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PAPER

Study on the thermal reactions of [60]fullerene with amino acids and amino acid esters†

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Thermal reactions of [60]fullerene with a series of amino acids and amino acid esters under aerobic and dark conditions have been investigated. Fulleropyrrolidines can be obtained from these reactions although an aldehyde is not added purposely. Possible reaction mechanisms involving uncommon C–N bond cleavages have been proposed to generate aldehydes, which then react with amino acids and amino acid esters to provide azomethine ylides, followed by 1,3-dipolar cycloaddition to [60]fullerene affording fulleropyrrolidines. Control experiments support our proposed mechanisms, and elucidate the innate nature of C–N bond cleavages of amino acids and amino acid esters.

Introduction

Many years have elapsed since the discovery of fullerenes, but their chemical modifications continue to be of great appeal due to the potential applications of fullerene derivatives in many fields of life and materials sciences.[1] Amino acids and their derivatives are important biological molecules. They have been utilized to functionalize [60]fullerene (C_{60}) *via* the Prato reaction, *i.e.*, 1,3-dipolar cycloaddition of azomethine ylides to C_{60}.[2] Azomethine ylides are generated *in situ* from the decarboxylation of iminium salts derived from the condensation of amino acids with aldehydes/ketones or from the formal 1,2-H shift of imines of amino acid esters. The formed fulleropyrrolidine derivatives have recently been employed as the acceptors of photovoltaic solar cells with a power conversion efficiency (PCE) of up to 3.44% and are superior to methyl [6,6]-phenyl-C61-butylate ([C60]-PCBM) under the same conditions.[3] Fulleropyrrolidines can also be further transformed to ionic fullerene derivatives and applied to supramolecular assemblies.[1d]

Compared to the extensive application of amino acids and their derivatives in the Prato reaction, much fewer reports on the functionalization of C_{60} using amino acids or amino acid esters alone have been described. Gan's group and others have disclosed a few photochemical reactions between amino acid esters and C_{60}.[4] Gan and co-workers have also investigated the reactions of amino acid esters with C_{60} in the presence of iodo reagents under ultrasonification.[5] We have explored the reaction of C_{60} with amino acid ester hydrochlorides by using triethylamine (Et_3N) as a base to remove HCl.[6,7] We found that the reaction in CS_2 at room temperature proceeded well and afforded fullerene products containing amino acid ester, thioamide and thiourea units.[6] In contrast, the reaction in refluxing *o*-dichlorobenzene (ODCB) gave fulleropyrrolidine derivatives containing the CH_3CH moiety originated from an unusual C–N bond cleavage of Et_3N. The fulleropyrrolidines were formed through the reaction of C_{60} with azomethine ylides from amino acids and acetaldehyde, which in turn were generated by the hydrolysis of the amino acid ester hydrochlorides in the presence of Et_3N and by the fragmentation/oxidization of Et_3N, respectively.[7] On the other hand, studies on the direct thermal reaction of C_{60} with amino acids themselves are scarce. Gan and co-workers investigated the reaction of C_{60} with glycine or alanine in the presence of sodium hydroxide and obtained complex mixtures of multiadducts.[8] Herein, we report the direct thermal reactions of C_{60} with a series of amino acids and amino acid esters in the absence of an aldehyde and under aerobic and dark conditions affording isolable monoadducts.[9,10] More importantly, we have gained a mechanistic insight into these reactions deduced from the structural motifs of isolated products and control experiments.

Results and discussion

In our preliminary communication,[10] we reported the thermal reaction of C_{60} with a few amino acids. In order to extend the substrate scope and better understand the reaction mechanism,

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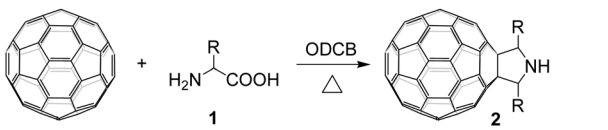
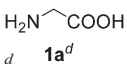
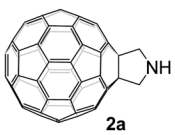
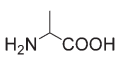
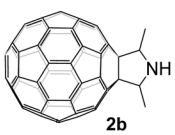
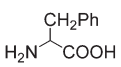
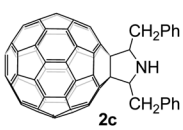
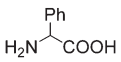
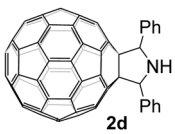
† Electronic supplementary information (ESI) available: NMR spectra of products **2a–2d**, **4a–4d**, **5b**, **5c**, **7a–7d**, **8a–8c**, **9** and **10c**. See DOI: 10.1039/c2ob26066b

we have extended the thermal reaction of C_{60} with more amino acids as well as that with amino acid esters. In contrast to the previous experimental procedure,[10] and for rational comparison amongst the reactions of C_{60} with different amino acids and amino acid esters, the concentration of C_{60} was kept constant; a sealed tube instead of a conventional flask was used for the reaction to prevent any loss of the volatile starting materials or *in situ* generated intermediates; the reaction temperature was 180 °C and 10 equiv. of amino acid/amino acid ester were used in most cases.

We first systematically explored the thermal reaction of C_{60} with representative *N*-unsubstituted amino acids, that is, glycine (**1a**), alanine (**1b**), phenylalanine (**1c**) and phenylglycine (**1d**). Among the employed *N*-unsubstituted amino acids, **1a–1c** are naturally occurring amino acids. To avoid the potential interference of a photochemical reaction,[4] the thermal reaction of C_{60} was conducted under dark conditions. Intriguingly, the products from the thermal reaction of C_{60} with **1a–1d** in refluxing ODCB in the presence of air proved to be *N*-unsubstituted fulleropyrrolidines **2a–2d**, instead of aminated fullerene derivatives.[8] It was found that the presence of oxygen was crucial for the thermal reaction, as strict exclusion of oxygen from the reaction mixture by a freeze–pump–thaw procedure failed to provide **2a–2d**.[11] The reaction conditions and product yields for the reaction of C_{60} with **1a–1d** are listed in Table 1. It should be pointed out that the reactions with both glycine and alanine were much more sluggish and required higher temperature than those with phenylalanine and phenylglycine, probably due to the lower solubility of the former two amino acids.

Table 1 Reaction conditions and product yields for the reaction of C_{60} with **1a–1d**[a]



Substrate **1**	T[b] (°C)	Reaction time (h)	Product **2**	Yield[c] (%)
 **1a**[d]	200	24	 **2a**	19 (51)
 **1b**	200	48	 **2b**	35 (56)[e]
 **1c**	180	12	 **2c**	19 (66)[f]
 **1d**	180	10	 **2d**	37 (66)[g]

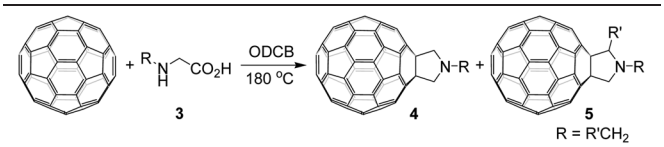
[a] Unless indicated otherwise, all reactions were performed with C_{60} (0.05 mmol) and 1 (0.5 mmol) in ODCB (6 mL). [b] Refers to the temperature of oil bath. [c] Isolated yield; those in parentheses were based on consumed C_{60}. [d] 1 mmol of **1a** was used. [e] *Trans*/*cis* ratio = 1 : 3.6. [f] *Trans*/*cis* ratio = 1.1 : 1. [g] *Cis* isomer only.

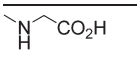
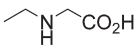
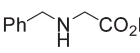
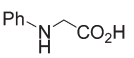
Products **2a–2d** are known compounds, and their identities were confirmed by comparison of their spectra with those reported in the literature.[12–14] The structures of adducts **2a–2d** are the same as those of products formed by the Prato reaction of C_{60}, **1a–1d** and the aldehydes generated *in situ* from **1a–1d** *via* the apparent elimination of the COOH and NH_2 groups. It should be noted that there are *trans* and *cis* isomers depending on the different orientation of the two R substituents when R ≠ H. Products **2b** and **2c** existed as a mixture of *trans* and *cis* isomers while product **2d** consisted of only the *cis* isomer. The exact same phenomenon was also observed for the corresponding Prato reactions.[13]

Secondly, typical *N*-substituted amino acids, *i.e.*, *N*-methylglycine (sarcosine) (**3a**), *N*-ethylglycine (**3b**), *N*-benzylglycine (**3c**) and *N*-phenylglycine (**3d**), were chosen to react with C_{60} in refluxing ODCB under aerobic and dark conditions. The reaction of C_{60} with **3b** and **3c** afforded two types (**4b**, **5b** and **4c**, **5c**) of monoadducts, whereas that with **3a** and **3d** provided only one type (**4a** and **4d**) of monoadducts. The reaction conditions and product yields for the reaction of C_{60} with **3a–3d** are listed in Table 2.

