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Synthesis and Reactions of 2,2-[60]Fullerenoalkanoyl Chlorides

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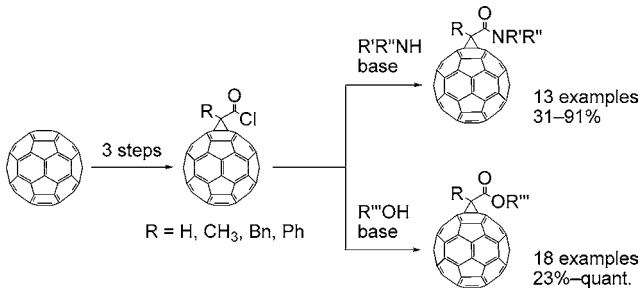

2,2-[60]Fullerenoalkanoyl chlorides (**1a**−**d**) were easily and securely prepared from the corresponding 2,2-[60]fullerenoalkanoic acids (**2a**−**d**) by the reaction with thionyl chloride in an unusual mixed solvent, CH_2Cl_2/dioxane. The characterization of **1a**−**d** by ^1H and ^{13}C NMR, FT-IR, and MALDI-TOF-MASS was conducted for the first time. The 2,2-[60]fullerenoalkanoyl chlorides thus obtained were readily converted to the corresponding amides and esters in moderate to excellent yields by the condensation with amines and alcohols, respectively. Upon applying the condensation, [60]fullerene−biomolecule hybrids were easily prepared.

Introduction

Methano[60]fullerenes are a class of the most extensively studied fullerene derivatives, because of easiness in handling, synthetic availability, and striking resemblance to [60]fullerene in physical properties.[1,2] For the preparation of methano[60]-fullerenes, several methods have been developed to date, such as the Bingel reaction,[2a,3] the addition−thermal decomposition of diazo compounds,[4] the addition−elimination of silylated nucleophiles derived from α-halocarbonyls,[2d,5] the addition−elimination of stabilized onium ylides,[2e,6] etc. Although these methods have been thoroughly studied and some of them have been widely used, they still have some limitations. In the Bingel reaction, the resultant methano[60]fullerenes usually possess two carbonyl groups or their equivalents at the bridgehead carbon, which may be a serious drawback for the preparation of simple, monofunctionalized [60]fullerene derivatives. In addition, a

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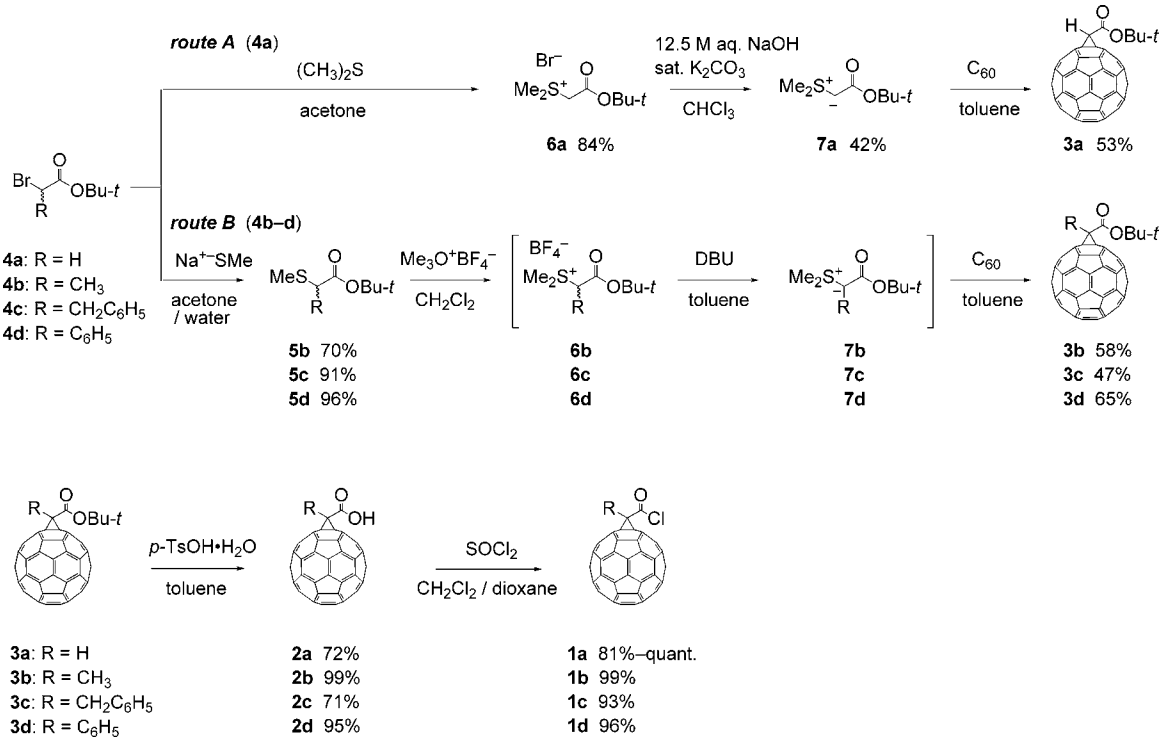
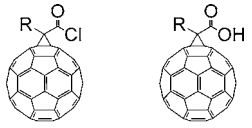
SCHEME 1. Synthesis of 2,2-[60]Fullerenoalkanoyl Chlorides 1a−d



