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Controlled [3+2] and [2+2] Cycloadditions of 1,3-Bifunctional Allenes with C_{60} by Using a Flow Reaction System

Mitsuhiro Ueda,*[a] Miho Hayama,[a] Hiroyuki Hashishita,[a] Aiko Munechika,[a] and Takahide Fukuyama[a]

Dedication ((optional))

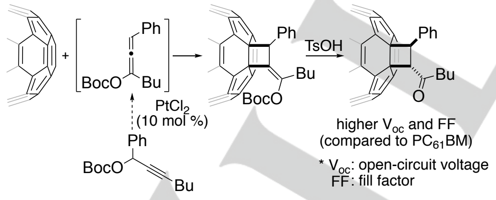
Abstract: The reaction of 1,2-diaryl-1,2-diketones, propiolic acid esters, and C_{60} in the presence of Et_3N gave cyclopentene-annulated fullerenes via [3+2] cycloaddition. They were formed in two Et_3N-promoted steps, namely, the generation of 1,3-bifunctional allenes and the cycloaddition of 1,3-bifunctional allenes with C_{60}. Interestingly, when a similar reaction was conducted using a flow packed-bed reactor in combination with a silica-supported tertiary amine, cyclobutane-annulated fullerenes were obtained via [2+2] cycloaddition.

Introduction

Ring-annulated fullerenes such as [6,6]-phenyl-C_{61}-butyric acid methyl ester (PCBM) exhibit outstanding performance as materials for organic solar cells[1] and organic-inorganic perovskite solar cells.[2] Their potential as materials for photovoltaics (PV) has triggered the development of efficient methods for the synthesis of novel ring-annulated fullerenes.[3,4,5]

In our previous work, we found that the allenol esters, which were generated *in situ* by the Pt-catalyzed 1,3-acyloxy migration of propargylic esters, reacted with C_{60} to give cyclobutane-annulated fullerenes as [2+2] cycloaddition products (Scheme 1).[3] The cyclobutane-annulated fullerenes were found to exhibit excellent performances as materials for organic photovoltaics (OPV) rather than PCBM-based devices. This inspired us to investigate other multi-substituted ring-annulated fullerenes.

Scheme 1. [2+2] Cycloaddition of the In Situ Generated Allenol Ester with C_{60} (Previous Work)



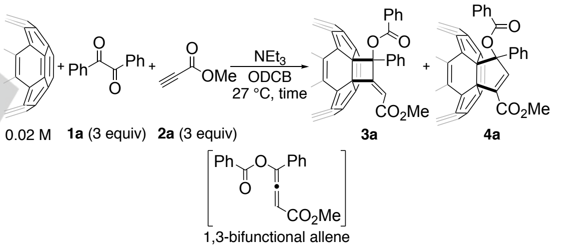
higher V_{oc} and FF (compared to $PC_{61}BM$)

* V_{oc}: open-circuit voltage
FF: fill factor

Results and Discussion

We commenced our next study by investigating the reaction of 1,3-bifunctional allenes, which are generated *in situ* by the Et_3N-catalyzed reaction of 1,2-diaryl-1,2-diketones with propiolic acid esters[6] and C_{60}. Contrary to our expectation, cyclopentene-annulated fullerene **4a** was formed as the major product instead of **3a** (**3a**:**4a** = 4:96, Table 1, entry 1).[7] A previous study has reported the formation of *mono-* and *di*-substituted cyclopentene-annulated fullerenes via phosphine-catalyzed [3+2] cycloadditions of allenoates with C_{60} (Scheme 2).[8] Our present findings provide access to further variations of functionalized cyclopentene-annulated fullerenes (Table 1). Optimization of the reaction conditions suggested that **4a** was selectively formed by the reaction in *o*-dichlorobenzene (ODCB) using 1 equiv Et_3N at 27 °C for 20 min (entry 3).

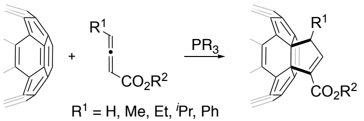
Table 1. Reaction of the In Situ Generated 1,3-Bifunctional Allene (from **1a** and **2a**) with C_{60}[a]



Entry	Equiv of NEt_3	Time	HPLC area (%)[b]			
			3a	**4a**	Others[c]	C_{60}
1	0.3	4 h	2	53	5	40
2	1	4 h	4	60	12	20
3	1	20 min	0	36 (32)[d]	2	62

[a] Reaction conditions: C_{60} (0.15 mmol), **1a** (3 equiv), **2a** (3 equiv), ODCB (7.5 mL), temperature: 27 °C. [b] Determined by the ratio of HPLC peak area. [c] Multiple cycloaddition products. [d] Isolated yield of **4a**.