Adducts **4a–4d**, **5b** and **5c** also prove to be fulleropyrrolidines. Among them, products **4a**,[12] **4b**,[15] **4c**[16] and **5c**[17] are known compounds, and their structures are confirmed by comparison of their spectral data with those reported previously. The HRMS spectra of **4d** and **5b** showed correct molecular ions. The ^{1}H NMR spectrum of **4d** exhibited the signals for a phenyl

Table 2 Reaction conditions and product yields for the reaction of C_{60} with **3a–3d**[a]



Substrate **3**	Reaction time (h)	Yield of **4**[b] (%)	Yield of **5**[b] (%)
 **3a**	10	30 (81)	—
 **3b**	2.5	33 (58)	11 (19)
 **3c**	28	22 (45)	23 (47)
 **3d**[c]	1.5	36 (71)	—

[a] Unless indicated otherwise, all reactions were performed with C_{60} (0.05 mmol) and **1** (0.5 mmol) in ODCB (6 mL) at 180 °C. [b] Isolated yield; those in parentheses were based on consumed C_{60}. [c] 0.1 mmol of **3d** was used.

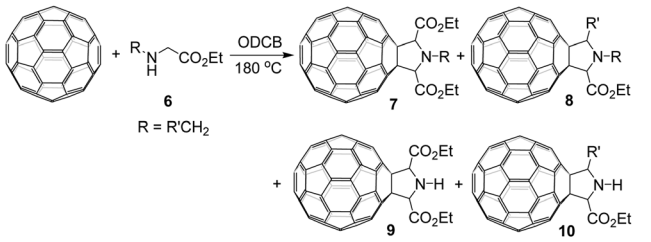
group and a singlet at 5.14 ppm for the two methylene groups. The ^{13}C NMR spectrum of **4d** displayed 16 lines for the 58 sp^2-carbons of the C_{60} skeleton along with a peak at 69.23 ppm for the two sp^3-carbons of the C_{60} core, consistent with its C_{2v} molecular symmetry. The ^1H NMR spectrum of **5b** gave two doublets at 4.88 and 3.98 ppm with J_{AB} = 9.2 Hz for the CH_2 group attached to the fullerene cage, two double quartets at 3.50 (J = 12.0, 7.4 Hz) and 2.73 (J = 12.0, 7.0 Hz) ppm, a triplet at 1.53 ppm (J = 7.2 Hz) for the ethyl group, a quartet at 4.02 ppm (J = 6.3 Hz), and a doublet at 1.95 ppm (J = 6.3 Hz) for the $CHCH_3$ moiety. The ^{13}C NMR spectrum of **5b** revealed 49 peaks in the 136–157 ppm range for the 58 sp^2-carbons of the C_{60} cage and two peaks at 75.89 and 69.20 ppm for the two sp^3-carbons of the C_{60} skeleton, consistent with its C_1 molecular symmetry. Adducts **4a–4d** appeared to be the Prato reaction products of C_{60}, **3** and CH_2O generated *in situ* from **3** through the apparent extrusion of the COOH and RNH moieties. Meanwhile, **5b** and **5c** might be similarly formed by the reaction of C_{60} with **3** and R′CHO (when R = R′CH_2), which was produced *via* an oxidative cleavage of the R′CH_2–N bond of **3**.

Finally, the corresponding *N*-substituted amino acid esters including sarcosine ethyl ester (**6a**), *N*-ethylglycine ethyl ester (**6b**), *N*-benzylglycine ethyl ester (**6c**) and *N*-phenylglycine ethyl ester (**6d**) were allowed to react with C_{60} under the same conditions as for *N*-substituted amino acids. Although **6c** and **6d** were commercially available, **6a** and **6b** were supplied as hydrochlorides. The *in situ* generation of **6a** and **6b** from their hydrochlorides in the presence of Et_3N during the reaction with C_{60} may cause hydrolysis of the amino acid ester hydrochlorides.[7] Therefore, **6a** and **6b** were prepared by the neutralization of sarcosine ethyl ester hydrochloride and *N*-ethylglycine ethyl ester hydrochloride with dilute aqueous solution of K_2CO_3 prior to use. The reaction conditions and product yields for the reaction of C_{60} with **6a–d** are listed in Table 3.

All adducts **7–10** were identified as fulleropyrrolidines. Among them, products **7a**,[17] **8a**,[4a] **9**[4a,17] and **10c**[18] are known compounds, and their structures are substantiated by comparison of their spectral data with those reported in the literature. Compounds **7b**, **7c**, **7d**, **8b** and **8c** exhibited correct molecular weights in their high-resolution mass spectra and the expected chemical shifts as well as the splitting patterns for all protons in their ^1H NMR spectra. In the ^{13}C NMR spectrum of **7b–7d**, there were no more than 28 peaks in the 135–154 ppm range for the 58 sp^2-carbons of the C_{60} cage and one peak at ~71 ppm for the two sp^3-carbons of the C_{60} skeleton, consistent with their C_2 molecular symmetry. In comparison, 51 lines in the range of 136–157 ppm for the 58 sp^2-carbons of the C_{60} cage along with two lines at *ca.* 71 and 75/76 ppm for the two sp^3-carbons of the C_{60} skeleton were observed in the ^{13}C NMR spectrum of **8b** and **8c**, agreeing with their C_1 molecular symmetry.

The reaction of C_{60} with amino acid esters was much more complex than that with the corresponding amino acids. Adducts **7** and **8** could be envisioned as the products from the reaction of C_{60} with **6** and aldehydes (EtO_2CCHO and R′CHO when R = R′CH_2), which were produced from apparent C–N oxidative cleavages of RNH–CH_2CO_2Et and R′CH_2–$NHCH_2CO_2Et$ (when R = R′CH_2), respectively. Meanwhile, **9** and **10** might be formed from the reaction of C_{60} with the *in situ* generated aldehydes and $NH_2CH_2CO_2Et$.

Table 3 Reaction conditions and product yields for the reaction of C_{60} with **6a–6d**[a]

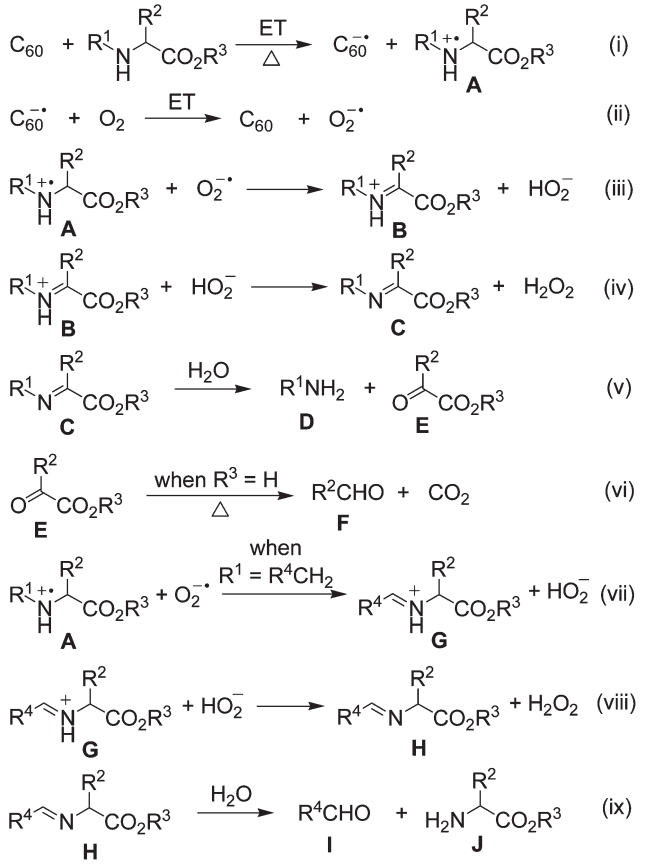


Substrate **6**	Reaction time (h)	Yield of **7**[b,c] (%)	Yield of **8**[b,c] (%)	Yield of **9**[b] (%)	Yield of **10**[b] (%)
6a	4	24 (44)	9 (16)	3 (5)[e]	—
6b	2	31 (56)	13 (24)	4 (7)[f]	—
6c	0.7	16 (30)	10 (19)	13 (25)[g]	0.7 (1)
6d[d]	75	11 (22)	—	—	—