strong base such as 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) is required to promote the reaction, and the substitutents to be introduced are limited to only robust ones.[3] On the other hand, the addition−thermal decomposition of diazo compounds proceeds under neutral conditions. This reaction, however, involves a complicated equilibrium between the [6,5]-open and [6,6]-closed structures of [60]fullerene.[4] Compared with these two methods, the addition−eliminations of silylated nucleophiles and onium ylides have some advantages for the synthesis of methano[60]fullerenes with various substituents. However, even in these advanced methods, strongly basic conditions have to be employed for the preparation of the corresponding cyclopropanating reagents, which diminish the functionality tolerance of these methods. In addition, the preparation of the cyclopropanating reagents usually requires considerable synthetic efforts.[5,6] Taking into account these aspects, a more efficient synthetic strategy has been required. One of such strategies would be as follows: At first, a methano-[60]fullerene possessing a reactive functional group is prepared as a universal precursor, and then the precursor is converted to various derivatives by conventional and reliable reactions in high yields.

As a key precursor for the creation of various [60]fullerene derivatives, 2,2-[60]fullerenoalkanoic acid (**2**) seems to meet the criteria; simple monofunctionalized structure, synthetic accessibility, and potential reactivity. In fact, several 2,2-[60]-fullerenoalkanoic acid amides and esters have been synthesized by treatment of [60]fullerenoacetic acid (**2**, R = H) with amines and alcohols, respectively, in the presence of a condensing agent.[4c,6d,6e] However, this method requires long reaction time, and the yields are not satisfactory in general, mainly due to the low solubility of the acid in common organic solvents and due to the low reactivity of the intermediate generated from **2** and the condensing agent. Moreover, such reactions were tried only for [60]fullerenoacetic acid (**2**, R = H). As an alternative and general series of key intermediates, we focused on 2,2-[60]-fullerenoalkanoyl chlorides (**1**), which are expected to be more



1 **2**

fascinating precursors, compared with **2**, from the viewpoints of solubility and reactivity.[4e,7] Recently, we briefly reported an efficient method for the preparation of [60]fullerenoacetyl chloride (**1**, R = H) and its application to the synthesis of several [60]fullerenenoacetic acid esters.[8] In this paper, we wish to report, in detail, a general method for the preparation of various 2,2-[60]fullerenoalkanoyl chlorides and their reactions with a number of amines and alcohols, including natural products and their derivatives, to successfully give the corresponding amides and esters in moderate to excellent yields.

Results and Discussion

Preparation of 2,2-[60]Fullerenoalkanoyl Chlorides (1a−d). As the precursor of [60]fullerenoacetyl chloride (**1a**), the *tert*-butyl ester **3a** was prepared by the cyclopropanation of C_{60} with the sulfonium ylide **7a**. For example, the (*tert*-butoxycarbonyl)methylsulfonium bromide **6a**-Br, prepared from *tert*-butyl bromoacetate (**4a**) and dimethyl sulfide, was converted to the sulfonium ylide **7a**, which was used for the cyclopropanation of C_{60} to give *tert*-butyl [60]fullerenoacetate (**3a**) (Scheme 1, route A).[6b−e] However, route A was unfortunately not applicable for the preparation of **3b−d**; the nucleophilic substitution of the 2-bromoalkanoates **4b−d** with dimethyl sulfide proceeded

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sluggishly, most likely due to the steric hindrance of **4b**−**d**. As an alternative method, **4b**−**d** were converted to the corresponding sulfonium salts through two steps by treatment with more reactive reagents; the 2-bromoalkanoates **4b**−**d** were allowed to react with sodium methanethioate to give the corresponding 2-(methylthio)alkanotates **5b**−**d**, which were then converted to the sulfonium tetrafluoroborates **6b**−**d**-BF_4 by treatment with trimethyloxonium tetrafluoroborate. Contrary to **6a**-Br, the sulfonium tetrafluoroborates **6b**−**d**-BF_4 showed moderate solubility in less polar organic solvents, such as toluene. Therefore, the sulfonium ylides **7b**−**d** were generated in situ upon treating **6b**−**d**-BF_4 with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene and allowed to directly react with C_{60} to give the target *tert*-butyl esters **3b**−**d** in satisfactory yields (Scheme 1, route B).[9]

The *tert*-butyl esters **3a**−**d** thus obtained were readily converted to the carboxylic acids **2a**−**d** through the cleavage of the ester moiety promoted by *p*-toluenesulfonic acid monohydrate (Scheme 1).[4c,6c,6e,9] As might be seen from their structures, the carboxylic acids **2a**−**d** were hardly soluble in most of common solvents, which was a serious obstacle for the isolation and further transformation of **2a**−**d**. We, therefore, surveyed many kinds of single and mixed solvent systems and finally found that CH_2Cl_2/dioxane (1:1 (v/v)) dissolved **2a**−**d** very well. With use of this mixed solvent, **2a**−**d** with satisfactory purity were easily isolated from the reaction mixture upon filtrating off materials insoluble in the mixed solvent (71−99%). This mixed solvent system was also found to be effective in the transformation of the carboxylic acids **2a**−**d** to the acyl chlorides **1a**−**d**; in the mixed solvent, **2a**−**d** were converted to the corresponding acyl chlorides **1a**−**d** in almost quantitative yields by treatment with thionyl chloride (Scheme 1).[9] Thus, the generality of the present method, developed for the preparation and isolation of 2,2-[60]fullerenoalkanoyl chlorides, was clearly demonstrated.