Scheme 2. Phosphine-Catalyzed [3+2] Cycloaddition of Allenoates with C_{60}



R^1 = H, Me, Et, ^{i}Pr, Ph
R^2 = Et, Bn

With the optimum conditions (entry 3, Table 1) in hand, we next explored the scope of the Et_3N-promoted [3+2] cycloaddition of **1** and **2** with C_{60} (Table 2). The reaction of 4,4'-dimethylbenzil (**1b**)

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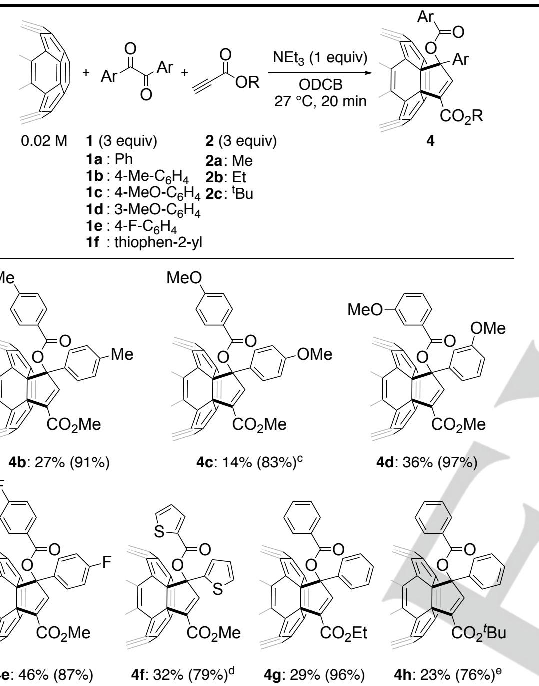
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate)) and **2a** with C_{60} produced the corresponding product **4b** in 27% yield. The reaction of 4,4'-dimethoxybenzil (**1c**) and **2a** with C_{60} also afforded the cyclopentene-annulated fullerene **4c**, albeit in a low yield (14%) due to the low solubility of **1c** in ODCB.[9] The reaction of 3,3'-dimethoxybenzil (**1d**) and **2a** with C_{60} gave the corresponding [3+2] cycloaddition product **4d** in 36% yield. The reaction of 4,4'-difluorobenzil (**1e**) and **2a** with C_{60} gave the cyclopentene-annulated fullerene **4e** in a good yield (46%). The reactivity of 2,2'-thenil (**1f**) was higher than that of **1a**, giving **4f** in 32% yield. Increasing the reaction time from 10 min to 20 min generated multiple cycloaddition products with increased yields.

Table 2. NEt_3-Promoted [3+2] Cycloaddition of the In Situ Generated 1,3-Bifunctional Allene (from **1** and **2**) with C_{60}[a]

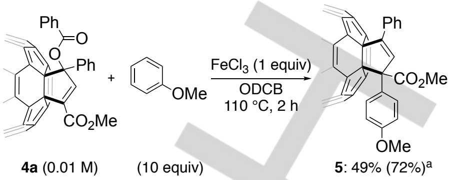


[a] Reaction conditions: C_{60} (0.15 mmol), **1** (3 equiv), **2** (3 equiv), NEt_3 (1 equiv), ODCB (7.5 mL), temperature: 27 °C, reaction time: 20 min. [b] Yields of **4** are the isolated yield. The values in parentheses are based on the amount of C_{60} consumed. [c] reaction time: 2 h. [d] reaction time: 10 min. [e] reaction time: 16 h.

Ethyl propiolate (**2b**) and tertiary butyl propiolate (**2c**) showed tolerance to the reaction conditions, furnishing the corresponding cyclopentene-annulated fullerenes **4g** and **4h** in 29% and 23% yields, respectively.

The obtained cyclopentene-annulated fullerenes **4** bore aryl carboxyl substituents, which could act as anionic leaving groups. Thus, **4a** was subjected to Friedel-Crafts type γ-addition with anisole and $FeCl_3$. As a result, the benzoyloxy group was successfully replaced by *p*-anisyl group to give 1,3-diaryl cyclopentene-annulated fullerene **5** in 49% isolated yield (Scheme 3).[10]

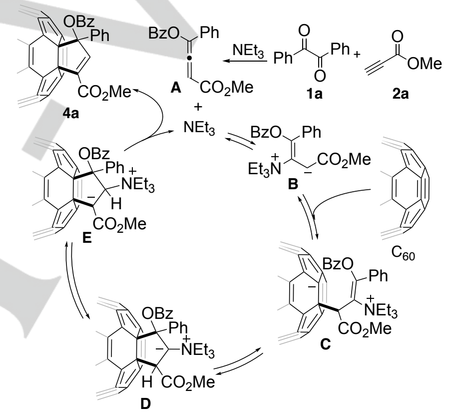
Scheme 3. Introduction of *p*-MeO-phenyl Group to **4a** by Fe-Promoted Friedel-Crafts Type γ-Addition



[a] Isolated yield of **5**. The value in parenthesis is HPLC yield of **5**.

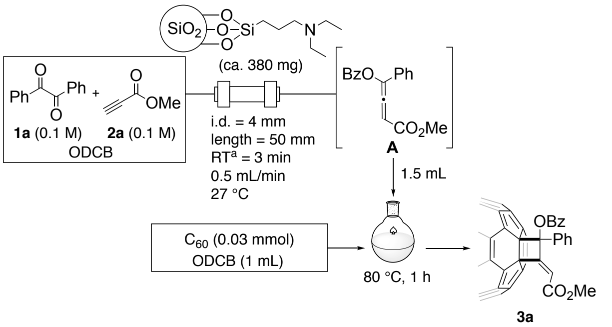
A plausible mechanism for the present [3+2] cycloaddition is illustrated in Scheme 4. The Et_3N-promoted reaction of benzil (**1a**) with methyl propiolate (**2a**) gives the 1,3-bifunctional allene **A**. Allene **A** in the presence of Et_3N is in equilibrium with the zwitterionic intermediate **B**, which reacts with C_{60} to give **D** via **C**. The subsequent 1,2-proton migration from **D** gives **E**. Finally, **E** liberates Et_3N to give **4a**.

