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Synthesis of methano[60]fullerene derivatives: the fluoride ion-mediated reaction of [60]fullerene with silylated nucleophiles

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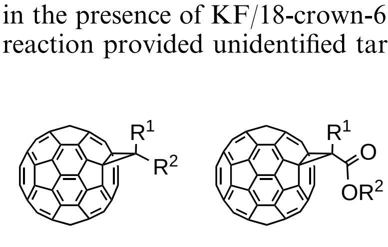
Abstract—A new reaction of [60]fullerene with silylated nucleophiles is described. The cyclopropanation of [60]fullerene with silylated nucleophiles, such as silyl ketene acetals, silyl ketene thioacetals, and silyl enol ethers, derived from α-halo carbonyl compounds, smoothly proceeded in the presence of KF/18-crown-6 to give the corresponding methano[60]fullerene derivatives in moderate to good yields. © 2001 Elsevier Science Ltd. All rights reserved.

The fascinating structure and properties of fullerenes have led to rapid development of their chemistry.[1] Among a large number of functionalized [60]fullerene compounds, methano[60]fullerene derivatives **1** have been one of the most intensively studied classes;[2] methano[60]fullerenes **2** having carboxyl group equivalent(s) are particularly interesting since they are applicable as versatile building blocks to the synthesis of [60]fullerene-containing functional compounds. Several methods for the synthesis of methano[60]fullerenes **2** have been developed:[3] (1) the addition–elimination reactions of α-halocarbanions generated in situ from active methylene compounds, so-called the Bingel reaction,[4] and of sulfonium ylides,[5] and (2) the addition of diazo compounds, followed by thermolysis or photolysis.[6] These reactions, however, have some limitation; the Bingel reaction inevitably requires basic reaction conditions and the substrates must be active methylene compounds, while the reaction of sulfonium ylides can be applied to the synthesis of only limited monosubstituted methano[60]fullerenes (**2**: $R^1 = H$) presumably due to the difficulty of the preparation and/or handling of disubstituted ylides, and the reaction of diazo compounds always yields fulleroides as by-products. Thus, a general method for the synthesis of various types of adducts **2** under neutral conditions has not been sufficiently established, in spite of the method being expected to show significant practical advantages (Fig. 1).

On the other hand, the fluoride ion-mediated reactions of silylated nucleophiles, such as silyl ketene acetals (SKAs), silyl ketene thioacetals (SKTAs), and silyl enol ethers (SEEs), which are isolable enolates, are widely used in carbon–carbon bond formations under nearly neutral conditions.[7] Then, we considered that by using 2-halogenated SKAs, SKTAs, or SEEs as α-halocarbanion equivalents, a fluoride ion-mediated cyclopropanation would proceed under neutral conditions via an addition–elimination to give various types of methano[60]fullerenes **2**.[8] This consideration promoted us to investigate the reaction of [60]fullerene with silylated nucleophiles having a halo group at the C2 position as a leaving group in the presence of fluoride ion (Table 1).[9]

At first, the reaction of [60]fullerene with an equimolar amount of SKA **3a**, derived from ethyl α-chloroacetate, was carried out in the presence of tetrabutylammonium fluoride (TBAF) or KF/18-crown-6 (runs 1 and 2). In both cases, the desired methano[60]fullerene **4a** was formed. Although the reaction in the presence of TBAF gave adduct **4a** in significantly higher isolated yield than that in the presence of KF/18-crown-6, the TBAF-mediated reaction provided unidentified tarry products;



1 **2**

Figure 1.

Keywords: fullerenes; cyclopropanation; ketene acetals; enol ethers.

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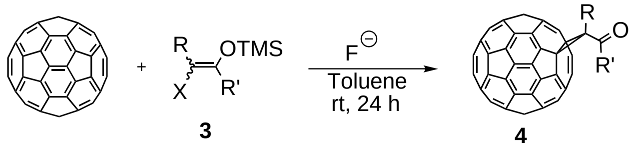
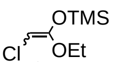
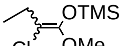
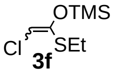
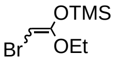
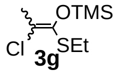
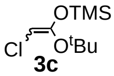
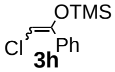
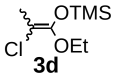
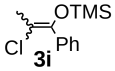
Table 1. Reactions of [60]fullerene with silylated nucleophiles in the presence of fluoride ion



3 **4**

Run	Substrate **3**	**3**/C_{60} (mol/mol)	Mediator[a]	Yield of **4**[b,c] (%)	Run	Substrate **3**	**3**/C_{60} (mol/mol)	Mediator[a]	Yield of **4**[b,c] (%)
1	 **3a**	1	TBAF	28 (68)[d]	7	 **3e**	5	KF/18-crown-6	67 (79)
2		1	KF/18-crown-6	20 (93)					
3		5	KF/18-crown-6	45 (86)	8	 **3f**	5	KF/18-crown-6	34 (82)
4	 **3b**	5	KF/18-crown-6	44 (88)	9	 **3g**	1	KF/18-crown-6	35 (74)
5	 **3c**	5	KF/18-crown-6	40 (71)	10	 **3h**	1	KF/18-crown-6	40 (72)
6	 **3d**	5	KF/18-crown-6	64 (79)	11	 **3i**	1	KF/18-crown-6	54 (96)

[a] An equimolar amount of TBAF (1M THF solution) or KF/18-crown-6 to substrate **3** was used.