Characterization of 2,2-[60]Fullerenoalkanoyl Chlorides (1a−d). In a conventional method, the acyl chloride **1a** has been prepared in situ and used without isolation;[4e] as far as we know, no characterization of **1a** has been reported. In contrast, the acyl chlorides **1a**−**d** thus prepared in the present study could be isolated, making it possible to conduct the characterization of **1a**−**d** by ^{1}H and ^{13}C NMR, FT-IR, and MALDI-TOF-MASS (Table 1). In the MALDI-TOF-MASS spectrum of each acyl chloride, a peak consistent with the calculated value was observed. Several unidentified peaks were also observed, most likely due to the decomposition/reaction of **1a**−**d** under the MALDI-TOF-MASS measurement conditions. In the IR spectra, the absorptions of the C═O groups were observed at 1771−1794 cm^{-1} for **1a**−**d**, of which the wavenumbers were similar to those for the absorptions of common acyl chlorides. Compared with the corresponding absorptions in the IR spectra of **2a**−**d** (C═O, 1700−1730 cm^{-1}), the absorptions of **1a**−**d** shifted to higher wavenumbers, indicating that the carboxyl groups of **2a**−**d** were converted to acyl chloride moieties, respectively. The ^{13}C NMR spectra of **1a**−**d** showed well-resolved 22−28 resonances of the fullerene core, which is in good agreement with the C_s symmetry of **1a**−**d**. In addition, the peaks assignable to the cyclopropane bridgehead carbon (40.79−62.70 ppm) and to the carbonyl carbon (166.40−167.98 ppm) were commonly observed for **1a**−**d**. In ^{1}H NMR spectra, all of the acyl chlorides **1a**−**d** gave one set of signals, respectively, indicating that **1a**−**d** was satisfactorily pure and that the contamination of the carboxylic acid **2a**−**d** was negligible.

TABLE 1. Physical Properties of the 2,2-[60]Fullerenoalkanoyl Chlorides 1a−d and the 2,2-[60]Fullerenoalkanoic Acids 2a−d[a]

	MALDI-TOF-MS (*m*/*z*)		IR (cm^{-1})	^{13}C NMR (δ/ppm)	
	calcd	found	C═O	carbonyl	bridgehead
1a	795.9716	795.9085	1780	167.30	40.79[b]
1b	809.9872	810.1824	1778	167.98	52.27[c]
1c	886.0185	886.2068	1794	166.41	58.03[c]
1d	872.0029	872.2001	1771	166.40	62.70[c]
2a	778.0055	778.1925	1700	166.80	40.32[b]
2b	792.0211	792.0426	1707	168.83	45.96[b]
2c	886.0185	886.2068	1718	167.46	51.61[b]
2d	854.0367	854.2013	1730	166.20	65.54[d]

[a] For the characterizaion of **1a**−**d** and **2a**−**d**, see ref 9. [b] THF-d_8/CS_2 = 1:1 (v/v). [c] $CDCl_3$/CS_2 = 1:1 (v/v). [d] $CDCl_3$/DMSO-d_6/CS_2 = 1:1:1 (v/v/v).

In general, acyl chlorides are rather sensitive to moisture and sometimes should be used within a short period after the preparation. However, the acyl chlorides **1a**−**d** could be stored at least for 1 day at −15 °C under argon atmosphere. Moreover, **1a**−**d** were fortunately soluble in less polar solvents, such as carbon disulfide, bromobenzene, and 1,2-dichlorobenzene, which might enlarge the potential utility of **1a**−**d** as substrates for various reactions.

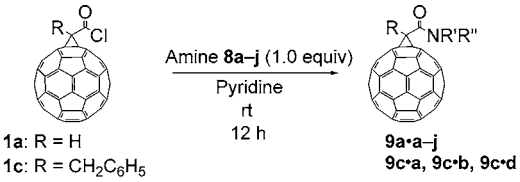
Condensation of 2,2-[60]Fullerenoalkanoyl Chlorides with Amines. The acyl chlorides **1a**−**d** were expected to be versatile precursors for the synthesis of various methano[60]fullerene derivatives, because of their high reactivity and good solubility in organic solvents. As one of the most fundamental reactions of acyl chlorides, we chose the condensation with amines to form the corresponding amides. For the condensation reaction, pyridine was selected as a solvent, because it is the most widely used solvent for general acyl chloride−amine condensations. Although the usage of an excess amount of an amine is sometimes effective for the condensation with sterically hindered acyl chlorides such as **1a**−**d**, we used an equimolar amount of an amine in the present reaction; the protocol developed here would be applicable for the condensation with precious amines.