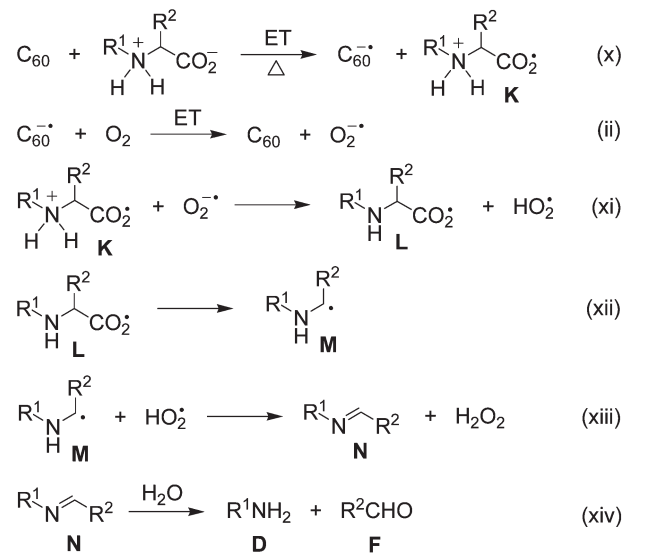
[a] Unless indicated otherwise, all reactions were performed with C_{60} (0.05 mmol) and **6** (0.5 mmol) in ODCB (6 mL) at 180 °C. [b] Isolated yield; those in parentheses were based on consumed C_{60}. [c] *Trans* isomer only. [d] 1.0 mmol of **6d** was used. [e] *Trans*/*cis* ratio = 1 : 3.6. [f] *Trans*/*cis* ratio = 1 : 3.5. [g] *Trans*/*cis* ratio = 1 : 3.3.

Primary and secondary amines can react with C_{60} thermally to give aminated products.[8,19] At first glance, it was surprising that fulleropyrrolidines were obtained from the direct thermal reaction of C_{60} with amino acids or amino acid esters in the absence of a purposely added aldehyde under aerobic and dark conditions. Although the exact pathways for the observed products from the thermal reaction of C_{60} with amino acids **1** and **3** as well as amino acid esters **6** remain to be clarified, structural motifs of the isolated products were sufficient to allow us to deduce the plausible reaction mechanisms (Schemes 1–3). The mechanisms for the formation of all potential intermediates involving C–N bond cleavages of amino acids and amino acid esters are generalized in Schemes 1 and 2, and the subsequent 1,3-dipolar cycloaddition reactions with C_{60} affording fulleropyrrolidines are shown in Scheme 3.

Electron transfer from amino acids/amino acid esters to C_{60} gives cation radical **A** and anion radical $C_{60}^{-\cdot}$ (step i),[7,19] the latter transfers an electron to O_2 to afford $O_2^{-\cdot}$ and regenerate C_{60} (step ii).[20] Hydrogen abstraction at the α-carbon adjacent to the carbonyl group of **A** by $O_2^{-\cdot}$ produces iminium cation **B** and HO_2^- (step iii),[4,7] subsequent proton transfer provides imine **C** and H_2O_2 (step iv). Under heating conditions, H_2O_2 can decompose to H_2O and O_2. Hydrolysis of **C** generates amine **D** and carbonyl compound **E** (step v).[7,21] When R^3 = H in **E**, it eliminates CO_2 to give aldehyde **F** upon heating (step vi).[22] Meanwhile, hydrogen abstraction at the α-carbon adjacent to R^4 (when $R^1 = R^4CH_2$) of **A** by $O_2^{-\cdot}$ attains iminium cation **G** and HO_2^- (step vii). Proton transfer from **G** to HO_2^- furnishes imine



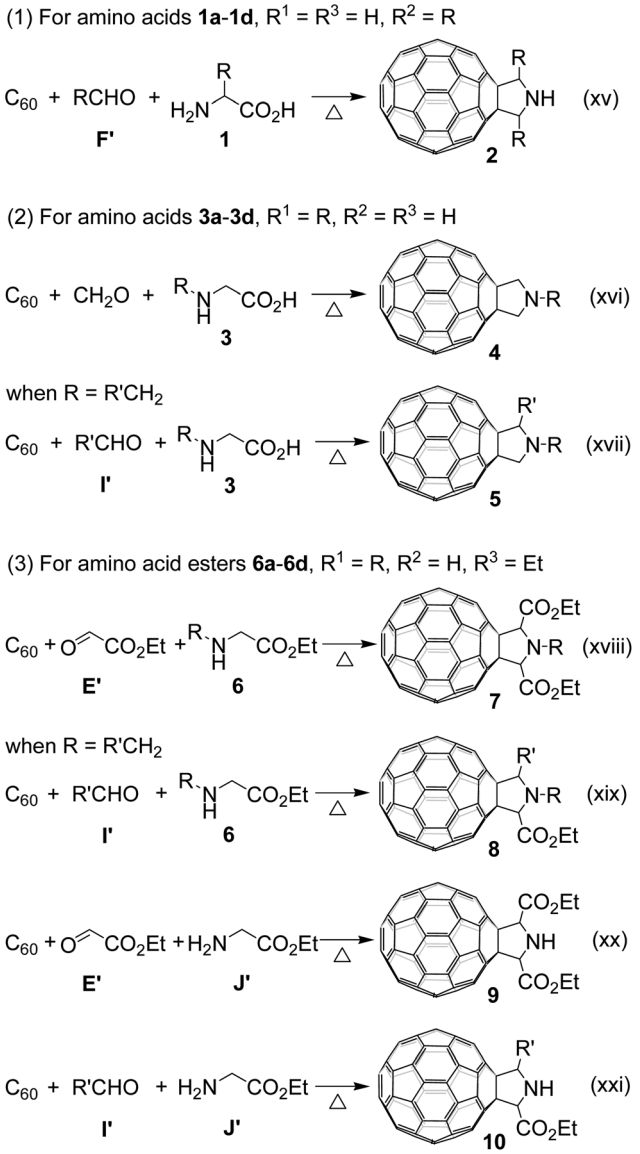
Scheme 1 Possible mechanisms for C–N bond cleavages of amino acids and amino acid esters.



Scheme 2 Alternative pathway to generate aldehydes from amino acids.

H and H_2O_2 (step viii), subsequent hydrolysis of **H** produces aldehyde **I** and amino acid/amino acid ester **J** (step ix).[7,21]

An alternative pathway leading to the formation of aldehydes R^2CHO (**F**) from amino acids is shown in Scheme 2. Electron transfer from a zwittionic amino acid to C_{60} affords the cationic radical **K** and $C_{60}^{-\cdot}$ (step x),[4b] followed by the same step ii to form $O_2^{-\cdot}$ and regenerate C_{60} (step ii). Proton transfer from **K** to $O_2^{-\cdot}$ furnishes radical **L** and $HO_2^{\cdot}$ (step xi). Loss of CO_2 from **L** gives radical **M** (step xii),[23] from which a hydrogen abstraction by $HO_2^{\cdot}$ provides imine **N** (step xiii). Hydrolysis of imine **N** produces amine R^1NH_2 (**D**) and R^2CHO (**F**) (step xiv).[7,21]



Scheme 3 1,3-Dipolar cycloaddition reactions with C_{60} affording fulleropyrrolidines.

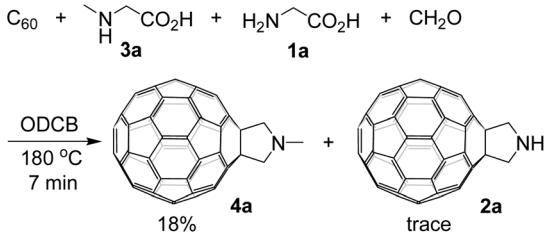
For amino acids **1a–1d**, $R^1 = R^3 = H$, $R^2 = R$, aldehyde RCHO (**F′**) is generated through steps i–vi and/or steps x–xiv. The 1,3-dipolar reaction of C_{60} with **1a–1d** and aldehyde **F′** leads to fulleropyrrolidines **2a–2d** (step xv). We previously found that the *cis*/*trans* isomeric ratio of **2b** and **2c** was heavily dependent on the reaction conditions.[13] The reaction of C_{60} with **1b** and acetaldehyde in refluxing toluene (110 °C) for 27 h led to 21% of *trans*-**2b** and 5% of *cis*-**2b**, and the isolated isomeric mixture of **2b** was then heated in refluxing ODCB (180 °C) for 12 h to afford a mixture dominated by the *cis* isomer.[13] The

direct reaction of C_{60} with **1b** at 200 °C for 2 d gave *cis*-**2b** as the major product (Table 1, entry 2). When the same reaction was conducted at lower temperature (180 °C for 4 d), *trans*-**2b** and *cis*-**2b** were obtained in 8% and 6% yields, respectively. A similar behavior was also observed for the reaction with **1c**. Thus, a higher reaction temperature tended to give a higher *cis*/*trans* isomeric ratio in our current cases. These experimental results support the above proposed mechanisms for the formation of aldehydes from amino acids, followed by 1,3-dipolar cycloaddition with C_{60} to produce fulleropyrrolidines.[13]