Scheme 4. Plausible Reaction Mechanism of the NEt_3-Promoted [3+2] Cycloaddition



In our previous study, allenol esters were found to react with C_{60} to give [2+2] cycloaddition products (Scheme 1).[3] In contrast, the present reaction of 1,3-bifunctional allenes with C_{60} prefers the [3+2] cycloaddition pathway. This can be attributed to the rapid generation of the zwitterionic intermediate **B** by the existing NEt_3. We speculated that the reaction of 1,3-bifunctional allene **A** with C_{60} would also give the [2+2] cycloaddition product if we could design amine-free conditions. This led us to examine the reaction on a flow packed-bed reactor using silica-supported tertiary amine. Thus, the formed allene was introduced into a batch reactor containing C_{60} (Scheme 5).[11,12,13]

Scheme 5. [2+2] Cycloaddition of the Ex Situ Generated 1,3-Bifunctional Allene with C_{60} in Amine-free Conditions

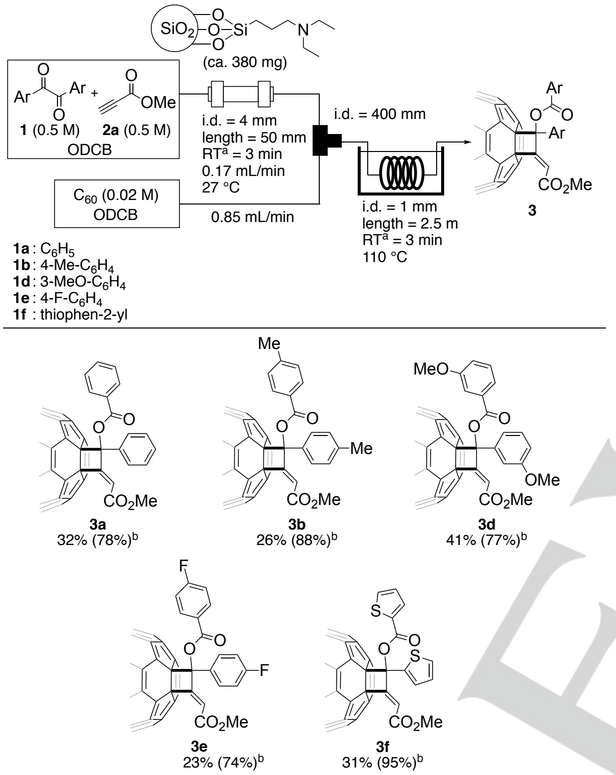


HPLC area (%)			
3a	**4a**	others[b]	C_{60}
31	0	4	65

[a] RT = residence time
[b] Multiple cycloaddition products

This worked quite well, and we then examined a serial flow reactor system consisting of a similar packed-bed reactor for allene generation and a flow tubular reactor for the subsequent [2+2] cycloaddition. To our delight, the *ex situ* generated allene **A** in the first column by silica-supported tertiary amine reacted with C_{60} in the second tubular reactor to give cyclobutane-annulated fullerene **3a** in a 32% yield (Scheme 6).[14] This continuous flow system could be extremely useful for the synthesis of other cyclobutane-annulated fullerenes **3**.

Scheme 6. [2+2] Cycloaddition of **1**, **2a**, and C_{60} Using a Flow Packed-bed Reactor in Combination with Silica-Supported Tertiary Amine[15,16]

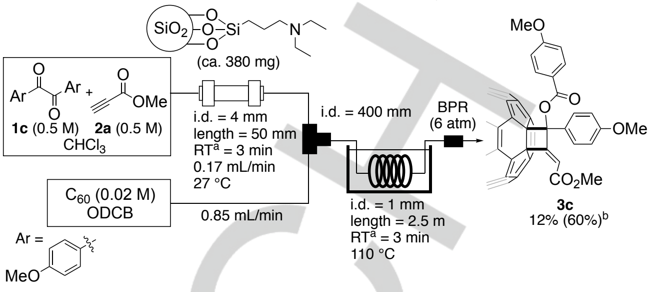


[a] RT = residence time
[b] Isolated yields of **3**. The values in parentheses are based on the amount of C_{60} consumed.

In a similar manner, the flow reaction of 4,4'-dimethylbenzil (**1b**), methyl propiolate (**2a**), and C_{60} using a silica-supported tertiary amine charged packed-bed reactor gave the desired cyclobutane-annulated fullerene **3b** in 26% yield. The reactivity of 3,3'-dimethoxybenzil (**1d**) and **2a** was higher than that of **1a** and **2a** (**3d**, 41%). The reaction of 4,4'-difluorobenzil (**1e**) and **2a** with C_{60} proceeded to form the cyclobutane-annulated fullerene **3e** in 23% yield. 2,2'-Thenil (**1f**) showed higher reactivity compared with **1a**, and a large amount of multiple cycloaddition products was formed at 110 °C. However, the yield of **3f** could be increased (31%) at a lower reaction temperature (60 °C).[17]

