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Synthesis of Organic Derivatives of Fullerenes

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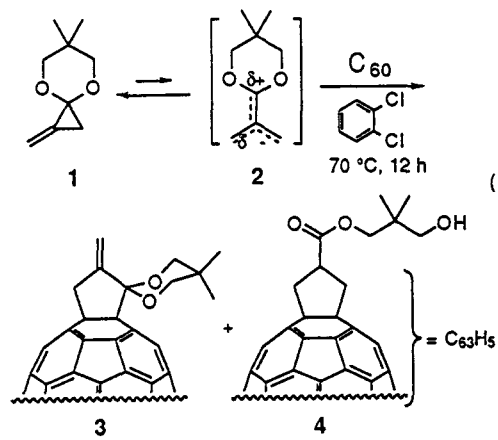
Abstract: A dipolarphilic character of C_{60} was exemplified in the [3 + 2] cycloaddition with a dipolar trimethylenemethane. The functional group of the cycloadduct was transformed without affecting the C_{60} core under weakly basic to strongly acidic conditions.

The unique structure and physical properties of C_{60} have resulted in an outburst of scientific investigation.[1] Much attentions have been focused on the derivatization of C_{60} to design and construct organic substructure on C_{60}.[2] Thus, it is required for the development of new methodologies to achieve the selective modification of C_{60} and its derivatives with and without affecting the C_{60} core. The wealth knowledge on the redox processes and the chemical reactivities disclosed the electrophilic and, hence, dipolarphilic nature of this molecule. We report herein the [3 + 2] cycloaddition of a dipolar trimethylenemethane (TMM) with C_{60},[3] that afford cyclopentanofullerenes with various useful functional groups. Selective transformations of the functional groups under weakly basic to strongly acidic condition are also reported.[4] These findings provide flexible synthetic routes to fullerenes of interests, such as biological active derivatives.[5]

[3 + 2] Cycloaddition[3]

A dipolar TMM (2) is generated by thermolysis of 2,2-dialkoxy-1-methylenecycloparpane (1), which reacts with an electron deficient olefin to afford a five-membered carbocyclic compound.[6] Thus, the methylenecyclopropane 1 was heated overnight in 1,2-dichlorobenzene at 70 ° C in the presence of an equimolar amount of C_{60}. Purification by column chromatography allowed the isolation of two products 3 and 4 in 34 and 27% yield, along with 35% unreacted C_{60} (eq 1).

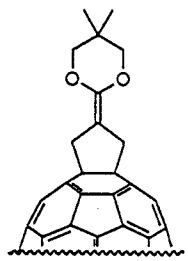


(1)

The α-methylene cyclopentanone acetal 3 has most likely formed *via* a single electron transfer from the TMM to C_{60}.[7] The ^1H NMR spectrum shows a singlet at 4.18 ppm for the CH_2 protons in

the five-membered ring, thus providing evidence for an attack onto the 6-6 (symmetrical) junction on C_{60}. The two vinyl protons resonate at 6.0 and 5.9 ppm as broad singlets whereas the axial and equatrial protons in the dioxane ring appear as an AB quartet (J = 11 Hz) and the methyl groups give two different singlets.

The ester **4** is a product of the silica-gel-catalyzed hydrolysis of the ketene acetal **5**, which is analogous to these formed by the reaction of **2** with acrylic esters.



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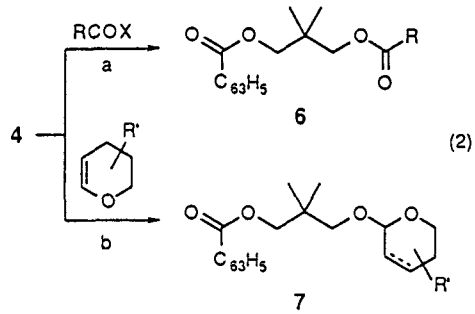
Chemical Derivatization of Organofullerenes[4]