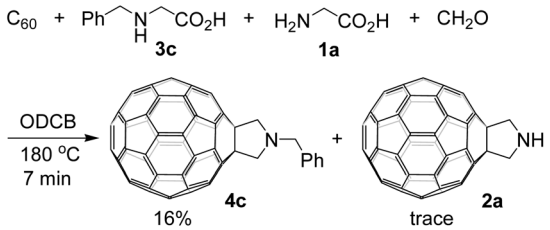
For amino acids **3a–3d**, R^1 = R, R^2 = R^3 = H, formaldehyde CH_2O is formed *via* steps i–vi and/or steps x–xiv, while aldehyde R′CHO (CH_2O, CH_3CHO and PhCHO for **3a**, **3b** and **3c**, respectively) can be produced through steps vii–ix when R = R′ CH_2. The cycloaddition reaction of C_{60} with **3a–3d** and CH_2O gives **4a–4d** (step xvi), while the reaction of C_{60} with **3a–3c** and R′CHO provides **5a–5c** (step xvii). In the case of **3a**, product **5a** was the same as adduct **4a**. Therefore, more pathways leading to **4a** may operate simultaneously. Similar steps vii–ix are impossible for **3d**, of which the phenyl group is directly attached to the nitrogen atom. As a result, the thermal reaction of C_{60} with **3d** afforded **4d** only. It should be noted that it was possible for H_2NCH_2COOH to react with CH_2O/R′CHO and C_{60} to give the corresponding *N*-unsubstituted fulleropyrrolidines. However, no more than a trace amount of, if any, *N*-unsubstituted fulleropyrrolidines could be isolated from the thermal reaction of C_{60} with **3a–3d** because the *in situ* generated CH_2O and R′CHO (**I′**) preferred to react with a large excess of amino acids **3a–3d** rather than the relatively small amount of the *in situ* formed H_2NCH_2COOH to furnish an azomethine ylide, which then underwent [2 + 3] cycloaddition reaction with C_{60} to provide **4a–4d** and **5b–5c**, respectively.

For amino acid esters **6a–6d**, R^1 = R, R^2 = H, R^3 = Et, EtO_2CCHO (**E′**) and R′CHO (**I′**, when R = R′CH_2) were obtained *via* steps i–v and vii–ix, respectively. Substrate **6d** bearing the Ph–N moiety cannot undergo steps vii–ix, and thus is unable to produce the corresponding R′CHO (**I′**) and $NH_2CH_2CO_2Et$ (**J′**). The reaction of C_{60} with **6a–6d** and **E′** affords **7a–7d** (step xviii), and that with **6a–6c** and **I′** furnishes **8a–8c** (step xix). For **6a–6c**, C_{60} can react with the *in situ* generated **J′** and EtO_2CCHO or R′CHO to provide **9** or **10** (steps xx and xxi), respectively. As expected, **9** was indeed obtained in all cases of **6a–6c**. However, only **10c** could be isolated because much more benzaldehyde and **J′** from **6c** might be produced than aldehydes (formaldehyde and acetaldehyde) and **J′** from **6a** and **6b** (*vide infra*).

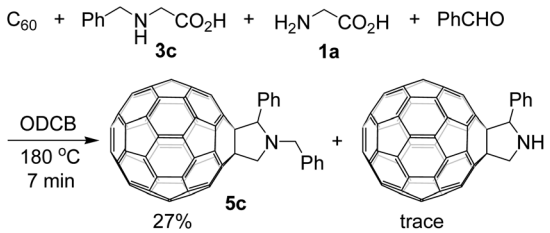
To better understand the product distribution for the thermal reaction of C_{60} with amino acids or amino acid esters, we performed additional experiments. Control experiments showed that the reaction of C_{60} with 1 equiv. of **3a**, 1 equiv. of $NH_2CH_2CO_2H$ and 1 equiv. of CH_2O at 180 °C for 7 min gave **4a** in 18% yield along with only a trace amount of **2a** (Scheme 4). In comparison, the reaction of C_{60} with 1 equiv. of **3c**, 1 equiv. of $NH_2CH_2CO_2H$ and 1 equiv. of CH_2O at 180 °C for 7 min afforded **4c** in 16% yield together with a very small amount of **2a** (Scheme 5); meanwhile the reaction of C_{60} with 1 equiv. of **3c**, 1 equiv. of $NH_2CH_2CO_2H$ and 1 equiv. of PhCHO at 180 °C for 7 min afforded **5c** in 27% yield along with a trace amount of the corresponding *N*-unsubstituted fulleropyrrolidine



Scheme 4 Thermal reaction of C_{60} with **1a**, **3a** and CH_2O.



Scheme 5 Thermal reaction of C_{60} with **1a**, **3c** and CH_2O.



Scheme 6 Thermal reaction of C_{60} with **1a**, **3c** and PhCHO.

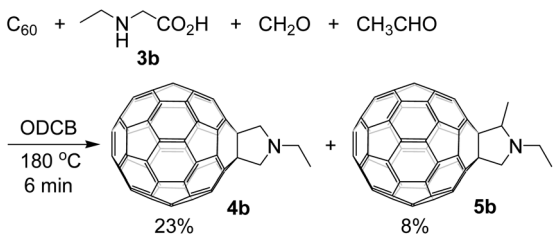
(Scheme 6). These experiments indicated that the reactivity of *N*-substituted glycine was higher than that of glycine. Therefore, it is understandable that we could not identify the *N*-unsubstituted fulleropyrrolidines from the reaction of C_{60} with **3a–3d** after taking into account the very small amount of the *in situ* generated glycine relative to that of **3a–3d**.

It was reported that fulleropyrrolidine **4a** was unexpectedly formed from the reaction of C_{60} with sarcosine and gossypol.[24] Product **4a** was also obtained from the reaction of C_{60} with sarcosine and 4,6-dimethoxysalicylaldehyde[25a] or hydroxyacetaldehyde.[25b] However, the authors did not provide any explanation of how **4a** was produced in their cases. Our current work shows that **4a** can be formed directly from the reaction of C_{60} with sarcosine *via* the aforementioned mechanisms, thus elucidating the origin for the formation of **4a** reported in the literature.[24,25] Control experiments showed that the reaction of C_{60} with 2 equiv. of **3a** under typical Prato reaction conditions (refluxing toluene, 2 h) afforded only a trace amount of **4a**. The same reaction in refluxing chlorobenzene for 2 h still gave a very small amount of **4a**. However, when the reaction time was prolonged to 48 h, as in the reaction of C_{60} with sarcosine and hydroxyacetaldehyde,[25b] **4a** was obtained in 20% yield along with 78% of unreacted C_{60}. These results suggest that although the formation of fulleropyrrolidines from the direct reaction of C_{60} with amino acids under typical Prato reaction conditions is negligible, a

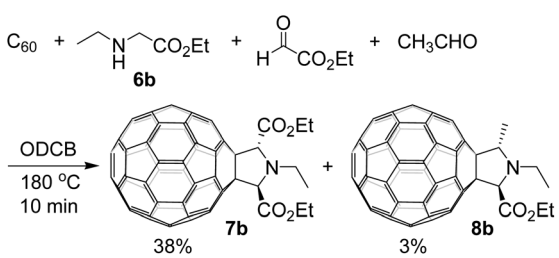
significant amount of fulleropyrrolidines can be generated at high reaction temperature and long reaction time.

It is obvious from the above results and discussion that both *N*-substituted glycines ($R'CH_2NHCH_2CO_2H$) and *N*-substituted glycine esters ($R'CH_2NHCH_2CO_2Et$) could undergo C–N bond cleavage at either side of the NH group. To further explore the innate nature of the C–N bond cleavage and product distribution, we have conducted additional control experiments. We found that the reaction of C_{60} with 1 equiv. of $CH_3CH_2NHCH_2CO_2H$ (**3b**), 1 equiv. of CH_2O and 1 equiv. of CH_3CHO at 180 °C for 6 min produced **4b** and **5b** in 23% and 8% yields, respectively (Scheme 7). The product ratio of **4b**/**5b** was 3 : 1 and happened to be the same as that from the direct thermal reaction of C_{60} with **3b** (Table 2, entry 2), suggesting that the same molar amount of CH_2O and CH_3CHO was generated from **3b**. In comparison, the reaction of C_{60} with 1 equiv. of CH_3CH_2-$NHCH_2CO_2Et$ (**6b**), 1 equiv. of EtO_2CCHO and 1 equiv. of CH_3CHO at 180 °C for 10 min produced **7b** and **8b** in 38% and 3% yields, respectively (Scheme 8). Combined with the product yields (**7b** and **8b** in 31% and 13% yields, respectively) for the thermal reaction of C_{60} with **6b** (Table 3, entry 2), it could be deduced that EtO_2CCHO and CH_3CHO were generated *in situ* from **6b** in a molar ratio of 1 : 5. Thus, the CH_3CH_2–NH bond was more easily to break *via* steps vii–ix in Scheme 1 than the NH–CH_2CO_2Et bond *via* steps i–v in Scheme 1. If **3b** in its thermal reaction with C_{60} proceeded only *via* the same routes as **6b**, it was expected that CH_2O and CH_3CHO should be formed also in a molar ratio of 1 : 5, in sharp contrast to the observed ratio of 1 : 1. Consequently, other routes, *i.e.*, steps x–xiv, must operate and contribute to the formation of CH_2O. The same processes shown in Scheme 2 should also occur for **1a–1d**, **3a**, **3c** and **3d** to provide the corresponding aldehydes.

