The solid-phase reaction of [60]fullerene: novel addition of organozinc reagents

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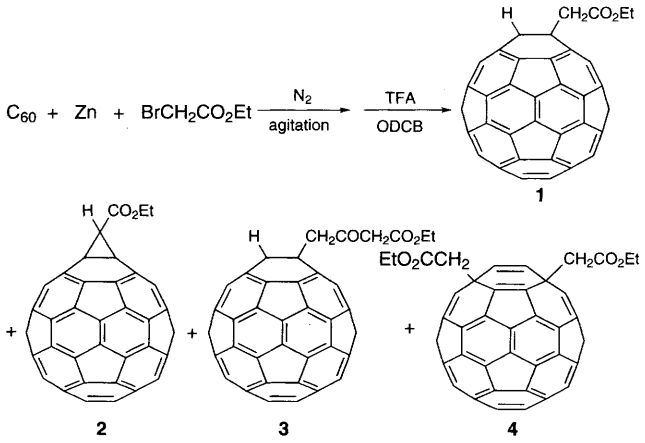
Reaction of ethyl bromoacetate and zinc with [60]fullerene in the absence of any solvent, followed by quenching with acid affords 1-ethoxycarbonylmethyl-1,2- dihydro-[60]fullerene along with other minor byproducts including 1,4-bis(ethoxycarbonylmethyl)-1,4-dihydro[60]fullerene; a detailed reaction mechanism is proposed.

Great progress in the functionalization of fullerenes has been made over the past few years.[1] However, the extremely low solubility of fullerenes in common solvents is apparently imposing some limitations on the investigation of chemical transformation of fullerenes in solution. In order to circumvent this difficulty, we explored a novel method of reacting [60]fullerene with nucleophiles in the absence of any solvent. It has already been demonstrated that various reactions can be successfully conducted in the solid state.[2] Nucleophilic addition to [60]fullerene was one of the first reactions investigated, and has since been proven to be a versatile method for derivatising fullerenes. A number of carbanionic nucleophiles, such as organolithiums,[3] Grignard reagents,[3b,4] cyanide,[5] carbanions derived from silyl enol ethers[6] and α- halogenocarbanions containing carbonyl,[7] alkynyl,[3c] cyano[8] and nitro[8b] groups, have been reported to react with [60]fullerene. To test and apply the methodology of solid-phase reaction to fullerene chemistry, we first investigated the nucleophilic addition of organozinc reagent to [60]fullerene, *i.e.* Reformatsky-type reaction, which has not been reported so far even in solution. Here, we describe the results of the first solid-phase reaction of [60]fullerene and propose a possible reaction mechanism for the formation of all isolated products.

As to the apparatus for our solid-phase reaction, we utilized the so-called 'vibrating mill', which was designed for the preparation of a well-mixed homogeneous powder by vigorously vibrating a stainless-steel capsule containing the sample and a stainless-steel ball with a frequency of 2800 cycles per minute.

A typical procedure is as follows: in a nitrogen bag, 50.2 mg of [60]fullerene, ethyl bromoacetate (5 equiv.), zinc dust (20 equiv.) and the stainless-steel ball were placed in the capsule. The above mixture was vigorously agitated for 20 min at room temperature, quenched with 0.5 ml of CF_3CO_2H in 20 ml of *o*-dichlorobenzene, and carefully separated by silica gel chromatography with hexane–toluene as the eluent to give the expected adduct **1** (17.2%) (62.5% based on consumed C_{60}) together with **2** (0.8%), **3** (3.9%), **4** (1.8%) and unreacted C_{60} (72.5%) (Scheme 1).



