, B.; Thebtaranonth, C.; Thebtaranonth, Y. *Tetrahedron Lett*. **1987**, *28*, 6671. (b) Bailey, W. J.; Hudson, R. L.; Yates, E. T. *J. Org. Chem.* **1963**, *28*, 828. (c) Bellus, D.; Weis, C. D. *Tetrahedron Lett*. **1973**, *12*, 999. (d) Hamon, D. P. G.; Spurr, P. R. *Synthesis* **1981**, 873. (e) Davidson, R. M.; Kenyon, G. L. *J. Org. Chem*. **1977**, *42*, 1030. (f) Semmelhack, M. F.; Helquist, P.; Jones, L. D.; Keller, L.; Mendelson, L.; Ryono, L. S.; Smith, J. G.; Stauffer, R. D. *J. Am. Chem. Soc*. **1981**, *103*, 6460. (g) Kiji, J.; Okano, T.; Fujii, E.; Tsuji, J. *Synthesis* **1997**, 869.
11. Lee, S. J.; Chien, C. J.; Chou, T. S. *Bull. Inst. Chem., Acad. Sin*. **1993**, *40*, 1. Our preparative method for **2** seems to be more convenient than that reported here (seven-step from 3-alkoxycarbonyl-4-keto-tetrahydrothiophene). By our method, [4+2] cycloaddition of **2a** with maleic anhydride and *p*-benzoquinone, which have comparable reactivity with C_{60}, was found to give the corresponding cycloadducts in 55% (lit. 23%^{10b}) and 73% (lit. 72%^{10d}) yields, respectively.
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13. δ 135.87, 138.63, 140.26, 141.72, 142.13, 142.21, 142.67, 143.17, 144.69, 145.06, 145.52, 145.66, 145.80, 146.31, 146.59, 147.72, 155.28.
14. In comparison with bis(methoxycarbonyl)-substituted **4a**, restricted flipping was observed in the bis(phenylsulfonyl)-substituted case (see Ref. 3c).
15. δ 135.85, 141.21, 142.54, 142.77, 142.95, 143.56, 144.02, 145.11, 145.42, 146.41, 146.48, 146.57, 147.19, 147.49, 148.53, 148.64, 155.44. Also observed are FAB-MS [*m/z* 844 (M^+), 720 (base)] and IR (1848, 1774, and 527cm^{-1}).