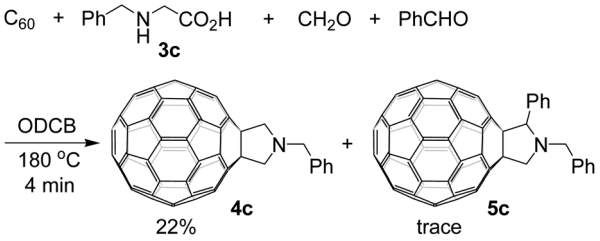
On the other hand, the reaction of C_{60} with 1 equiv. of $PhCH_2NHCH_2CO_2H$ (**3c**), 1 equiv. of CH_2O and 1 equiv. of PhCHO at 180 °C for 4 min afforded **4c** in 22% yield together with a trace amount of **5c** (Scheme 9), while the reaction of C_{60} with 1 equiv. of $PhCH_2NHCH_2CO_2Et$ (**6c**), 1 equiv. of EtO_2CCHO and 1 equiv. of PhCHO at 180 °C for 3 min afforded **7c** in 31% yield along with a trace amount of **8c** (Scheme 10). The observation of **5c** (23%) and **8c** (10%) in the direct reaction of C_{60} with **3c** and **6c** (entry 3, Tables 2 and 3), respectively, suggested that the $PhCH_2$–NH bond was much more facile to cleave than the NH–CH_2CO_2H and NH–CH_2CO_2Et bonds in substrates **3c** and **6c**, respectively, and thus provided significantly more PhCHO than CH_2O (for **3c**)/EtO_2CCHO (for **6c**). The reactivity for the hydrogen abstraction in step vii should follow the order of CH_3–NH < CH_3CH_2–NH < $PhCH_2$–NH. Therefore, more benzaldehyde is expected to form from **3c** than acetaldehyde from **3b** due to the more reactive benzylic position of the former. It is reasonable to assume that the amount of the *in situ* generated CH_2O *via* steps i–vi is not strongly affected by the *N*-alkyl group of **3b** and **3c**. Consequently, the product ratio of **5c**/**4c** is expected to be higher than that of **5b**/**4b**, fully consistent with our experimental results (Table 2, entries 2 and 3). Similar to amino acids **3**, the formation of EtO_2CCHO *via* steps i–v is little affected by the *N*-alkyl group of **6**, while the production of R′CHO *via* steps vii–ix should be more favorable for **6c** than that for **6b**, which in turn is more facile than for **6a**, corroborating the observed product distribution of **8c**/**7c** > **8b**/**7b** > **8a**/**7a** (see Table 3). In addition, product **10** was observed only in the case of **6c**, further supporting that much more PhCHO from **6c** was produced than CH_2O from **6a** and CH_3CHO from **6b**, respectively.



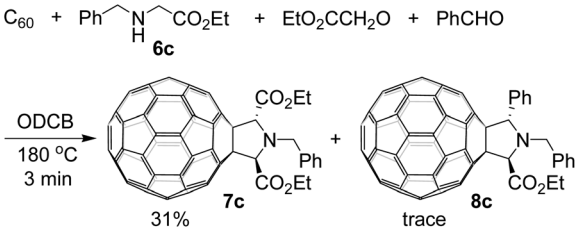
Scheme 7 Thermal reaction of C_{60} with **3b**, CH_2O and CH_3CHO.



Scheme 8 Thermal reaction of C_{60} with **6b**, EtO_2CCHO and CH_3CHO.



Scheme 9 Thermal reaction of C_{60} with **3c**, CH_2O and PhCHO.



Scheme 10 Thermal reaction of C_{60} with **6c**, EtO_2CCHO and PhCHO.

Conclusions

Fulleropyrrolidines are commonly obtained by the Prato reaction, *i.e.*, the reaction of C_{60} with an amino acid or amino acid ester with an aldehyde. In the present work, we have demonstrated that the direct thermal reaction of C_{60} with amino acids or amino acid esters in refluxing ODCB without the purposely added aldehydes under aerobic and dark conditions can also afford

fulleropyrrolidines. Plausible reaction mechanisms involving unusual C–N bond cleavages are proposed to explain the formation of intermediates from the employed amino acids and amino acid esters, and subsequent addition of the azomethine ylides to C_{60} furnishes fulleropyrrolidines. All isolated products from the reaction mixtures can be well explained by the proposed reaction mechanisms. Control experiments shed light on the innate nature of the C–N bond cleavages of amino acids and amino acid esters and support the proposed reaction mechanisms. Our current work also clarifies the origin of the unexpected formation of *N*-methylfulleropyrrolidine from the reaction of C_{60} with sarcosine and gossypol, 4,6-dimethoxysalicylaldehyde or hydroxyacetaldehyde reported in the literature.

Experimental

Thermal reaction of C_{60} with glycine

A 25 mL tube containing a mixture of C_{60} (36.1 mg, 0.05 mmol) and glycine (76.2 mg, 1.0 mmol) in ODCB (6 mL) was wrapped with aluminum foil, sealed up, and then heated in an oil bath preset at 200 °C for 24 h (monitored by TLC). After removal of the solvent *in vacuo*, flash chromatography of the residue on a silica gel column with carbon disulfide as the eluent to afford unreacted C_{60} (22.7 mg, 63%), then with a mixture of carbon disulfide and dichloromethane to give fulleropyrrolidine **2a**[12] (7.4 mg, 19%). ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 4.78 (s, 4H).

Thermal reaction of C_{60} with alanine

By the same procedure as above, the reaction of C_{60} (36.0 mg, 0.05 mmol) with alanine (46.0 mg, 0.52 mmol) at 200 °C for 48 h gave unreacted C_{60} (13.4 mg, 37%) and fulleropyrrolidine **2b**[13] (13.8 mg, 35%) as a mixture of *cis* and *trans* isomers in a ratio of 3.6 : 1. *cis*-**2b**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 4.79 (q, J = 6.6 Hz, 2H), 2.02 (d, J = 6.6 Hz, 6H). *trans*-**2b**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 5.06 (q, J = 6.8 Hz, 2H), 2.04 (d, J = 6.8 Hz, 6H).

Thermal reaction of C_{60} with phenylalanine

By the same procedure as above, the reaction of C_{60} (35.9 mg, 0.05 mmol) with phenylalanine (82.2 mg, 0.50 mmol) at 180 °C for 12 h gave unreacted C_{60} (25.6 mg, 71%) and fulleropyrrolidine **2c**[13] (8.7 mg, 19%) as a mixture of *cis* and *trans* isomers in a ratio of 1 : 1.1. *cis*-**2c**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 7.40 (d, J = 7.2 Hz, 4H), 7.30 (t, J = 7.5 Hz, 4H), 7.21 (t, J = 7.3 Hz, 2H), 4.74 (dd, J = 10.6, 3.0 Hz, 2H), 3.87 (dd, J = 13.4, 3.0 Hz, 2H), 3.35 (dd, J = 13.4, 10.6 Hz, 2H), 2.63 (br s, 1H). *trans*-**2c**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 7.27–7.24 (m, 10H), 5.11 (dd, J = 11.1, 3.5 Hz, 2H), 3.68 (dd, J = 13.3, 3.5 Hz, 2H), 3.50 (dd, J = 13.3, 11.1 Hz, 2H), 2.63 (br s, 1H).

Thermal reaction of C_{60} with phenylglycine

By the same procedure as above, the reaction of C_{60} (36.2 mg, 0.05 mmol) with phenylglycine (75.4 mg, 0.50 mmol) at 180 °C for 10 h gave unreacted C_{60} (16.1 mg, 44%) and fulleropyrrolidine **2d**[13] (17.2 mg, 37%); ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 7.95 (d, J = 7.2 Hz, 4H), 7.39 (t, J = 7.5 Hz, 4H), 7.30 (t, J = 7.3 Hz, 2H), 5.95 (s, 2H), 3.11 (br s, 1H).