Scheme 1

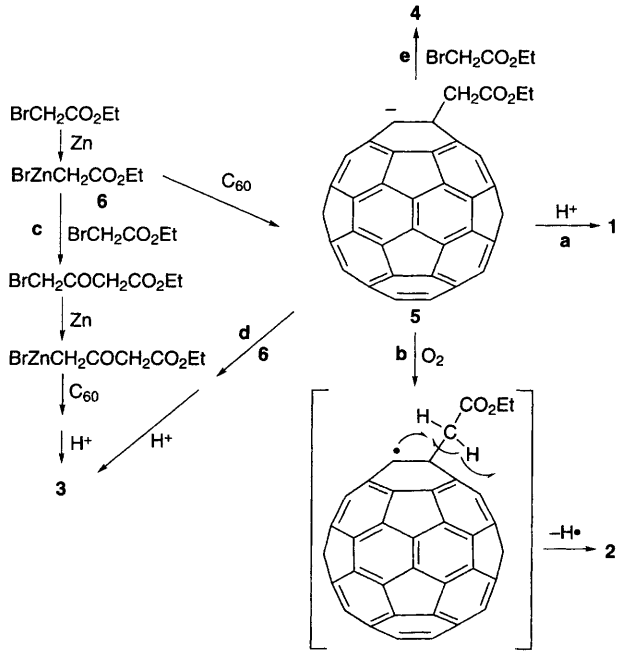
Adducts **3**† and **4**‡ are new compounds, while **1**§,[9] and **2**[10] have been previously reported and their structures are confirmed by their spectroscopic data. The only inconsistency with the reported data is found in the ^{13}C NMR spectrum of compound **1**. The assignments of the three peaks between δ 66 and 59[9b] are now correctly assigned to the CH_2 of the ethyl group, the sp^3-C and the CH of the fullerene skeleton, respectively, based on DEPT experiment and the off-resonance ^{13}C NMR spectrum.

The ^1H NMR and mass spectra of adduct **3** are consistent with its proposed structure. A smaller set of peaks,¶ which could be assigned to the enol isomer of **3**, are also observed in its ^1H NMR spectrum. The ^{13}C NMR spectrum‖ of **3** shows a similar pattern to that of **1** for the fullerene skeleton, together with additional peaks at δ 199.60 and 56.76 for another carbonyl and methylene carbon, respectively, indicating its C_s symmetry. Further evidence supporting the assigned structure of **3** is that the chemical shifts for the fragment $COCH_2CO_2Et$ of **3** are very close to those of ethyl acetoacetate in both the ^1H and ^{13}C NMR spectra. The FT-IR spectrum of **3** displays two absorptions at 1740 and 1718 cm^{-1} for the ester and ketone groups.

Product **4** is identified as a bisadduct by mass spectral analysis. In addition, the typical AB quartet for the methylene attached to fullerene cage in the ^1H NMR spectrum and a similar ^{13}C NMR pattern to those of reported 1,4-adducts,[4,11,12] *i.e.* 31 peaks for sp^2-carbons (among them 4 peaks appear with half-intensity) and 1 peak for sp^3-carbons for the fullerene cage, strongly support the idea that compound **4** is a 1,4-adduct and has a C_s symmetry with a plane of symmetry bisecting the six-membered ring. It seems to be a general trend that the sp^3-carbons of the fullerene cage for 1,4-bisadducts with two identical alkyl addends undergo upfield shift by *ca.* 5–7 ppm compared with those of corresponding monosubstituted 1,2-dihydrofullerenes.[4,11,13] The yellow colour of adduct **4** in solution and the broad peak around 443 nm in its UV–VIS spectrum are also typical for 1,4-adducts.[4,11,12]

The effect of reaction time was examined in the range of 10 to 60 min with the same reagent ratio as shown above. It was found that the conversion of [60]fullerene reached the maximum value of 40% at the reaction time of 40 min and that the relative yield of byproduct **3** among the formed products increased with reaction time at the expense of the main product **1**. For example, the yields of **1** and **3** were 13 and 8%, respectively, when the reaction was allowed to proceed for 1 h.

1,4-Bisadduct **4** was also synthesized by the reaction of 2-(ethoxycarbonylmethyl)-1,2-dihydro[60]fulleren-1-ide **5**, generated by deprotonation of **1** in THF using 1 equiv. of Bu^tOK, with 20 equiv. of ethyl bromoacetate for 2 h at 70 °C. Chromatography on silica gel using toluene as the eluent



Scheme 2

afforded 47% of **4** along with 41% of recovered **1**. Adduct **4** was obtained as a single product without any formation of the isomeric 1,2-adduct. This might have resulted from kinetic control, but, at the same time, agrees with the results of AM1 calculations, which indicate that the heat of formation of **4** (767.31 kcal mol^{-1}) is 0.44 kcal mol^{-1} less than that of its corresponding 1,2-adduct (767.75 kcal mol^{-1}).

From the above results, a possible reaction mechanism for the formation of all isolated products is proposed and shown in Scheme 2. Reformatsky reagent, $BrZnCH_2CO_2Et$, reacts with [60]fullerene to give the vital intermediate **5**, which is quenched with acid to afford the main product **1** (pathway **a**). A small amount of **2** is formed, most probably *via* pathway **b**, owing to the presence of trace O_2 during agitation of the reaction mixture and/or during the quenching procedure. Both pathway **c** and pathway **d** could contribute to the formation of adduct **3**. The concentration of intermediate **5** would increase with the reaction time and thus increases the possibility of pathway **d** leading to a relatively higher yield of adduct **3** after a prolonged reaction. The 1,4-adduct **4** should be formed by the nucleophilic substitution of ethyl bromoacetate by **5** (pathway **e**), as shown by the above designed synthesis of **4**.