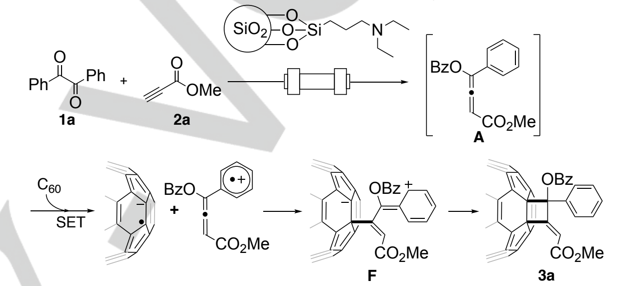
Due to the poor solubility of 4,4'-dimethoxybenzil (**1c**) in *o*-dichlorobenzene, the solvent was changed to $CHCl_3$ in the case of **1c** and **2a**.[9] This required a back-pressure regulator (6 atm) to suppress the gas evolution. In this way, the flow reaction of 4,4'-dimethoxybenzil (**1c**), methyl propiolate (**2a**), and C_{60} gave the desired cyclobutane-annulated fullerene **3c,** albeit in 12% yield (Scheme 7).

Scheme 7. [2+2] Cycloaddition of **1c**, **2a**, and C_{60} Using a Flow Packed-bed Reactor in Combination with Silica-Supported Tertiary Amine



[a] RT = residence time
[b] Isolated yield of **3c**. The value in parenthesis is based on the amount of C_{60} consumed.

Scheme 8. Plausible Reaction Mechanism of [2+2] Cycloaddition



A plausible mechanism for the [2+2] cycloaddition is illustrated in Scheme 8. The reaction of **1a** with **2a** by silica-supported tertiary amine generates the 1,3-bifunctional allene **A**. Under amine-free conditions, a single-electron transfer from the aryl group of **A** to C_{60} occurs to give a radical ion-pair consisting of the radical anion $C_{60}^{\bullet-}$ and a radical cation of **A**. $C_{60}^{\bullet-}$ reacts with the radical cation of **A** to give the [2+2] cycloaddition product **3a** via the zwitterionic intermediate **F**.[3]

Conclusions

In conclusion, we have developed the [3+2] cycloaddition of *in situ* generated 1,3-bifunctional allenes with C_{60} in the presence of Et_3N. In addition, the [2+2] cycloaddition of the same *in situ* generated 1,3-bifunctional allenes was achieved using a continuous flow packed-bed reactor and silica-supported tertiary amine. It is expected that the flow protocol developed in this work would prove to be a powerful tool for the synthesis of other ring-annulated fullerenes. Further studies on the application of these products in the field of materials science are currently in progress.

Experimental Section

Typical Procedure for NEt_3-Promoted [3+2] Cycloaddition of *in-situ* Generated 1,3-Bifunctional Allene with C_{60}

To a 50 mL screw capped test tube, C_{60} (0.15 mmol, 0.360 g), benzil (**1a**, 0.45 mmol, 3 equiv), methyl propiolate (**2a**, 0.45 mmol, 3 equiv), NEt_3 (0.15 mmol, 1 equiv), and ODCB (7.5 mL) were added. The mixture was stirred for 20 min at 27 °C. The reaction was monitored by analytical HPLC. After 20 min, MeOH was added to the reaction mixture, and the

10.1002/ejoc.201901072

sediment was filtered and washed with MeOH. The residue was purified by silica gel column chromatography eluting first with hexane to remove C_{60}, and then with toluene (R_f = 0.7 with toluene). The combined fractions were concentrated under reduced pressure giving the desired cyclopentene-annulated fullerene derivatives **4a** as a solid.

4a: Brown solid (47.6 mg, 32% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (3H, s), 7.34-7.38 (1H, m), 7.45-7.54 (4H, m), 7.61-7.67 (1H, m), 7.81 (2H, d, J = 7.2 Hz), 8.13 (2H, d, J = 7.6 Hz), 8.61 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.79, 74.77, 80.75, 98.58, 126.22, 127.66, 127.86, 128.95, 129.04, 129.31, 129.93, 130.07, 130.18, 130.23, 130.69, 132.73, 133.88, 134.36, 134.43, 134.57, 135.02, 135.50, 135.17, 139.21, 139.47, 140.06, 140.53, 141.88, 141.91, 142.01, 142.13, 142.55, 142.85, 142.97, 143.05, 144.80, 145.30, 145.89, 146.00, 146.16, 146.22, 146.33, 146.39, 146.63, 147.50, 147.67, 147.81, 148.43, 151.60, 152.50, 153.21, 153.75, 164.09, 164.83.
HRMS (ESI) m/z calcd for $C_{78}H_{14}O_4$ [M + Na^+]: 1037.0784, found: 1037.0761.

4b: Brown solid (42.2 mg, 27% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.34 (3H, s), 2.43 (3H, s), 4.02 (3H, s), 7.24-7.26 (2H, m), 7.28-7.31 (2H, m), 7.67 (2H, d, J = 8.4 Hz), 8.01 (2H, d, J = 6.4 Hz), 8.59 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.45, 21.90, 52.76, 74.72, 80.84, 98.39, 125.44, 126.07, 127.47, 128.37, 128.48, 129.18, 129.64, 130.00, 130.25, 134.99, 135.39, 135.97, 137.18, 137.66, 138.74, 139.25, 139.39, 139.43, 140.01, 141.63, 141.85, 142.01, 142.45, 142.53, 142.62, 142.81, 142.95, 143.26, 143.45, 144.70, 144.75, 145.25, 145.36, 145.76, 145.86, 146.19, 146.30, 146.34, 146.53, 146.60, 147.47, 147.64, 147.83, 148.47, 151.66, 152.62, 152.62, 153.42, 153.97, 164.16, 164.93.
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_4$ [M + Na^+]: 1065.1097, found 1065.1094.