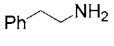
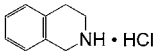
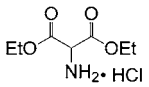
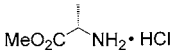
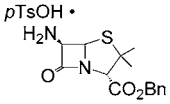
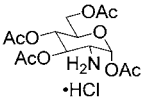
The α carbon of the acyl chloride moiety of **1a** is secondary, whereas those of **1b**−**d** are tertiary. Because such a structural difference would have some effect on the reactivity of the acyl chlorides, we selected **1a** and **1c** as representative substrates to examine their reactivity. Thus, the condensations of **1a** and **1c** with three types of amines, a primary amine, a primary amine with a bulky substituent, and a secondary amine (**8a**, **8b**, and **8d**, respectively), were first conducted. The amines (1.0 equiv) smoothly reacted with the acyl chlorides **1a** and **1c** in pyridine at room temperature. Although the acyl chlorides **1a** and **1c** were not sufficiently soluble in pyridine, the reactions gradually proceeded, and the mixtures turned from suspensions to dark brown solutions, indicating the conversion of **1a** and **1c** to the corresponding amides.

As shown in Table 2, the corresponding amides were successfully obtained in moderate to excellent yields by the condensation of **1a** with amines: The reaction with a typical primary amine, 2-phenylethylamine (**8a**), gave the corresponding

(9) Methano[60]fullerene derivatives **1a**−**d**, **2a**−**d**, and **3a**−**d** were characterized by ^{1}H and ^{13}C NMR, FT-IR, and MALDI-TOF-MS spectroscopies. In the cases of some 2,2-[60]fullereneoalkanoic acid amides (**9**) and esters (**11**), the ^{13}C NMR spectra could not be obtained because of their poor solubility in most solvents, and the identification was carried out by ^{1}H NMR, FT-IR, and MALDI-TOF-MS (see Experimental Section and Supporting Information).

TABLE 2. Condensation of the 2,2-[60]Fullerenoalkanoyl Chlorides 1a and 1c with Various Amines 8a−j[a]



entry	acyl chloride	amine		yield /%	entry	acyl chloride	amine		yield /%
1	**1a**		**8a**	87	9	**1a**		**8f**	83
2	**1c**			53					
3[b]	**1a**		**8b**	77	10	**1a**		**8g**	85
4[b]	**1c**			31					
5[b]	**1a**		**8c**	78	11	**1a**		**8h**	91
6	**1a**		**8d**	80	12	**1a**		**8i**	75
7	**1c**			50					
8	**1a**		**8e**	82	13[b]	**1a**		**8j**	19 (43[c])

[a] For the characterization of **9**, see ref 9. [b] The reaction was conducted in the presence of DMAP (1.0 equiv). [c] The reaction was conducted at 50 °C.

amide **9a·a** in 87% yield (entry 1). The same reaction conditions were applicable for the reactions with a secondary amine, diethylamine (**8d**, entry 6). On the other hand, only a poor yield was achieved when a hindered amine, *tert*-butylamine (**8b**), was used. Therefore, to improve the yield, 4-(dimethylamino)-pyridine (DMAP, 1.0 equiv) was added as an activator of the acyl chloride **1a**.[10] As a result, the corresponding amide was obtained in good yield (entry 3). In a similar manner, amides containing a C_{60} core were obtained by the reaction of **1a** with hindered and functionalized primary amines and secondary amines (entries 5 and 8−10). Moreover, as demonstrated by the reaction with diethyl aminomalonate (**8g**), the reaction conditions were tolerant to an ester group (entry 10). The amide **9a·g** thus obtained would have a potential of further transformations, such as the nucleophilic reactions of the stabilized tertiary carbanion and the hydrolysis/decarboxylation of the ethoxycarbony moiety.[11]

Even though the steric hindrance of the α-substituents of **1c** seems to have an unfavorable effect on the efficiency of the reaction, the condensation of **1c** proceeded smoothly under the same conditions. The condensation of **1c** with the primary amine **8a**, the secondary amine **8b**, and the hindered amine **8c** afforded the corresponding amides **9c·a**, **9c·b**, and **9c·d** in acceptable yields (Table 2, entries 2, 4, and 6; 31−53%).

The same procedure was applied for the synthesis of [60]-fullerene−biomolecule hybrids from **1a** and the derivatives of natural products possessing an amino group (entries 11−13) on the basis of the consideration that the resultant amides would be attractive as potential bioactive materials.[12] The condensation with methyl L-alaninate hydrogen chloride (**8h**) gave the corresponding amide **9a·h** in excellent yield (entry 11). The enantiomeric purity of **9a·h** thus obtained was confirmed to be >99% by ^{1}H NMR spectroscopy, using Eu(hfc)$_3$ as a chiral shift reagent. In a similar manner, the [60]fullerene−penicilline hybrid **9a·i** was prepared in moderate yield (entry 12). In the case of the condensation with 1,3,4,6-tetra-*O*-acetyl-D-glucosamine hydrogen chloride (**8j**), however, an elevated temperature was required to achieve an acceptable yield even in the presence of DMAP, most likely due to the steric hindrance (entry 13).