Thermal reaction of C_{60} with sarcosine

By the same procedure as above, the reaction of C_{60} (36.0 mg, 0.05 mmol) with sarcosine (44.3 mg, 0.50 mmol) at 180 °C for 10 h gave unreacted C_{60} (22.6 mg, 63%) and fulleropyrrolidine **4a**[12] (11.7 mg, 30%). ^{1}H NMR (300 MHz, CS_2/$CDCl_3$): δ = 4.37 (s, 4H), 2.97 (s, 3H).

Thermal reaction of C_{60} with *N*-ethylglycine

By the same procedure as above, the reaction of C_{60} (36.1 mg, 0.05 mmol) with *N*-ethylglycine (52.2 mg, 0.51 mmol) at 180 °C for 2.5 h gave unreacted C_{60} (15.4 mg, 43%) and a mixture of **4b** and **5b**, which was further separated by recycling HPLC (10 × 250 mm Cosmosil Buckyprep column; flow rate 3 mL min^{-1}; injection volume 5 mL; toluene as eluent) to afford fulleropyrrolidines **4b**[15] (13.1 mg, 33%) and **5b** (4.5 mg, 11%). **4b**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 4.40 (s, 4H), 3.15 (q, J = 7.2 Hz, 2H), 1.55 (t, J = 7.2 Hz, 3H). **5b**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 4.88 (d, J = 9.2 Hz, 1H), 4.02 (q, J = 6.3 Hz, 1H), 3.98 (d, J = 9.2 Hz, 1H), 3.50 (dq, J = 12.0, 7.4 Hz, 1H), 2.73 (dq, J = 12.0, 7.0 Hz, 1H), 1.95 (d, J = 6.3 Hz, 3H), 1.53 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CS_2/DMSO-d_6 with Cr(acac)$_3$ as relaxation reagent, all 1C unless indicated): δ = 156.69, 154.58, 154.23, 153.42, 147.34 (2C), 146.98, 146.84, 146.70, 146.43, 146.39, 146.28, 146.26, 146.22, 146.17, 146.06 (2C), 145.92, 145.75, 145.65 (3C), 145.52, 145.43, 145.38 (2C), 145.33, 145.28, 144.90, 144.77, 144.52 (2C), 143.28, 143.16, 142.80, 142.77, 142.74, 142.72, 142.38 (3C), 142.34, 142.29, 142.28, 142.20, 142.18, 142.17, 142.06, 141.85, 141.81, 140.39, 140.32 (2C), 139.88, 137.72, 136.68, 136.13, 135.93, 75.89 (sp^3-*C* of C_{60}), 71.77 (N*C*HCH$_3$), 69.20 (sp^3-*C* of C_{60}), 66.49 (*C*H$_2$N), 46.64 (N*C*H$_2$CH$_3$), 17.35 (CH*C*H$_3$), 13.76 (NCH$_2$*C*H$_3$); FT-IR ν/cm^{-1} (KBr) 2962, 2923, 1506, 1451, 1426, 1377, 1332, 1186, 766, 699, 572, 525; UV-vis ($CHCl_3$) λ_{max}/nm (lg ε) 257 (4.92), 323 (4.40), 431 (3.43), 704 (2.55); HRMS (MALDI TF-ICR): m/z calcd for $C_{65}H_{11}N$: 805.0891; found: 805.0895.

Thermal reaction of C_{60} with *N*-benzylglycine

By the same procedure as above, the reaction of C_{60} (36.1 mg, 0.05 mmol) with *N*-benzylglycine (82.5 mg, 0.50 mmol) at 180 °C for 28 h gave unreacted C_{60} (18.3 mg, 51%), fulleropyrrolidines **4c**[16] (9.4 mg, 22%) and **5c**[17] (10.7 mg, 23%). **4c**: ^{1}H NMR (300 MHz, CS_2/$CDCl_3$): δ = 7.69 (d, J = 7.1 Hz, 2H), 7.46 (t, J = 7.3 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 4.43 (s, 4H), 4.30 (s, 2H); ^{13}C NMR (75 MHz, CS_2/$CDCl_3$ with Cr(acac)$_3$ as relaxation reagent): δ = 154.76 (4C), 147.13 (2C), 146.09 (4C), 145.90 (8C), 145.52 (2C), 145.30 (4C), 145.13 (4C), 144.41 (4C), 142.95 (2C), 142.49 (4C), 142.10 (4C), 141.92 (4C), 141.74 (4C), 140.04 (4C), 137.77 (1C, aryl C), 136.15 (4C), 128.68 (2C, aryl C), 128.65 (2C, aryl C), 127.55 (1C, aryl C),

70.54 (2C, sp^3-*C* of C_{60}), 67.47 (2C, *C*H_2), 58.82 (1C, N*C*H_2). **5c**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 7.93 (br s, 2H), 7.68 (d, J = 7.4 Hz, 2H), 7.50–7.43 (m, 4H), 7.40–7.33 (m, 2H), 5.21 (s, 1H), 4.86 (d, J = 9.4 Hz, 1H), 4.59 (d, J = 13.4 Hz, 1H), 4.16 (d, J = 9.4 Hz, 1H), 3.67 (d, J = 13.4 Hz, 1H); ^{13}C NMR (75 MHz, CS_2/$CDCl_3$ with Cr(acac)$_3$ as relaxation reagent, all 1C unless indicated): δ = 156.32, 154.04, 153.39, 153.33, 147.29 (2C), 146.79, 146.40, 146.29, 146.26, 146.20, 146.17, 146.14, 146.12, 146.09, 145.93 (2C), 145.74, 145.53 (2C), 145.51, 145.49, 145.35, 145.30, 145.25 (2C), 145.22, 145.13, 144.70, 144.62, 144.39, 144.36, 143.15, 142.98, 142.67, 142.58, 142.55 (2C), 142.34, 142.24, 142.14, 142.12, 142.10, 142.07, 142.01, 141.99, 141.92, 141.82, 141.64, 141.54, 140.18, 140.14, 139.89, 139.45, 137.85 (aryl C), 136.99 (aryl C), 136.84, 136.51, 135.92, 135.71, 129.46 (2C, aryl C), 128.86 (2C, aryl C), 128.82 (2C, aryl C), 128.74 (2C, aryl C), 128.66 (aryl C), 127.56 (aryl C), 81.54 (*C*HPh), 77.37 (sp^3-*C* of C_{60}), 68.68 (sp^3-*C* of C_{60}), 66.69 (*C*H_2), 56.84 (N*C*H_2).

Thermal reaction of C_{60} with *N*-phenylglycine

By the same procedure as above, the reaction of C_{60} (36.0 mg, 0.05 mmol) with *N*-phenylglycine (16.2 mg, 0.11 mmol) at 180 °C for 1.5 h gave unreacted C_{60} (17.6 mg, 49%) and fulleropyrrolidine **4d** (15.1 mg, 36%). ^{1}H NMR (300 MHz, CS_2/$CDCl_3$): δ = 7.41 (t, J = 7.4 Hz, 2H), 7.25 (d, J = 7.7 Hz, 2H), 7.00 (t, J = 7.3 Hz, 1H), 5.14 (s, 4H); ^{13}C NMR (75 MHz, CS_2/$CDCl_3$ with Cr(acac)$_3$ as relaxation reagent): δ = 153.77 (4C), 146.82 (2C), 145.74 (4C), 145.54 (4C), 145.30 (4C), 145.09 (2C), 145.02 (4C), 144.75 (4C), 144.01 (4C), 142.57 (2C), 142.12 (4C), 141.67 (4C), 141.54 (4C), 141.37 (4C), 139.72 (4C), 135.63 (4C), 129.14 (2C, aryl C), 120.18 (1C, aryl C), 116.10 (2C, aryl C), 69.23 (2C, sp^3-*C* of C_{60}), 62.63 (*C*H_2N); FT-IR ν/cm^{-1} (KBr) 2921, 1597, 1501, 1466, 1427, 1353, 1216, 1187, 751, 687, 558, 526; UV-vis ($CHCl_3$) λ_{max}/nm (lg ε) 256 (5.05), 308 (4.55), 430 (3.53), 703 (2.09); HRMS (MALDI TF-ICR): m/z calcd for $C_{68}H_9N$: 839.0735; found: 839.0732.