4c: Brown solid (22.6 mg, 14% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (3H, s), 3.87 (3H, s), 4.02 (3H, s), 6.97 (4H, m), 7.71 (2H, d, J = 9.2 Hz), 8.06 (2H, d, J = 8.8 Hz), 8.59 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.77, 55.39, 55.71, 74.65, 81.04, 98.14, 113.74, 114.20, 114.42, 114.58, 114.87, 122.44, 127.45, 127.86, 128.46, 132.28, 132.53, 133.00, 133.88, 133.95, 134.08, 134.90, 135.33, 135.91, 137.20, 139.33, 139.39, 139.44, 140.07, 141.65, 141.85, 141.88, 142.09, 142.13, 142.36, 142.47, 142.62, 142.81, 142.95, 143.11, 143.25, 144.56, 144.74, 145.24, 145.35, 145.40, 145.49, 145.61, 145.75, 145.85, 145.95, 146.19, 146.26, 146.34, 46.51, 146.59, 147.48, 147.64, 147.79, 148.48, 151.64, 152.69, 152.86, 153.51, 153.74, 154.03, 159.73, 164.09, 164.19, 164.60.
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_6$ [M + Na^+]: 1097.0996, found 1097.1035.

4d: Brown solid (58.1 mg, 36% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (6H, s), 4.02 (3H, s), 6.87-6.90 (1H, m), 7.15-7.19 (2H, m), 7.33-7.34 (1H, m), 7.37-7.42 (2H, m), 7.68 (1H, dd, J = 2.8, 1.6 Hz), 7.74 (1H, dt, J = 7.6, 1.2 Hz), 8.60 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.81, 55.59 (two peaks overlap), 74.73, 80.61, 98.41, 112.89, 113.51, 121.39, 122.08, 122.78, 123.41, 127.85, 129.95, 130.18, 130.49, 130.67, 131.24, 134.35, 135.93, 137.03, 139.17, 139.43, 139.99, 141.61, 141.86, 141.94, 142.04, 142.12, 142.44, 142.53, 142.61, 142.83, 142.88, 142.93, 143.10, 143.21, 143.30, 144.37, 144.64, 144.76, 144.18, 145.26, 145.32, 145.41, 145.50, 145.50, 145.59, 145.74, 145.87, 145.97, 146.21, 146.30, 146.30, 146.52, 146.59, 147.46, 147.77, 148.40, 151.58, 152.40, 152.97, 152.83, 159.84, 160.18, 164.03, 164.64.
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_6$ [M + Na^+]: 1097.0996, found 1097.0995.

4e: Brown solid (72.5 mg, 46% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 (3H, s), 7.16 (4H, t, J = 8.0 Hz), 7.77 (2H, dd, J = 8.8, 5.2 Hz), 8.13 (2H, dd, J = 8.8, 5.6 Hz), 8.56 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$) δ 52.88, 74.69, 80.62, 98.18, 116.23 (d, J_{CF} = 22.0 Hz), 116.45 (d, J_{CF} = 21.0 Hz), 126.20, 126.23, 127.97, 128.02, 132.82 (d, J_{CF} = 9.5 Hz), 135.01, 135.40, 135.79, 136.50, 136.53, 137.04, 139.35, 139.48, 140.09, 141.54, 141.60, 141.66, 141.86, 141.90, 141.92, 142.09, 142.12, 142.43, 142.52, 142,63, 142.84, 142.86, 142.89, 143.01, 143.15, 143.22, 143.30, 143.32, 144.35, 144.65, 144.74, 145.00, 145.32,145.46, 145.52, 145.63, 145.67, 145.79, 145.82, 145.88, 146.00, 146.23, 146.34, 146.38, 146.41, 146.59, 146.61, 147.49, 147.67, 148.35, 151.32, 152.26, 152.84, 153.42, 162.81 (d, J_{CF} = 247.2 Hz), 163.84, 163.91, 166.39 (d, J_{CF} = 253.0 Hz).
HRMS (ESI) m/z calcd for $C_{78}H_{12}O_4F_2$ [M + Na^+]: 1073.0596, found 1073.0592.

4f: Brown solid (49.3 mg, 32% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.92 (3H, s), 7.12-7.17 (2H, m), 7.45 (1H, d, J = 5.2 Hz), 7.49 (1H, s), 7.64 (1H, dd, J = 4.4, 0.8 Hz Hz), 7.73 (1H, dd, J = 3.6, 0.8 Hz), 7.92 (1H, dd, J = 3.6, 1.2 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 53.56, 78.83, 81.14, 95.71, 127.56, 127.72, 127.86, 128.29, 129.24, 132.72, 134.06, 135.01, 135.64, 135.83, 136.10, 136.71, 137.06, 139.48, 139.55, 139.86, 140.07, 141.71, 141.75, 141.82, 141.88, 141.95, 142.17, 142.26, 142.60, 142.77, 142.89, 143.08, 143.20, 143.38, 144.51, 144.69, 144.92, 145.49, 145.55, 145.67, 145.81, 145.84, 146.28, 146.33, 146.62, 146.68, 147.20, 147.25, 147.56, 147.64, 147.69, 150.87, 151.67, 152.07, 153.22, 161.28, 169.34.
HRMS (ESI) m/z calcd for $C_{74}H_{10}O_4S_2$ [M + H^+]: 1027.0093, found 1027.6360.