In order to investigate the stability of the C_{60} group against bond forming reaction conditions, we first examined esterification reactions under mildly basic conditions (eq 2a). When the alcohol **4** was treated with a mixture of benzoyl chloride (2 equiv) and pyridine (2 equiv) in toluene at 50 °C for 3 h, the benzoate **6a** was isolated in 62% yield by silica gel chromatography (Table I, entry 1a). The same benzoate could be obtained more conveniently by condensation with benzoic acid (2 equiv) and dicyclohexylcarbodiimide (DCC) (2 equiv) and 4-dimethylaminopyridine (DMAP, 0.2 equiv) in CH_2Cl_2 at room temperature (entry 1b). Similarly, methacrylic ester **6b** was prepared in quantitative yield (entry 2).

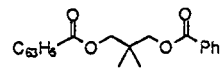
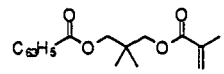
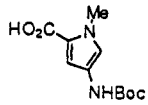
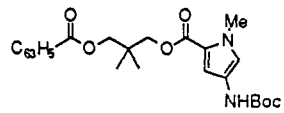
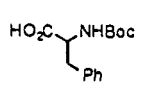
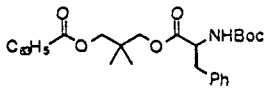
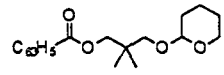
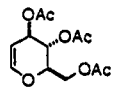
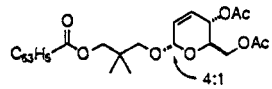
In relation to our interests in the biological activities of fullerenes, we have examined the possibility of connecting the fullerene unit to amino acids. Thus, condensation with the *N*-Boc-protected 4-aminopyrrolecarboxylic acid gave the ester **6c** (entry 3) and that with *N*-Boc-phenylalanine gave the ester **6d** (entry 4). These compounds were found to be stable compounds, offering good prospects for the design and synthesis of biochemical tools based on fullerene chemistry. Throughout the present studies, we have noted that excess reagents were necessary to achieve full conversion of **4** within a reasonable period of time, since low solubility of **4** necessitated the use of a relatively low concentration of reactants (ca. 0.01 M).



C-O bond formation could also be achieved under acidic conditions (eq 2b). For instance, the tetrahydropyranyl ether **7a** was prepared by treatment of **4** with dihydropyran (20 equiv) and *p*-toluenesulfonate (0.2 equiv) in high yield (entry 5). The acidic etherification conditions were found to be useful for glycosidation of the **4** with a glycal. Thus, the reaction of **4** with tri-*O*-acetylglycal (10 equiv) shown in entry 6 in the presence of *p*-toluenesulfonic acid (0.4 equiv) afforded the sugar derivative **7b** as a 4:1 mixture of α and β-anomers.

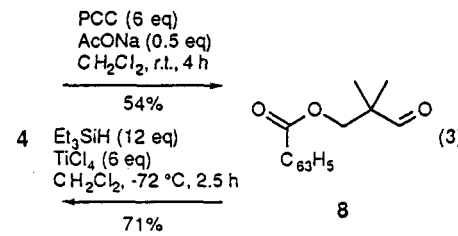
Oxidation and reduction of oxygen functionalities could also be achieved in

Table II. Synthesis of Organofullerenes.[a]

entry	reagents	product	%yield[b]
1a	PhCOCl, pyridine	 **6a**	62
1b	$PhCO_2H$, DCC/DMAP	**6a**	100
2	 DCC/DMAP	 **6b**	100
3	 DCC/DMAP	 **6c**	64
4	 DCC/DMAP	 **6d**	81
5	 PPTS	 **7a**	85
6	 TsOH	 **7b**	62

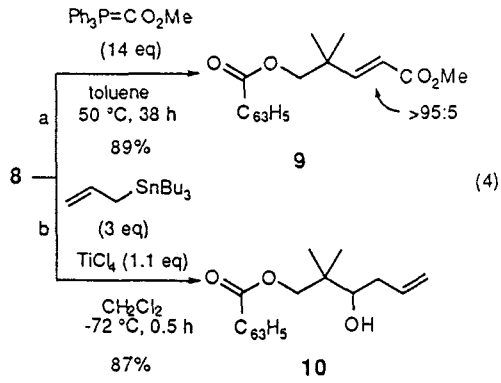
[a]The reaction was carried out in CH_2Cl_2 at room temperature except for entry 1a, where it was carried out in toluene at 50 °C. [b]Based on pure isolated material.