Thermal reaction of C_{60} with sarcosine ethyl ester

By the same procedure as above, the reaction of C_{60} (36.0 mg, 0.05 mmol) with sarcosine ethyl ester (57.3 mg, 0.49 mmol) at 180 °C for 4 h gave unreacted C_{60} (16.2 mg, 45%), **7a**[17] (11.0 mg, 24%), **8a**[4a] (3.9 mg, 9%) and **9** as a mixture of *cis*-isomer[4a,17] (1.1 mg, 2.4%) and *trans*-isomer[4a] (0.3 mg, 0.7%). **7a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (s, 2H), 4.42 (dq, J = 10.8, 7.1 Hz, 2H), 4.33 (dq, J = 10.8, 7.1 Hz, 2H), 3.10 (s, 3H), 1.28 (t, J = 7.1 Hz, 6H). **8a**: ^{1}H NMR (300 MHz, CS_2/$CDCl_3$): δ = 4.96 (d, J = 9.5 Hz, 1H), 4.79 (s, 1H), 4.41 (dq, J = 10.8, 7.2 Hz, 1H), 4.31 (dq, J = 10.8, 7.1 Hz, 1H), 4.25 (d, J = 9.5 Hz, 1H), 3.02 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). *cis*-**9**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.51 (d, J = 13.6 Hz, 2H), 4.48 (t, J = 13.6 Hz, 1H, NH), 4.43 (dq, J = 10.8, 7.1 Hz, 2H), 4.32 (dq, J = 10.8, 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 6H). *trans*-**9**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.01 (d, J = 9.0 Hz, 2H), 4.42 (dq, J = 10.8, 7.1 Hz, 2H), 4.33 (dq, J = 10.8, 7.1 Hz, 2H), 4.21 (t, J = 9.0 Hz, 1H, NH), 1.28 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, CS_2/$CDCl_3$ with Cr(acac)$_3$ as relaxation reagent, all 2C unless indicated): δ = 169.17 (*C*═O), 153.30, 149.98, 146.47, 145.69, 145.65, 145.35, 145.33, 145.18, 144.87, 144.83 (4C), 144.75, 144.66, 144.61, 143.79, 143.62, 142.46, 142.09, 142.05, 141.55 (6C), 141.49, 141.26, 141.18, 139.41, 138.94, 135.86, 134.92, 75.70 (sp^3-*C* of C_{60}), 73.09 (*C*HCO_2), 61.24 (O*C*H_2CH$_3$), 13.91 (OCH$_2$*C*H$_3$); FT-IR ν/cm^{-1} (KBr) 2923, 1739, 1566, 1520, 1429, 1373, 1279, 1199, 1027, 942, 803, 751, 592, 527; UV-vis ($CHCl_3$) λ_{max} nm (lg ε) 251 (4.97), 325 (4.50), 428 (3.47), 693 (2.62); HRMS (MALDI TF-ICR): m/z calcd for $C_{68}H_{13}NO_4$: 907.0845; found: 907.0842.

Thermal reaction of C_{60} with *N*-ethylglycine ethyl ester

By the same procedure as above, the reaction of C_{60} (36.1 mg, 0.05 mmol) with *N*-ethylglycine ethyl ester (67.8 mg, 0.52 mmol) at 180 °C for 2 h gave unreacted C_{60} (16.2 mg, 45%), **7b** (14.5 mg, 31%), **8b** (5.6 mg, 13%) and **9** as a mixture of *cis*-isomer[4a,17] (1.4 mg, 3.0%) and *trans*-isomer[4a] (0.4 mg, 0.9%). **7b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.92 (s, 2H), 4.41 (dq, J = 10.8, 7.1 Hz, 2H), 4.31 (dq, J = 10.8, 7.1 Hz, 2H), 3.52 (dq, J = 11.8, 7.5 Hz, 1H), 3.16 (dq, J = 11.8, 7.0 Hz, 1H), 1.57 (t, J = 7.3 Hz, 3H), 1.28 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ with Cr(acac)$_3$ as relaxation reagent, all 2C unless indicated): δ = 170.56 (*C*═O), 153.85, 151.14, 147.54, 146.51, 146.45, 146.19 (4C), 146.14, 145.95, 145.74 (4C), 145.61, 145.44, 145.39, 144.66, 144.62, 143.20, 142.84, 142.76, 142.33, 142.25, 142.11, 142.02, 141.95, 141.87, 140.12, 139.68, 137.28, 136.61, 74.21 (*C*HCO_2), 71.64 (sp^3-*C* of C_{60}), 61.63 (O*C*H_2CH$_3$), 43.40 (1C, N*C*H_2CH$_3$), 14.45 (OCH$_2$*C*H$_3$), 13.71 (1C, NCH$_2$*C*H$_3$). FT-IR ν/cm^{-1} (KBr) 2970, 1727, 1509, 1427, 1366, 1337, 1263, 1166, 1093, 1012, 802, 573, 523; UV-vis ($CHCl_3$) λ_{max}/nm (lg ε) 256 (5.00), 311 (4.52), 429 (3.53), 695 (2.84); HRMS (MALDI TF-ICR): m/z calcd for $C_{70}H_{17}NO_4$: 935.1158; found: 935.1165. **8b**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 5.56 (s, 1H), 5.40 (q, J = 6.4 Hz, 1H), 4.35 (dq, J = 10.8, 7.1 Hz, 1H), 4.27 (dq, J = 10.8, 7.1 Hz, 1H), 3.43 (dq, J = 12.0, 7.5 Hz, 1H), 3.10 (dq, J = 12.0, 7.0 Hz, 1H), 1.90 (d, J = 6.4 Hz, 3H), 1.52 (t, J = 7.3 Hz, 3H), 1.29 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CS_2/DMSO-d_6 with Cr(acac)$_3$ as relaxation reagent, all 1C unless indicated): δ = 169.90 (*C*═O), 156.25, 154.46, 153.92, 151.48, 147.48, 147.35, 146.83, 146.81, 146.77, 146.45, 146.44, 146.41, 146.31, 146.20, 146.17, 146.09, 146.06, 145.82, 145.65, 145.63 (2C), 145.61, 145.49, 145.45, 145.42, 145.37 (2C), 145.24, 144.80 (2C), 144.63, 144.47, 143.26, 143.14, 142.84, 142.78 (2C), 142.70, 142.40, 142.33, 142.32 (2C), 142.23, 142.18 (2C), 142.07, 141.97, 141.91, 141.84 (2C), 140.42, 140.30, 139.89, 139.66, 137.67, 137.08, 136.51, 136.31, 75.05 (sp^3-*C* of C_{60}), 73.42 (*C*HCO_2), 71.36 (sp^3-*C* of C_{60}), 67.20 (*C*HCH_3), 61.02 (O*C*H_2CH$_3$), 42.25 (N*C*H_2CH$_3$), 18.15 (*C*HCH_3), 14.99 (OCH$_2$*C*H$_3$), 14.73 (NCH$_2$*C*H$_3$). FT-IR ν/cm^{-1} (KBr) 2964, 2921, 1729, 1509, 1450, 1429, 1377, 1336, 1169, 574, 524; UV-vis ($CHCl_3$) λ_{max}/nm (lg ε) 256 (4.93), 320 (4.40), 430 (3.43), 701 (2.46); HRMS (MALDI TF-ICR): m/z calcd for $C_{68}H_{15}NO_2$: 877.1103; found: 877.1112.

Thermal reaction of C_{60} with *N*-benzylglycine ethyl ester

By the same procedure as above, the reaction of C_{60} (35.9 mg, 0.05 mmol) with *N*-benzylglycine ethyl ester (96.7 mg,