[b] Isolated yield. [c] Values in parentheses are based on consumed C_{60}. [d] Unidentified products were also formed.

as the result, its selectivity was rather lower than that of the (KF/18-crown-6)-mediated reaction. The yield of adduct **4a**, produced by the (KF/18-crown-6)-mediated reaction, increased with increasing amounts of SKA **3a** maintaining the high selectivity; finally methano[60]fullerene **4a** was obtained in moderated yield by using fivefold excess of SKA **3a** (run 3). Thus, KF/18-crown-6 was found to be more suitable than TBAF as the fluoride ion source.

Next, the (KF/18-crown-6)-mediated reactions with various types of SKAs were carried out (runs 4–7). The reaction with 2-brominated SKA **3b** (run 4) gave methano[60]fullerene **4a** in almost the same yield as that with 2-chlorinated SKA **3a** (run 3). This result indicates that 2-chlorinated SKAs are better than 2-brominated SKAs as silylated nucleophiles from the viewpoint of ease of preparation and handling. The reactivity of SKA **3c**, derived from the *t*-butyl ester, was a little lower than that of SKA **3a**, derived from the ethyl ester (run 5), presumably due to a steric repulsion between the *t*-butyl group and the [60]fullerene core at the stage of the first addition reaction. 2-Alkylated SKAs **3d**,**e**, derived from α-chloropropanoic and α-chlorobutanoic acid ethyl esters, showed higher reactivity than non-substituted SKA **3a**, and their reactions gave adducts **4d**,**e** in good yields (runs 6 and 7). This higher reactivity would arise from higher nucleophilicity of the carbon at the C2 position influenced by the substituent. These reactions are the first examples of the synthesis of methano[60]fullerenes **2** substituted by an alkyl group and an alkoxycarbonyl group.

Similar reactions with several silylated nucleophiles other than SKAs were carried out (runs 8–11). The reactions with SKTAs **3f**,**g** also proceeded smoothly to afford methano[60]fullerenes **4f**,**g** in moderate yields (runs 8 and 9). SEEs **3h**,**i** also underwent an addition–elimination reaction to give the corresponding adducts **4h**,**i** (runs 10 and 11).[10] However, the reaction with fivefold excess of SKTA **3g** or SEEs **3h**,**i** yielded a complex mixture, from which [60]fullerene could not be recovered; thus, the reaction was carried out by using an equimolar amount of SKTA **3g** or SEEs **3h**,**i** to give the corresponding methano[60]fullerene in acceptable yield. In contrast, even when the reaction of (3-chloroallyl)trimethylsilane was conducted at 80°C for 12 h, unreacted [60]fullerene was recovered quantitatively, due to the less reactivity of the silylated nucleophile.

The present (KF/18-crown-6)-mediated reaction of [60]fullerene with 2-chlorinated SKAs, SKTAs, and SEEs has several advantages, compared with conventional methods for the synthesis of methano[60]fullerenes. (1) The reaction gave methano[60]fullerenes **4a**–**g**,**i** which could not be synthesized by the Bingel reaction; for example, the Bingel reactions with ethyl α-chloroacetate and α-chloropropanoate did not give methano[60]fullerenes even at 60°C in the presence of fivefold excess of DBU. 2) The reaction could be applied for substrates, giving disubstituted methano[60]fullerenes **2** ($R^1 \neq H$), which could not be obtained by the reactions of diazo compounds and sulfonium ylides.[5,6] (3) Alkylthiocarbonylated methano[60]fullerenes could be synthesized first time.

In conclusion, various types of methano[60]fullerenes were efficiently synthesized under neutral conditions by the (KF/18-crown-6)-mediated cyclopropanation of [60]fullerene with 2-chlorinated SKAs, SKTAs, and SEEs.

Acknowledgements

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9. A typical reaction procedure for methano[60]fullerene **4d**: To a solution of [60]fullerene (72 mg, 0.1 mmol), SKA **3d** (105 mg, 0.5 mmol) and KF (29 mg, 0.5 mmol) in dry toluene (72 mL) was added 18-crown-6 (132 mg, 0.5 mmol). After this solution was stirred at rt for 24 h under Ar, the mixture was directly chromatographed on silica gel (eluent: hexane to chloroform) to give adduct **4d** (52.5 mg, 64%). ^{1}H NMR ($CDCl_3/CS_2$, 300 MHz): 1.51 (3H, t, $J=7.2$ Hz), 2.53 (3H, s), 4.51 (2H, q, $J=7.2$ Hz) ppm. ^{13}C NMR ($CDCl_3/CS_2$, 75 MHz): 14.18, 15.33, 44.04, 62.12, 76.36 (×2), 137.65, 137.80, 140.40, 140.62, 141.55, 141.63, 141.71, 141.77, 142.45, 142.53, 142.60, 142.64, 142.66, 142.78, 143.19, 143.41, 143.77, 144.07, 144.10, 144.18, 144.30, 144.37, 144.68, 144.71, 144.73 (×2), 145.06, 145.80, 147.07, 167.27 ppm. IR (KBr): 1740 (C=O), 523 (C_{60}) cm^{-1}. FAB-MSS: 820 (M^+). The other products (**4a**–**c**,**e**–**i**) were also identified by NMR, IR, and MSS spectroscopies.
10. There is only one report on the fluoride ion-promoted reaction of [60]fullerene with a silyl enol ether [(CH_2=CPh(OTMS)], giving methano[60]fullerene **4h**. However, the reaction is distinct from the present reaction; the reaction proceeds in air at a little higher temperature (60°C) via a radical intermediate. In addition, the yield of adduct **4h** is low (13% based on consumed [60]fullerene): Shu, L.-H.; Wang, G.-H.; Wu, H.-M. *J. Chem. Soc., Chem. Commun.* **1995**, 367.