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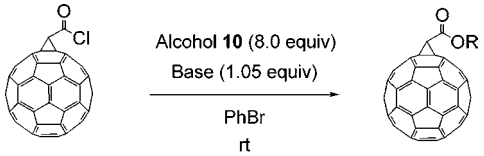
TABLE 3. Effect of a Base on the Condensation of 2,2-[60]Fullerenoacetyl Chloride (1a) with Alcohols



1a **11a**

entry	alcohol	base	yield/%
1	methanol (**10a**)	triethylamine	89
2	ethanol (**10b**)	triethylamine	82
3	2-propanol (**10e**)	triethylamine	49
4	2-propanol (**10e**)	*N*,*N*-diisopropylethylamine	52
5	2-propanol (**10e**)	*N*-methylmorporine	34
6	2-propanol (**10e**)	4-(dimethylamino)pyridine	61
7	2-propanol (**10e**)	pyridine	38

Condensation of 2,2-[60]Fullerenoalkanoyl Chlorides with Alcohols. To demonstrate further utility of the acyl chlorides **1a**−**d** as precursors for the synthesis of [60]fullerene−functional molecule hybrids, we next targeted the condensation with alcohols. Due to the low nucleophilicity of alcohols compared with amines, the conditions for the amide formation mentioned above are not necessarily applicable for ester formation. Therefore, we examined the parameters, such as the reaction solvent, the amount of alcohols, and the base, by using **1a**. The amide formation from **1a** and amines proceeded efficiently in pyridine, even though **1a** was not sufficiently soluble in pyridine. However, the ester formation from **1a** and alcohols was very slow. On the basis of this result, we decided to apply a homogeneous system in the presence of a base to increase the concentration of the substrate **1a**. Among less polar solvents with suitable dissolvability for **1a**, we selected bromobenzene, because of better stability under basic conditions and ease in evaporation. In addition, an excess amount of an alcohol (8.0 equiv) was used for the condensation, taking into account the low nucleophilicity of the alcohol.

One of the crucial factors of this condensation reaction was the choice of a base (Table 3). At first, triethylamine was used as a base, which is widely employed for the general condensation of acyl chlorides with alcohols. In the presence of triethylamine (1.05 equiv), the acyl chloride **1a** readily reacted with simple primary alcohols, such as methanol (**10a**) and ethanol (**10b**), to give the corresponding esters in high yields (entries 1 and 2). Contrary to this, in the case of 2-propanol (**10e**), the reaction did not give a satisfactory result, most likely due to the lower reactivity arising from the steric hindrance between the [60]fullerene core and **10e** (entry 3). Therefore, several bases were tested for the condensation of **1a** with **10e**. Table 3 indicates that the basicity of a base used is an important but not crucial factor for the effective ester formation. When aliphatic tertiary amines with strong basicity were used (entries 3−5), the yields were comparable with or a little better than that in the presence of pyridine with low basicity (entry 7). Worth noting is the fact that an exceptionally good yield was realized when DMAP was used as the base (entry 8) despite DMAP being classified as a base weaker than triethylamine, *N*,*N*-diisopropylethylamine, and *N*-methylmorpholine. These results suggest that DMAP promoted the condensation not only as a base possessing sufficient basicity, but also as an activator of **1a**, as observed in the amide formation from **1a** and hindered amines.[10]

To prove the generality of this condensation reaction, we conducted the condensations of **1a** and **1c** with various alcohols.[12] As shown in Table 4, the acyl chloride **1a** smoothly reacted with the primary and secondary alcohols **10a**−**e** under mild conditions to give the corresponding esters in good to excellent yields (entries 1, 2, and 4−6). Moreover, less-reactive alcohols such as the phenols **10f** and **10g** were applicable for the condensation (entries 8 and 10). The acyl chloride **1c** could also condense with the primary alcohol **10b**, the secondary alcohol **10e**, and the phenol **10f** to give the corresponding esters **11c·b**, **11c·e**, and **11c·f** in moderate to excellent yields (entries 3, 7, and 9). The reactivity of **1c** was, however, lower than that of **1a**, especially in the reaction with sterically hindered alcohols such as **10e**, which is in good agreement with the case of the amide formation.

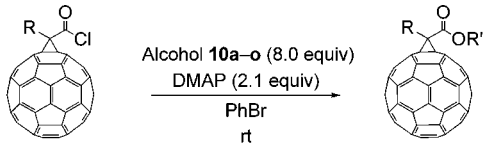
The effectiveness of the condensation thus observed prompted us to use natural products and their derivatives containing a hydroxy group as substrates. As expected, the condensations of **1a** with (+)-menthol (**10h**), (−)-borneol (**10i**), geraniol (**10j**), cholesterol (**10k**), and the glucose derivative **10*l*** readily proceeded to give the corresponding esters **11a·h**−**11a·*l***, although the yields were influenced to some extent by the steric congestion around their hydroxy group (entries 11−15). In the case of geraniol (**10j**), however, an unidentified byproduct was generated, presumably due to the exceptional reactivity of its hydroxy group at the allylic position. Taking this aspect into consideration, pyridine (1.05 equiv) was used in the place of DMAP; the byproduct was not detected by TLC monitoring, and the yield was highly improved, as was expected (entry 13).

[60]Fullerene−nucleoside/nucleotide hybrids have attracted current attention as promising reagents for genetic therapy.[12a,b,e] Therefore, the condensation of **1a** with three kinds of nucleoside derivatives **10m**−**o**, possessing a hydroxy group at their 3′- or 5′-position, was attempted (entries 16−18). Steric hindrance was again found to be one of the determinant factors of this condensation. For example, the acyl chloride **1a** was easily condensed with the 5′-OH of **10m** (entry 16), whereas the yield of the ester **11a·n** decreased when **1a** was allowed to react with the more hindered 3′-OH in **10n** (entry 17). In the case of uridine derivatives, an additional protective group should be introduced at their 2′-position, which generally brings serious influence on the reactivity of the 3′-OH. In fact, the condensation of **1a** with **10o** proceeded sluggishly to afford the corresponding ester **11a·o** in only 23% yield (entry 18). These results indicate that the present protocol for the condensation is applicable for the synthesis of [60]fullerene−nucleoside hybrids, although less-hindered protecting group(s) should be selected for the 2′-, 3′-, and/or 5′-hydroxy group of nucleosides to achieve high yields.