Preliminary results indicate that magnesium can replace zinc and cause an obvious change of product distribution, with adduct **3** as the main product in the Reformatsky-type reaction, and that this reaction can also occur with diethyl bromomalonate or allyl bromide in place of ethyl bromoacetate.

We are grateful for financial support by the Inamori Foundation and a Grant-in-Aid for the Scientific Research on Priority Areas (No. 07213217) from the Ministry of Education, Science and Culture, Japan. We also thank Miss Michiko Kanai of Thermoquest Co. for the measurements of some mass spectra.

Footnotes

† *Spectroscopic data* for **3**: MS (ESI) *m/z* 850 (M^-, 100%), 720 (C_{60}^-, 17); $\nu_{max.}$(KBr)/cm^{-1} 2923, 2852, 1740, 1718, 1461, 1425, 1309, 1260, 1182, 1096, 1026, 807, 577, 528; $\lambda_{max.}$(cyclohexane)/nm (log ε) 212 (5.08), 256 (5.00), 308 (4.49), 323 (4.48), 432 (3.54), 706 (2.67); δ_H (300 MHz, CS_2–$CDCl_3$, 2:1) 6.58 (s, 1 H, CH), 4.74 (s, 2 H, CH_2CO), 4.34 (q, *J* 7.1 Hz, CH_2CH_3), 3.88 (s, 2 H, CH_2COO), 1.41 (t, *J* 7.2 Hz, CH_2CH_3); δ_C (75.4 MHz, CS_2–$CDCl_3$, 1:1) (number of carbon atoms) 199.60 (1, CO), 166.68 (1, COO), 153.85 (2), 153.37 (2), 147.44 (1), 147.16 (1), 146.94 (2), 146.32 (2), 146.24 (2), 146.09 (4), 145.79 (2), 145.52 (2), 145.49 (2), 145.32 (2), 145.30 (2), 145.26 (2), 144.78 (2), 144.40 (2), 143.17 (2), 142.51 (2), 142.43 (2), 142.04 (2), 142.00 (2), 141.82 (2), 141.59 (2), 141.54 (4), 140.15 (2), 140.06 (2), 137.01 (2), 136.48 (2), 61.86 (1, CH_2CH_3), 60.68 (1, sp^3-C of C_{60} core), 59.22 (1, CH of C_{60} core), 56.76 (1,CH_2CO), 49.59 (1,CH_2COO), 14.29 (1,CH_2CH_3).

‡ *Spectroscopic data* for **4**: MS (DCI) *m/z* 894 (M^-, 100%), 720 (C_{60}^-, 4); $\nu_{max.}$(KBr)/cm^{-1} 2976, 2927, 1735, 1460, 1428, 1368, 1186, 1021, 571, 528; $\lambda_{max.}$(cyclohexane)/nm (log ε) 211 (5.13), 257 (5.00), 324 (4.50), 443 (3.81), 684 (2.52); δ_H(300 MHz, $CDCl_3$) 4.41 (q, *J* 7.2 Hz, 4 H, CH_2CH_3), 4.13, 4.04 (ABq, *J* 15.0 Hz, 4 H, CH_2COO), 1.40 (t, *J* 7.2 Hz, 6 H, CH_2CH_3); δ_C(75.4 MHz, $CDCl_3$) (number of carbon atoms) 169.86 (2, COO), 155.30 (2), 150.52 (2), 148.73 (2), 148.06 (2), 147.25 (2), 147.15 (2), 147.08 (2), 146.99 (2), 145.60 (2), 145.43 (2), 145.24 (2), 144.99 (2), 144.79 (2), 144.66 (1), 144.46 (2), 144.43 (2), 144.28 (2), 144.06 (2), 143.94 (2), 143.62 (2), 143.32 (2), 143.26 (2), 143.11 (2), 142.70 (1), 142.65 (2), 142.33 (2), 142.09 (1), 141.84 (2), 140.93 (1), 138.99 (2), 138.93 (2), 61.57 (2,CH_2CH_3), 54.81 (sp^3-C of C_{60} core), 46.84 (2, CH_2COO), 14.44 (2, CH_2CH_3).