4g: Brown solid (44.8 mg, 29% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.46 (3H, t, J = 7.6 Hz), 4.48 (2H, q, J = 7.6 Hz), 7.36 (1H, t, J = 7.2 Hz), 7.45-7.51 (4H, m), 7.63 (1H, t, J = 8.0 Hz), 7.81 (2H, d, J = 7.2 Hz), 8.14 (2H, dd, J = 8.4, 1.6 Hz), 8.60 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 14.42, 62.16, 74.73, 80.74, 98.52, 126.16, 128.94, 129.29, 130.21, 133.86, 134.97, 135.43, 135.91, 137.12, 139.15, 139.32, 140.03, 140.54, 141.51, 141.62, 141.81, 141.97, 142.08, 142.42, 142.50, 142.54, 142.60, 142.68, 142.80, 142.93, 143.08, 143.24, 143.31, 144.34, 144.62, 144.71, 144.75, 145.26, 145.39, 145.45, 145.45, 145.58, 145.71, 145.82, 145.94, 146.13, 146.27, 146.31, 146.27, 146.31, 146.52, 146.58, 147.44, 147.62, 147.87, 147.49, 151.62, 152.51, 153.24, 153.80, 163.62, 164.78.
HRMS (ESI) m/z calcd for $C_{79}H_{16}O_4$ [M + Na^+]: 1051.0941, found 1051.0924.

4h: Brown solid (36.5 mg, 23% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (9H, s), 7.36 (1H, q, J = 7.6 Hz), 7.44-7.54 (4H, m), 7.61-7.67 (1H, m), 7.81 (2H, d, J = 7.6 Hz), 8.15 (2H, d, J = 7.6 Hz), 8.48 (1H, s).
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.61, 28.43, 83.72, 85.38, 98.42, 125.44, 127.85, 128.37, 128.91, 129.17, 129.24, 130.06, 130.23, 130.28, 130.68, 133.12, 133.80, 135.03, 135.46, 135.89, 137.11, 138.01, 139.14, 139.21, 139.28, 140.04, 140.70, 141.54, 141.64, 141.67, 141.71, 141.80, 141.86, 141.99, 142.10, 142.18, 142.46, 142.50, 142.60, 142.80, 142.95, 143.11, 143.22, 144.18, 144.39, 144.63, 144.72, 144.82, 145.18, 145.27, 145.43, 145.47, 145.59, 145.71, 145.75, 145.81, 145.91, 145.96, 146.20, 146.29, 146.33, 146.37, 146.54, 146.61, 147.47, 147.63, 147.89, 148.70, 149.38, 151.89, 152.76, 153.42, 154.05, 162.84, 164.73,
HRMS (ESI) m/z calcd for $C_{81}H_{20}O_4$ [M + Na^+] 1079.1254, found 1079.1243.

5: Brown solid (24.5 mg, 49% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.84 (3H, s), 3.99 (3H, s), 6.93 (1H, s), 7.01 (2H, dt, J = 8.8, 3.2 Hz), 7.43-7.52 (3H, m), 7.83 (2H, dt, J =6.4, 1.6 Hz), 8.02 (2H, dt, J = 9.2, 3.2 Hz)
^{13}C NMR (100 MHz, $CDCl_3$): δ 53.26, 55.44, 74.12, 78.52, 80.29, 114.32, 128.59, 128.78, 129.89, 130.16, 132.16, 132.95, 134.42, 134.77, 135.70, 135.99, 136.33, 139.09, 139.13, 139.80, 140.02, 141.59, 141.76, 141.86, 141.90, 142.03, 142.71, 142.86, 143.07, 143.20, 144.35, 144.75, 144.51, 144.70, 145.03, 145.23, 145.31, 145.41, 145.46, 145.69, 145.88, 145.06, 146.11, 146.18, 146.21, 146.26, 146.39, 146.41, 146.44, 146.93, 147.39, 147.57, 148.85, 152.41, 153.65, 154.72, 155.53, 159.47, 173.05
HRMS (ESI) m/z calcd for $C_{78}H_{16}O_3$ [M + Na^+]: 1023.0992, found 1023.1000.

The structure of **5** was determined by HMBC, HMQC, and NOESY analysis.

Typical Procedure for [2+2] Cycloaddition of 1, 2a and C_{60} by Using a Flow Packed-Bed Reactor in Combination with Silica-Supported Tertiary Amine

Silica-supported tertiary amine (380 mg) was packed into a stainless steel column (i.d. = 4 mm, length = 2.5 m). An *o*-dichlorobenzene solution of **1a** (0.5 M) and **2a** (0.5 M) was feed into a column reactor at 27 °C to form 1,3-bifunctional allene (0.17 mL/min, RT = 3 min), and the resultant mixture was mixed with an *o*-dichlorobenzene solution of C_{60} (0.02 M, 0.85 mL/min) using a T-shaped micromixer (stainless-steel made, 400 μm channel diameter). The reaction mixture was passed through a residence time unit (110 °C, i.d. = 1 mm, length = 2.5 m, RT = 3 min). Consequently, we obtained the [2+2] cycloaddition product **3a** in 32% yield after the purification by silica gel column chromatography eluting first with hexane to remove C_{60}, and then with toluene (R_f = 0.7 with toluene).