Conclusion

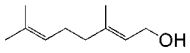
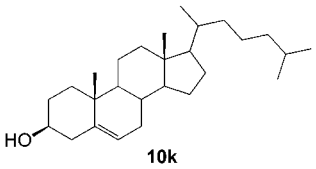
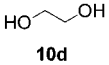
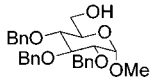
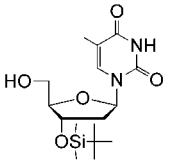
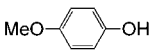
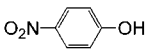
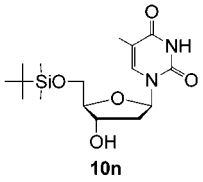
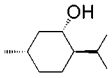
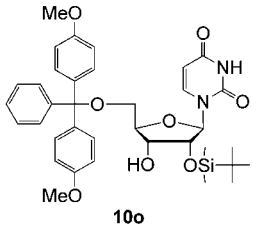
Four kinds of 2,2-[60]fullerenoalkanoyl chlorides (**1a**−**d**) were easily and securely prepared from the corresponding 2,2-[60]fullerenoalkanoic acids (**2a**−**d**) by the reaction with thionyl chloride in an unusual mixed solvent, CH_2Cl_2/dioxane. The acyl chlorides **1a** and **1c** were found to be readily converted to the corresponding amides **9** and esters **11** by the condensation with amines and alcohols, respectively. The condensation was applicable to the preparation of [60]fullerene−biomolecule hybrids; by the reaction of **1a** with natural products and their derivatives possessing an amino or hydroxy group, the target amides and esters were obtained in moderate to excellent yields. The hybrids thus obtained are expected to be attractive motifs

TABLE 4. Condensation of the 2,2-[60]Fullerenoalkanoyl Chlorides 1a and 1c with Various Alcohols 10a−o[a]



1a: R = H
1c: R = $CH_2C_6H_5$

11a•a–o
11c•b, 11c•e, 11c•f

entry	acyl chloride	alcohol	time / h	yield /%	entry	acyl chloride	alcohol	time / h	yield /%
1[b]	**1a**	CH_3OH **10a**	3	96	13	**1a**	 **10j**	12	53 (88[d])
2[b]	**1a**	CH_3CH_2OH **10b**	3	93					
3[b]	**1c**		3	53					
4[b]	**1a**	 **10c**	3	84	14	**1a**	 **10k**	12	76
5[b c]	**1a**	 **10d**	12	84	15	**1a**	 **10l**	12	66
6	**1a**	 **10e**	6	80	16	**1a**	 **10m**	12	70
7	**1c**		6	49					
8	**1a**	 **10f**	3	90					
9	**1c**		3	quant.					
10	**1a**	 **10g**	12	73	17	**1a**	 **10n**	12	44
11	**1a**	 **10h**	6	66	18	**1a**	 **10o**	12	23
12	**1a**	 **10i**	6	77					

[a] For the characterization of **11**, see ref 9. [b] DMAP (1.05 equiv) was used as a base. [c] Solvent; PhBr/THF = 1:1 (v/v). [d] Base; pyridine (1.05 equiv). Reaction time; 3 h.

for the studies on [60]fullerene-containing bioactive materials. Furthermore, the method demonstrated here might be applied for the preparation of combinatorial libraries composed of methano[60]fullerene derivatives, taking into account the simplicity, mild reaction conditions, and substrate tolerance.

Experimental Section

***tert*-Butyl 2-(Methylthio)-3-phenylpropionate (5c).** To an acetone solution (10 mL) of *tert*-butyl 2-bromo-3-phenylpropionate (**4c**, 4.2 g, 14.7 mmol) was added an aqueous solution of sodium methanethioate (15 wt %, 7.5 mL, 16.2 mmol) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 24 h. The reaction mixture was concentrated to ca. 8 mL under reduced pressure, and the resultant residue was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were successively washed with water (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to silica gel column chromatography (hexane/AcOEt = 10:1 (v/v)) to afford **5c** (3.36 g, 13.3 mmol, 91%) as a colorless

oil. IR (neat) 2977, 2923, 1722, 1495, 1455, 1392, 1368, 1256, 1142, 979, 960, 847, 744, 699 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.37 (s, 9H), 2.16 (s, 3H), 2.87−2.94 (m, 1H), 3.10−3.18 (m, 1H), 3.32−3.37 (m, 1H), 7.19−7.29 (m, 6H, overlapped with internal $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ 14.02, 27.88, 37.19, 49.69, 81.28, 126.62, 128.32, 129.00, 138.25, 170.81.