the presence of the fullerene core (eq 3). Thus, oxidation of the hydroxyl group in 4 with pyridinium chlorochromate (PCC) in CH_2Cl_2 at room temperature cleanly (TLC) afforded the aldehyde 8 in 54% isolated yield. Swern oxidation, on the other hand, resulted in recovery of 4. While attempted conversion of 8 back to 4 with diisobutylaluminum hydride was unsuccessful due to competitive reaction with the C_{60} core, reduction under acidic conditions proved to be successful. Thus, reduction of the aldehyde group of 8 with Et_3SiH (12 equiv) in the presence of $TiCl_4$ (6 equiv) in CH_2Cl_2 at -72 °C afforded 4 in 74% yield. The C_{60} core remained intact despite the use of excess reducing agent.



The possibility of C-C bond elongation reaction was next examined for the aldehyde group in 8. Initial attempts to add alkyllithium and magnesium reagents failed due to competitive reaction with the C_{60} moiety. It was rather disappointing that much milder conditions using fluoride activation technology also failed to realize selective C-C bond formation at the aldehyde group. Hence, the aldol reaction of 8 with the trimethylsilyl ketene acetal of methyl isobutyrate in the presence of tris-(diethylamino)sulfur(trimethylsilyl)difluoride gave several products due to reactions at the C_{60} moiety. We found, however, that a stabilized ylid does react selectively with the aldehyde group to give the unsaturated ester 9 as an *E*-isomer (>95:5) in 89% yield (eq 4a). Lewis-acid mediated reaction was also found to be effective for C-C bond formation. The reaction of the aldehyde 8 with allyltributyltin (3 equiv) and $TiCl_4$ (1.1

equiv) at -72 °C gave the homoallylic alcohol **10** in 87% yield (eq 4b).



While the parent C_{60} is sparingly soluble in various solvents, the fullerene derivatives described above were found to be much more soluble than C_{60} in aromatic hydrocarbons, halogenated and ethereal solvents. While there was a possibility that the polar groups attached in the present studies may interact with the C_{60} core in either an intramolecular or intermolecular manner, the ^1H NMR spectroscopy, which provides a measure of the spatial proximity between the C_{60} and a nearby proton,[2c] indicated no sign of anomaly due to such interactions.

References

1 *Fullerenes Synthesis, Properties, and Chemistry of Large Carbon Clusters*; Hammond, G.; Kuck, V. J., Eds.; ACS Symposium Series 481; American Chemical Society: Washington, DC, 1992. The fullerene issue: *Acc. Chem. Res.* **1992**, 25 (3). Taylor, R.; Walton, D. R. M. *Nature* **1993**, *363*, 685.

2. Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157.

3. 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.

4. Yamago, S.; Tokuyama, H.; Nakamura, E.; Prato, M.; Wudl, F. *J. Org. Chem.* in press.

5. Sijbesma, R.; Srdanov, G.; Wudl, F.; Castoro, J. A.; Wilkins, C.; Friedman, S. H.; DeCamp, D. L.; Kenyon, G. L. *J. Am. Chem. Soc.* in press, Friedman, S. H.; DeCamp, D. L.; Sijbesma, R.; Srdanov, G.; Wudl, F.; Kenyon, G. L. *J. Am. Chem. Soc.* in press, Tokuyama, H.; Yamago, S.; Nakamura, E.; Shiraki, T.; Sugiura, Y. *J. Am. Chem. Soc.* in press.

6. Ejiri, S.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 8708, Yamago, S.; Nakamura, E. *J. Org. Chem.* **1990**, *55*, 5553.

7. Yamago, S.; Ejiri, S,; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 5344.