3a: Brown solid (32% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.79 (3H, s), 5.55 (1H, s), 7.48-7.60 (6H, m), 8.16-8.20 (4H, m).
^{13}C NMR (100 MHz, $CDCl_3$): δ 51.46, 78.03, 83.46, 90.73, 96.64, 126.54, 127.03, 128.31, 128.72, 129.10, 129.29, 129.57, 130.38, 130.74, 131.24, 131.69, 137.30, 139.11, 139.38, 139.59, 139.72, 140.08, 140.18, 140.61, 141.79, 141.94, 142.10, 142.20, 142.38, 142.45, 142.59, 142.76, 142.89, 143.04, 143.32, 143.40, 143.98, 144.23, 144.41, 144.49, 145.30, 145.34, 145.46, 145.54, 145.56, 145.61, 145.66, 145.77, 145.97, 146.04, 146.17, 146.19, 146.28, 146.33, 146.38, 146.49, 146.61, 146.92, 147.15, 147.30, 148.29, 148.91, 149.39, 149.87, 150.74, 151.28, 153.12, 154.95, 165.14, 165.42.
HRMS (ESI) m/z calcd for $C_{78}H_{14}O_4$ [M + Na$^+$]: 1037.0784, found: 1037.0777.

3b: Brown solid (26% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.42 (6H, s), 3.79 (3H, s), 5.54 (1H, s), 7.37 (4H, t, *J* = 6.8 Hz), 8.06 (4H, t, *J* = 8.0 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 21.68, 22.09, 51.57, 78.21, 83.47, 90.54, 92.00, 96.72, 115.13, 121.59, 126.51, 127.01, 127.66, 128.37, 128.87, 129.18, 129.45, 129.53, 129.85, 130.01, 130.17, 130.48, 130.81, 134.36, 136.06, 136.73, 137.32, 138.98, 139.14, 139.50, 139.65, 139.71, 140.12, 140.20, 140.46, 141.74, 141.85, 141.99, 142.50, 142.81, 142.94, 144.31, 144.48, 144.57, 145.18, 145.30, 145.36, 145.41, 145.45, 145.53, 145.59, 145.68, 146.03, 146.10, 146.24, 146.38, 146.54, 146.77, 146.97, 147.13, 147.22, 147.36, 148.60, 149.23, 149.77, 150.28, 151.23, 151.80, 165.51, 166.00.
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_4$ [M + Na$^+$]: 1065.1097, found 1065.1093.

3c: Brown solid (12% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (3H, s), 3.88(3H, s), 3.89 (3H, s), 5.61 (1H, s), 7.02-7.07 (2H, m), 7.49 (2H, dt, *J* = 8.4, 2.0 Hz), 7.70-7.74 (3H, m), 7.79 (1H, dq, *J* = 7.6, 1.2 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 51.60, 55.51, 55.77, 77.36, 83.55, 90.45, 96.65, 114.14, 114.42, 114.47, 114.72, 115.07, 123.59, 123.86, 125.43, 126.43, 127.95, 128.35, 128.58, 129.16, 132.50, 136.71, 137.23, 137.99, 138.97, 139.12, 139.67, 139.74, 140.14, 140.21, 141.73, 141.76, 141.86, 141.99, 142.15, 142.20, 142.26, 142.39, 142.50, 142.59, 142.69, 142.80, 142.93, 143.03, 143.10, 144.28, 144.47, 144.55, 144.62, 145.34, 145.44, 145.51, 145.57, 145.68, 146.07, 146.20, 146.39, 146.52, 146.86, 147.07, 147.21, 147.36, 148.57, 149.21, 149.82, 150.38, 160.38, 161.16, 165.49, 166.19,
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_6$ [M + Na$^+$]: 1097.0996, found 1097.0994.

3d: Brown solid (41% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.81 (3H, s), 3.888 (3H, s), 3.894 (3H, s), 5.61 (1H, s), 7.02-7.07 (2H, m), 7.49 (2H, dt, *J* = 8.4, 2.0 Hz), 7.72-7.74 (3H, m), 7.79 (1H, dq, *J* = 7.6, 1.2 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 51.60, 55.62, 55.74, 78.05, 83.29, 90.84, 96.55, 112.88, 112.94, 114.68, 114.77, 115.92, 119.04, 119.58, 130.04, 130.39, 132.63, 133.08, 136.65, 137.39, 138.95, 139.16, 139.62, 139.67, 140.13, 140.16, 141.72, 141.82, 142.00, 142.12, 142.16, 142.22, 142.25, 142.41, 142.47, 142.51, 142.65, 142.82, 142.94, 143.03, 143.11, 144.28, 144.46, 144.54, 145.25, 145.36, 145.45, 145.50, 145.58, 145.62, 145.67, 145.72, 146.03, 146.10, 146.18, 146.20, 146.23, 146.39, 146.44, 146.54, 146.90, 147.08, 147.21, 147.35, 148.33, 148.94, 149.50, 149.83, 159.73, 160.25, 165.32, 165.40, 165.46.
HRMS (ESI) m/z calcd for $C_{80}H_{18}O_6$ [M + Na$^+$]: 1097.0996, found 1097.0995.
The *E*/*Z* configuration of **3d** was determined by HMBC, HMQC, and NOESY analysis.