***tert*-Butyl [60]Fullerenoacetate (3a).** *tert*-Butyl (dimethylsulfanylidene)acetate (**7a**) was prepared from *tert*-butyl bromoacetate (**5a**) according to the procedure in the literature.[6b−e] To a toluene solution (200 mL) of [60]fullerene (200 mg, 0.28 mmol) was added a toluene solution (5 mL) of **7a** (40 mg, 0.23 mmol) at room temperature. After being stirred at room temperature for 18 h, the reaction mixture was concentrated under reduced pressure. The resultant residue was subjected to preparative thin-layer chromatography developed with hexane/toluene (1:1 (v/v)) to afford **3a** as a brown solid (101 mg, 0.12 mmol, 53%) and unreacted [60]-fullerene (53 mg). IR (KBr) 2973, 2923, 1730, 1366, 526 cm^{-1}; ^1H NMR ($CDCl_3/CS_2$ = 1:1 (v/v)) δ 1.78 (s, 9H), 4.70 (s, 1H); ^{13}C NMR ($CDCl_3/CS_2$ = 1:1 (v/v)) δ 28.05, 40.29, 70.80, 83.26, 136.03, 140.28, 140.68, 140.92, 141.81, 141.87, 142.00, 142.22, 142.59, 142.74, 142.78, 142.87, 143.06, 143.49, 143.72, 144.14, 144.37, 144.42, 144.55, 144.83, 144.89, 144.97, 144.99, 145.41, 145.70, 148.25, 164.52; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{66}H_{10}O_2$ calcd 834.0681, found 834.1663.

***tert*-Butyl 2,2-[60]Fullereno-3-phenylpropionate (3c).** To a CH_2Cl_2 solution (12 mL) of **5c** (252 mg, 1.0 mmol) was added trimethyloxonium tetrafluoroborate (148 mg, 1.0 mmol) at room temperature. After being stirred at room temperature for 24 h, the resultant CH_2Cl_2 solution of [1-(*tert*-butoxycarbonyl)-2-phenylethyl]-dimethylsulfonium tetrafluoroborate (**6c**-BF_4) (0.083 M) was used for the following reaction without further purification.

To a toluene solution (72 mL) of [60]fullerene (72 mg, 0.10 mmol) were successively added a CH_2Cl_2 solution of **6c**-BF_4 (0.083 M, 1.8 mL, 0.15 mmol) and a toluene solution (0.56 mL) of 1,8-diazabicyclo[5.4.0]undec-7-ene (25.8 mg, 0.17 mmol) at room temperature. After being stirred at room temperature for 18 h, the reaction mixture was subjected to silica gel plug filtration (toluene), and the filtrate was concentrated under reduced pressure. The resultant residue was subjected to preparative thin-layer chromatography developed with CS_2 to afford **3c** as a brown solid (43.9 mg, 0.047 mmol, 47%) and unreacted [60]fullerene (33.0 mg, 46%). IR (KBr) 2972, 2924, 1726, 1453, 1427, 1366, 1184, 1153, 1130, 838, 754, 696, 525 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (s, 9H), 4.20 (s, 2H), 7.33−7.44 (m, 3H), 7.63−7.65 (m, 2H); ^{13}C NMR ($CDCl_3/CS_2$ = 1:1 (v/v)) δ 27.83, 35.17, 50.68, 76.28, 83.41, 127.28, 128.67, 129.22, 136.60, 137.79, 138.02, 140.72, 141.01, 141.98, 142.03, 142.11, 142.77, 142.85, 142.94, 142.98, 143.03, 143.09, 143.56, 143.77, 144.13, 144.47, 144.53, 144.61, 144.68, 144.72, 145.05, 145.10, 145.15, 145.41, 146.52, 147.90, 165.46; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{73}H_{16}O_2$ calcd 924.1150, found 924.3105.

[60]Fullerenoacetic Acid (2a). A toluene solution (150 mL) of **3a** (214 mg, 0.26 mmol) and *p*-TsOH·H_2O (88 mg, 0.52 mmol) was refluxed for 8 h to afford a suspension. The brown solid thus precipitated was collected by filtration (ADVANTEC, filter paper 5A) and washed successively with toluene (100 mL) and water (30 mL). The residual solid was dissolved in CH_2Cl_2/dioxane (1:1 (v/v), 30 mL), and the insoluble mass was filtered off (ADVANTEC, filter paper 5A). The filtrate was concentrated to dryness to afford **2** as a brown solid (145 mg, 0.19 mmol, 72%). IR (KBr) 3420, 1700, 520 cm^{-1}; ^1H NMR (THF-d_8/CS_2 = 1:1 (v/v)) δ 5.18 (s, 1H); ^{13}C NMR (THF-d_8/CS_2 = 1:1 (v/v)) δ 40.32, 72.10, 136.99, 141.37, 141.65, 142.61, 142.70, 142.81, 143.09, 143.36, 143.49, 143.56, 143.65, 143.87, 144.30, 144.55, 144.85, 145.04, 145.12, 145.20, 145.27, 145.43, 145.59, 145.67, 145.72, 145.75, 145.89, 146.32, 147.14, 149.56, 166.80; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{62}H_2O_2$ calcd 778.0055, found 778.1925.