§ *Selected spectroscopic data* for **1**: δ_C (75.4 MHz, CS_2–$CDCl_3$, 3:1) (number of carbon atoms) 169.68 (1, COO), 153.79 (2), 153.22 (2), 147.32 (1), 147.05 (1), 146.75 (2), 146.21 (2), 146.15 (2), 145.99 (2), 145.97 (2), 145.62 (2), 145.43 (4), 145.22 (4), 145.14 (2), 144.59 (2), 144.31 (2), 143.04 (2), 142.39 (2), 142.35 (2), 141.98 (2), 141.88 (2), 141.75 (2), 141.44 (6), 140.07 (2), 139.99 (2), 136.56 (2), 136.24 (2), 61.48 (1, OCH_2), 60.93 (1, sp^3-C of C_{60} core), 59.05 (1, CH of C_{60} core), 49.32 (1, CH_2COO), 14.62 (1, CH_3).

¶ δ_H 6.88 (s, 1 H, CH), 5.59 (s, 1 H, C=CH), 4.30 (q, *J* 7.2 Hz, 2 H, CH_2CH_3), 4.29 (s, CH_2), 1.38 (t, *J* 7.2 Hz, CH_2CH_3).

‖ The peaks corresponding to the enol isomer were too weak to be accounted.

References

1 For recent reviews, see: A. Hirsch, *Synthesis*, 1995, 895; F. Diederich and C. Thilgen, *Science*, 1996, **271**, 317.
2 For a review, see: F. Toda, *Synlett*, 1993, 303.
3 (*a*) P.J. Fagan, P. J. Krusic, D. H. Evans, S. A. Lerke and E. Johnston, *J. Am. Chem. Soc.*, 1992, **114**, 9697; (*b*) A. Hirsch, T. Grösser, A. Skiebe and A. Soi, *Chem. Ber.*, 1993, **126**, 1061; (*c*) H. L. Anderson, R. Faust, Y. Rubin and F. Diederich, *Angew. Chem. Int. Ed. Engl.*, 1994, **33**, 1366; (*d*) K. Komatsu, Y. Murata, N. Takimoto, S. Mori, N. Sugita and T. S. M. Wan, *J. Org. Chem.*, 1994, **59**, 6101; (*e*) Y. Murata, K. Motoyama, K. Komatsu and T. S. M. Wan, *Tetrahedron*, 1996, **52**, 5077.
4 H. Nagashima, H. Terasaki, E. Kimura, K. Nakajima and K. Itoh, *J. Org. Chem.*, 1994, **59**, 1246; H. Nagashima, H. Terasaki, Y. Saito, K. Jinno and K. Itoh, *J. Org. Chem.*, 1995, **60**, 4966.
5 M. Keshavarz-K., B. Knight, G. Srdanov and F. Wudl, *J. Am. Chem. Soc.*, 1995, **117**, 11371.
6 L.-H. Shu, G.-W. Wang, S.-H. Wu and H.-M. Wu, *J. Chem. Soc., Chem. Commun.*, 1995, 367.
7 C. Bingel, *Chem. Ber.*, 1993, **126**, 1957.
8 (*a*) A. M. Benito, A. D. Darwish, H. W. Kroto, M. F. Meidine, R. Taylor and D. R. M. Walton, *Tetrahedron Lett.*, 1996, **37**, 1085; (*b*) M. Keshavarz-K., B. Knight, R. C. Haddon and F. Wudl, *Tetrahedron*, 1996, **52**, 5149.
9 (*a*) H. Tokuyama, H. Isobe and E. Nakamura, *J. Chem. Soc., Chem. Commun.*, 1994, 2753; (*b*) K. Mikami, S. Matsumoto, A. Ishida, S. Takamuku, T. Suenobu and S. Fukuzumi, *J. Am. Chem. Soc.*, 1995, **117**, 11134.
10 (*a*) L. Isaacs, A. Wehrsig and F. Diederich, *Helv. Chim. Acta*, 1993, **76**, 1231; (*b*) Y. Wang, J. Cao, D. I. Schuster and S. R. Wilson, *Tetrahedron Lett.*, 1995, **36**, 6843.
11 S. Miki, M. Kitao and K. Fukunishi, *Tetrahedron Lett.*, 1996, **37**, 2049.
12 G. Schick, K.-D. Kampe and A. Hirsch, *J. Chem. Soc., Chem. Commun.*, 1995, 2023.
13 J. Chen, R.-F. Cai, Z.-E. Huang, H.-M. Wu, S.-K. Jiang and Q.-F. Shao, *J. Chem. Soc., Chem. Commun.*, 1995, 1553.

Received, 18th June 1996; Com. 6/04257K