3e: Brown solid (23% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (3H, s), 5.53 (1H, s), 7.24-7.32 (4H, m), 8.16-8.23 (4H, m).
^{13}C NMR (100 MHz, $CDCl_3$): δ 51.70, 77.36, 90.98, 96.42, 100.13, 113.83, 114.66, 116.07 (d, J_{CF} = 21.9 Hz), 116.62 (d, J_{CF} = 22.0 Hz), 116.68, 117.34, 122.83, 123.43, 127.63, 127.81, 128.53 (d, J_{CF} = 8.6 Hz), 129.23 (d, J_{CF} = 8.6 Hz), 129.55, 129.65, 129.68, 129.76, 130.07, 132.00, 132.07, 132.88, 133.02, 133.18, 136.21, 136.76, 136.80, 138.18, 139.05, 139.80, 141.79, 142.09. 142.24, 142.39, 143.15, 144.49, 145.40, 145.79, 146.09, 146.15, 146.29, 146.45, 146.60, 147.30, 148.00, 148.50, 148.62, 149.08, 149.45, 149.60, 152.22, 152.30, 156.19, 156.74, 157.86, 160.37, 160.80, 162.24, 163.99 (d, J_{CF} = 250.1 Hz), 164.94 (d, J_{CF} = 259.6 Hz), 166.85.
HRMS (ESI) m/z calcd for $C_{78}H_{12}O_4F_2$ [M + Na$^+$]: 1073.0596, found 1073.0560.

3f: Brown solid (31% yield).
^{1}H NMR (400 MHz, $CDCl_3$): δ 3.74 (3H, s), 5.54 (1H, t, *J* = 2.0 Hz), 6.54 (1H, dd, *J* = 6.0, 2.4 Hz), 6.66 (1H, dd, *J* = 6.0, 1.6 Hz), 6.99 (1H, s), 7.16-7.20 (1H, m), 7.68 (1H, d, *J* = 4.8 Hz), 8.03 (1H, d, *J* = 3.6 Hz).
^{13}C NMR (100 MHz, $CDCl_3$): δ 52.33, 62.83, 67.91, 71.11, 108.16, 111.58, 112.75, 116.09, 116.37, 118.67, 124.27, 128.26, 128.68, 129.17, 132.13, 133.84, 135.30, 135.87, 136.73, 139.42, 139.62, 139.77, 139.96, 140.21, 141.52, 141.68, 141.74, 141.78, 141.85, 141.99, 142.03, 142.35, 142.38, 142.50, 142.61, 142.89, 142.92, 143.04, 143.14, 143.21, 143.25, 143.80, 144.68, 144.76, 144.88, 144.91, 144.97, 145.53, 145.58, 145.66, 145.73, 145.82, 145.88, 146.08, 146.34, 146.45, 146.53, 146.58, 146.75, 146.79, 146.82, 147.02, 147.75, 147.83, 147.85, 150.99, 151.03, 151.17, 151.24, 154.82, 155.54, 157.23, 165.57 (two peaks over-lap).
HRMS (ESI) m/z calcd for $C_{74}H_{10}O_4S_2$ [M + Na$^+$]: 1048.9913, found 1048.9915.

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Keywords: [3+2] cycloaddition • [2+2] cycloaddition • 1,3-bifunctional allene • flow packed-bed reactor • silica-supported tertiary amine

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[14] The mixture of **1a**, **2a**, C_{60} and silica-supported tertiary amine in batch system gave cyclopentene-annulated fullerene **4a** selectively.

[15] Silica-supported tertiary amine: 380 mg (amine: ca. 0.27 mmol, see: ref. 10-f). Catalyst loading: 106 mol % for **1a** (RT = 3 min, flow rate = 0.17 mL/min).

[16] The lower temperature conditions (80 °C) in a residence time unit occurred to decrease the conversion.

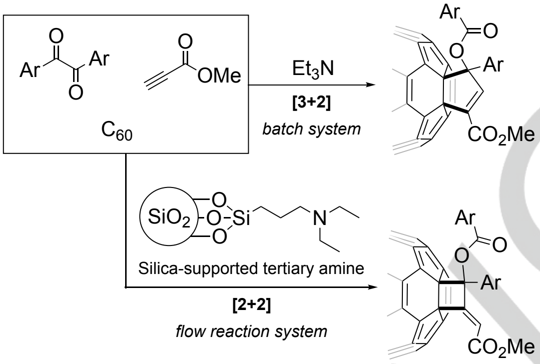
[17] The flow reaction of **1e**, **2a** and C_{60} at 60 °C gave **3e** in lower yield due to the low conversion.

Entry for the Table of Contents (Please choose one layout)

Layout 1:

COMMUNICATION

The reaction of 1,2-diaryl-1,2-diketones, propiolic acid esters, and C_{60} in the presence of Et_3N gave cyclopentene-annulated fullerenes via [3+2] cycloaddition. Interestingly, cyclobutane-annulated fullerenes were obtained via [2+2] cycloaddition when a similar reaction was conducted using a flow packed-bed reactor in combination with a silica-supported tertiary amine.



Silica-supported tertiary-amine*

Mitsuhiro Ueda, Miho Hayama, Hiroyuki Hashishita, Aiko Munechika, Takahide Fukuyama*

Page No. – Page No.

Controlled [3+2] and [2+2] Cycloadditions of 1,3-Bifunctional Allenes with C_{60} by Using a Flow Reaction System

*one or two words that highlight the emphasis of the paper or the field of the study