0.50 mmol) at 180 °C for 40 min gave unreacted C_{60} (16.9 mg, 47%), **7c** (8.2 mg, 16%), **8c** (5.0 mg, 10%) and **9** as a mixture of *cis*-isomer[4a,17] (4.5 mg, 10%) and *trans*-isomer[4a] (1.5 mg, 3%), and **10c**[18] (0.3 mg, 0.7%). **7c**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, J = 7.2 Hz, 2H), 7.47 (t, J = 7.5 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 5.80 (s, 2H), 4.74 (d, J = 13.1 Hz, 1H), 4.37–4.30 (m, 4H), 4.14 (d, J = 13.1 Hz, 1H), 1.25 (t, J = 6.9 Hz, 6H); ^{13}C NMR (75 MHz, CS_2/$CDCl_3$ with Cr(acac)$_3$ as relaxation reagent, all 2C unless indicated): δ = 169.82 (*C*═O), 153.49, 150.73, 147.17, 146.17, 146.11, 145.84 (4C), 145.78, 145.66, 145.41, 145.39, 145.27, 145.09, 145.03, 144.32, 144.28, 142.85, 142.51, 142.43, 141.98, 141.92, 141.82, 141.67, 141.62, 141.50, 139.79, 139.30, 137.35 (1C, aryl C), 136.82, 136.10, 128.78 (aryl C), 128.56 (aryl C), 127.68 (1C, aryl C), 73.05 (*C*HCO$_2$), 71.26 (sp^3-*C* of C_{60}), 61.18 (O*C*H$_2$CH$_3$), 52.27 (1C, N*C*H$_2$), 14.27 (OCH$_2$*C*H$_3$); FT-IR ν/cm^{-1} (KBr) 2923, 1731, 1567, 1520, 1375, 1279, 1146, 1095, 1027, 941, 803, 751, 679, 592, 526; UV-vis ($CHCl_3$) λ_{max} nm (lg ε) 256 (5.01), 310 (4.52), 429 (3.36), 693 (1.81); HRMS (MALDI TF-ICR): m/z calcd for $C_{75}H_{19}NO_4$: 997.1314; found: 997.1308. **8c**: ^{1}H NMR (300 MHz, CS_2/$CDCl_3$): δ = 7.89 (br s, 2H), 7.65 (d, J = 7.3 Hz, 2H), 7.46–7.28 (m, 6H), 6.64 (s, 1H), 5.43 (s, 1H), 4.50 (d, J = 13.8 Hz, 1H), 4.39 (dq, J = 10.7, 7.1 Hz, 1H), 4.28 (dq, J = 10.7, 7.1 Hz, 1H), 4.05 (d, J = 13.8 Hz, 1H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CS_2/acetone-d_6 with Cr(acac)$_3$ as relaxation reagent, all 1C unless indicated): δ = 170.34 (*C*OO), 156.23, 154.25, 153.96, 151.31, 147.67, 147.54, 147.06, 146.87, 146.62 (2C), 146.51, 146.45, 146.37, 146.33, 146.29, 146.20 (2C), 145.92, 145.83 (3C), 145.78, 145.58, 145.53, 145.49, 145.45 (2C), 145.36, 144.96, 144.86, 144.74, 144.63, 143.40, 143.25, 142.98, 142.87 (2C), 142.82, 142.45 (3C), 142.41, 142.36, 142.29, 142.28 (2C), 142.03, 141.99, 141.90, 141.85, 140.41, 140.34, 139.80, 139.73, 138.25, 137.59, 137.34, 136.58, 136.42, 136.38, 129.35 (4C, aryl C), 129.22 (2C, aryl C), 128.87 (3C, aryl C), 128.22 (1C, aryl C), 77.32 (*C*HPh), 76.02 (sp^3-*C* of C_{60}), 73.04 (*C*HCO$_2$), 70.89 (sp^3-*C* of C_{60}), 61.30 (O*C*H$_2$CH$_3$), 51.90 (N*C*H$_2$), 14.93 (OCH$_2$*C*H$_3$); FT-IR ν/cm^{-1} (KBr) 1731, 1493, 1454, 1428, 1188, 1166, 1138, 1027, 906, 732, 700, 575, 527; UV-vis ($CHCl_3$) λ_{max} nm (lg ε) 257 (4.98), 311 (4.53), 431 (3.44), 703 (1.90); HRMS (MALDI TF-ICR): m/z calcd for $C_{78}H_{19}NO_2$: 1001.1416; found: 1001.1422. **10c**: ^{1}H NMR (400 MHz, CS_2/$CDCl_3$): δ = 7.76 (d, J = 7.2 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 5.85 (s, 1H), 5.61 (s, 1H), 4.43 (dq, J = 10.8, 7.1 Hz, 1H), 4.34 (dq, J = 10.8, 7.1 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H).

Thermal reaction of C_{60} with ethyl *N*-phenylglycinate

By the same procedure as above, the reaction of C_{60} (36.3 mg, 0.05 mmol) with ethyl *N*-phenylglycinate (182.4 mg, 1.02 mmol) at 180 °C for 75 h gave unreacted C_{60} (18.1 mg, 50%) and fulleropyrrolidine **7d** (5.3 mg, 11%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (t, J = 7.7 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.12 (t, J = 7.2 Hz, 1H), 6.54 (s, 2H), 4.26–4.16 (m, 4H), 1.15 (t, J = 7.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$ with Cr(acac)$_3$ as relaxation reagent, all 2C unless indicated): δ = 169.81 (*C*═O), 153.04, 150.17, 147.20, 146.13, 146.09, 145.82 (4C), 145.46, 145.40 (4C), 145.32 (4C), 145.06 (3C), 144.99, 144.26, 144.19, 142.82, 142.46, 142.38, 141.93, 141.86, 141.62 (4C), 141.50, 141.46, 139.89, 139.33, 136.57, 135.88, 129.21 (aryl C), 122.13 (1C, aryl C), 118.68 (aryl C), 74.12 (*C*HCO$_2$), 70.75 (sp^3-*C* of C_{60}), 61.57 (O*C*H$_2$CH$_3$), 13.89 (OCH$_2$*C*H$_3$). FT-IR ν/cm^{-1} (KBr) 2923, 1734, 1598, 1498, 1461, 1368, 1340, 1292, 1262, 1180, 1015, 757, 692, 576, 526; UV-vis ($CHCl_3$) λ_{max}/nm (lg ε) 257 (5.03), 310 (4.52), 429 (3.41), 691 (2.14); HRMS (MALDI TF-ICR): m/z calcd for $C_{74}H_{17}NO_4$: 983.1158; found: 983.1163.

Reaction of C_{60} with sarcosine, glycine and formaldehyde

A 25-mL tube containing a mixture of C_{60} (72.1 mg, 0.10 mmol), sarcosine (8.9 mg, 0.10 mmol), glycine (7.5 mg, 0.10 mmol) and formaldehyde solution (7.2 μL, 0.10 mmol) in ODCB (10 mL) was wrapped with aluminum foil, sealed up, and ultrasonicated until C_{60} was dissolved, and then heated in an oil bath preset at 180 °C for 7 min. The usual workup gave unreacted C_{60} (48.1 mg, 67%), **4a**[12] (14.3 mg, 18%) and a trace amount of **2a**.[12]

Reaction of C_{60} with *N*-benzylglycine, glycine and formaldehyde

By the same procedure as above, the reaction of C_{60} (72.1 mg, 0.10 mmol) with *N*-benzylglycine (16.5 mg, 0.10 mmol), glycine (7.5 mg, 0.10 mmol) and formaldehyde solution (7.2 μL, 0.10 mmol) at 180 °C for 7 min gave unreacted C_{60} (41.4 mg, 57%), **4c**[16] (13.8 mg, 16%), and a trace amount of **2a**.[12]

Reaction of C_{60} with *N*-benzylglycine, glycine and benzaldehyde

By the same procedure as above, the reaction of C_{60} (72.0 mg, 0.10 mmol), *N*-benzylglycine (16.5 mg, 0.10 mmol), glycine (7.5 mg, 0.10 mmol) and benzaldehyde (10 μL, 0.10 mmol) at 180 °C for 7 min gave unreacted C_{60} (45.3 mg, 63%), **5c**[17] (25.4 mg, 27%) and a trace amount of the corresponding *N*-unsubstituted fulleropyrrolidine.

Reaction of C_{60} with *N*-ethylglycine, formaldehyde and acetaldehyde

By the same procedure as above, the reaction of C_{60} (71.9 mg, 0.10 mmol), *N*-ethylglycine (10.3 mg, 0.10 mmol), formaldehyde solution (7.2 μL, 0.10 mmol) and acetaldehyde solution (12 μL, 0.10 mmol) at 180 °C for 6 min gave unreacted C_{60} (28.7 mg, 40%), **4b**[15] (18.5 mg, 23%) and **5b** (6.4 mg, 8%).

Reaction of C_{60} with *N*-ethylglycine ethyl ester, ethyl glyoxalate and acetaldehyde

By the same procedure as above, the reaction of C_{60} (72.0 mg, 0.10 mmol), *N*-ethylglycine ethyl ester (13.1 mg, 0.10 mmol), ethyl glyoxalate solution (20.5 μL, 0.10 mmol) and acetaldehyde solution (12 μL, 0.10 mmol) at 180 °C for 10 min gave unreacted C_{60} (34.5 mg, 48%), **7b** (35.5 mg, 38%) and **8b** (2.6 mg, 3%).

Reaction of C_{60} with *N*-benzylglycine, formaldehyde and benzaldehyde

By the same procedure as above, the reaction of C_{60} (36.1 mg, 0.05 mmol), *N*-benzylglycine (8.4 mg, 0.05 mmol), formaldehyde (3.6 μL, 0.05 mmol) and benzaldehyde (5.2 μL, 0.05 mmol) in ODCB (6 mL) at 180 °C for 4 min gave unreacted C_{60} (27.1 mg, 75%), **4c**[16] (9.4 mg, 22%) and a trace amount of **5c**.[17]

Reaction of C_{60} with *N*-benzylglycine ethyl ester, ethyl glyoxalate and benzaldehyde

By the same procedure as above, the reaction of C_{60} (35.9 mg, 0.05 mmol), *N*-benzylglycine ethyl ester (9.7 mg, 0.05 mmol), ethyl glyoxalate (10 μL, 0.05 mmol) and benzaldehyde (5.2 μL, 0.05 mmol) in ODCB (6 mL) at 180 °C for 3 min gave unreacted C_{60} (21.0 mg, 58%), **7c** (15.3 mg, 31%) and a trace amount of **8c**.

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