2,2-[60]Fullereno-3-phenylpropionic Acid (2c). The title compound was synthesized from **3c** through a procedure similar to that for the preparation of **2a** (71% yield). IR (KBr) 3435, 2918, 2848, 1718, 1637, 1494, 1428, 1252, 1185, 1119, 1078, 870, 734, 698, 525 cm^{-1}; ^1H NMR (THF-d_8/CS_2 = 1:1 (v/v)) δ 4.28 (s, 2H), 7.29−7.44 (m, 3H), 7.67−7.69 (m, 2H); ^{13}C NMR (THF-d_8/CS_2 = 1:1 (v/v)) δ 35.63, 51.61, 77.41, 127.93, 129.50, 129.90, 137.79, 138.92, 139.06, 141.40, 141.76, 142.84, 142.88, 142.93, 143.55, 143.62, 143.73, 143.76, 143.81, 143.93, 144.36, 144.60, 144.87, 145.21, 145.25, 145.33, 145.47, 145.63, 145.82, 145.87, 146.09, 146.34, 147.66, 149.12, 167.46; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{69}H_8O_2$ calcd 868.0524, found 868.1671.

[60]Fullerenoacetyl Chloride (1a). A solution of **2a** (50 mg, 0.064 mmol) and thiony chloride (5.0 mL, 67 mmol) in CH_2Cl_2/dioxane (1:1 v/v, 40 mL) was refluxed for 5 h to afford a black precipitate. The precipitate was collected by filtration (ADVANTEC, filter paper 5A) and washed with CH_2Cl_2/dioxane (1:1 v/v, 100 mL). The residual solid was dissolved in CS_2 (20 mL), and the insoluble mass was filtered off (ADVANTEC, filter paper 5A). The filtrate was concentrated to dryness to afford **1a** as a black solid (51 mg, 0.064 mmol, quant.). IR (KBr) 1780, 520 cm^{-1}; ^1H NMR ($CDCl_3/CS_2$ = 1:1 (v/v)) δ 5.23 (s, 1H); ^{13}C NMR (THF-d_8/CS_2 = 1:1 (v/v)) δ 40.79, 72.63, 137.45, 141.79, 142.09, 143.07, 143.14, 143.26, 143.54, 143.80, 143.93, 144.00, 144.30, 144.74, 144.99, 145.28, 145.47, 145.56, 145.65, 145.73, 146.02, 146.12, 146.15, 146.19, 146.36, 146.79, 147.67, 150.08, 167.30; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{62}HClO$ calcd 795.9716, found 795.9085.

2,2-[60]Fullereno-3-phenylpropionyl Chloride (1c). A solution of **2c** (50 mg, 0.057 mmol) and thiony chloride (4.5 mL, 60 mmol) in CH_2Cl_2/dioxane (1:1 v/v, 40 mL) was refluxed for 5 h. The reaction mixture was concentrated under reduced pressure, and the resultant residue was triturated with hexane, collected by filtration (ADVANTEC, filter paper 5A), and washed with hexane (50 mL). The residual solid was dissolved in CS_2 (20 mL), and the insoluble mass was filtered off (ADVANTEC, filter paper 5A). The filtrate was concentrated to dryness to afford **1c** as a black solid (47.6 mg, 0.053 mmol, 93%). IR (KBr) 2923, 1794, 1509, 1427, 1184, 912, 878, 736, 694, 654, 524 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.37 (s, 2H), 7.36−7.47 (m, 3H), 7.63−7.65 (m, 2H); ^{13}C NMR ($CDCl_3/CS_2$ = 1:1 (v/v)) δ 34.75, 58.03, 75.36, 127.99, 128.98, 129.20, 134.77, 137.64, 138.32, 140.98, 141.18, 141.79, 141.98, 142.04, 142.12, 142.84, 142.95, 143.00, 143.16, 143.54, 143.73, 144.46, 144.56, 144.60, 144.67, 144.72, 144.76, 144.80, 145.04, 145.14, 145.19, 145.22, 145.75, 166.41; MALDI-TOF-MASS (dithranol) for $[M]^+$ $C_{69}H_7ClO$ calcd 886.0185, found 886.2068.

General Procedure for the Condensation of the 2,2-[60]-Fullerenoalkanoyl Chlorides 1 with the Amines 8. To a suspension of **1** (0.0188 mmol) in pyridine (15 mL) was added the amine or ammonium salt **8** (0.0188 mmol) at room temperature, and mixture was stirred at room temperature for 12 h. The reaction mixture was concentrated under reduced pressure, and residual pyridine was azeotropically removed with toluene (30 mL). The resultant residue was subjected to preparative thin-layer chromatography developed with CS_2/CH_2Cl_2 to afford the corresponding amide **9** as a brown solid.

General Procedure for the Condensation of the 2,2-[60]-Fullerenoalkanoyl Chlorides 1 with the Alcohols 10. To a bromobenzene solution (15 mL) of **1** (0.0188 mmol) were added the alcohol **10** (0.15 mmol) and 4-(dimethylamino)pyridine (2.4−4.8 mg, 0.0197−0.0395 mmol) at room temperature. The mixture was stirred for 3−12 h and concentrated under reduced pressure. The resultant residue was subjected to preparative thin-layer chromatography developed with CS_2/CH_2Cl_2 to afford the corresponding ester **11** as a brown solid.

Supporting Information Available: Synthetic procedures and characterization data for the new compounds **1b**, **1d**, **2b**, **2d**, **3b**, **3d**, **5b**, **5d**, **9a·a**−**j**, **9c·a**, **9c·b**, **9c·d**, **11a·a**−**o**, **11c·b**, **11c·e**, and **11c·f** and ^1H and ^{13}C NMR spectra of **1a**−**d**, **2a**−**d**, **3a**−**d**, **5b**−**d**, **9a·a**, **9c·a**, **11a·b**, and **11c·b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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