JOC Notes

Methodology for the Preparation of C1-Monoalkylated 1,2-Dihydro[C_{70}] Derivatives: Formation of the "Other" Regioisomer

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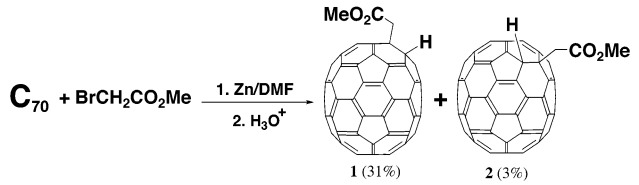
Abstract: Deprotonation of 1,2-$C_{70}H_2$ with TBAOH, followed by alkylation with methyl bromoacetate, results in formation of a C1-monoalkylated 1,2-dihydro-C_{70} derivative. The position of the alkyl group (C1) was established by NMR spectroscopy and comparison with literature spectra of C2-monoalkylated analogs. Presumably, C1-alkylation is the major process due to selective deprotonation of 1,2-$C_{70}H_2$ at C1. Substitution of benzyl bromide for methyl bromoacetate results in rapid dialkylation, unless the amount of base is carefully controlled, in which case C1-monobenzylation is the major process. This methodology for alkylation at C1 is complimentary to methods for the C2-monoalkylation of C_{70} with Zn and methyl bromoacetate.

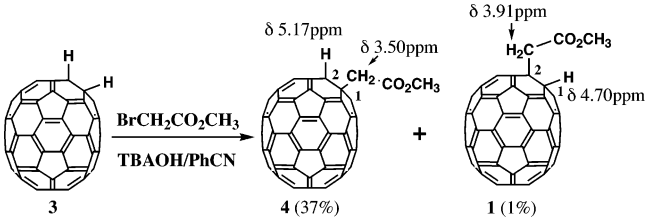
Although fullerene anions ("fullerides")[1] are used in a number of methods for the formation of dialkylated fullerenes,[2] there are many fewer that produce monoalkylated fullerene derivatives from C_{60} anions. It is possible to prepare monoalkylated fullerenes by alkylation of C_{60}^{n-} anions prepared by electrochemical reduction,[2d] by photoinduced charge transfer,[3] by chemical reduction,[4] and by deprotonation of hydrogenated fullerenes.[2g]

There are even fewer reports of monoalkylation of C_{70} anions. Reactions of this lower-symmetry fullerene can produce (at least in principle) many more isomers than are produced in similar reactions on the icosahedral C_{60}. We have recently demonstrated that treatment of C_{70} with Zn and reactive alkyl halides results in monoalkylation at C2.[4b] Alkylation with methyl bromoacetate occurs preferentially at C2 (**1**), although a small amountof the C5-alkylated (6-H) isomer **2** was isolated (Scheme 1).[5]

SCHEME 1



SCHEME 2



Although the C1−C2 bond is usually the most reactive bond in C_{70}, it is not clear why C2 alkylation is preferred over C1 alkylation. Blank experiments with preformed Reformatsky reagents suggested that the result above is not due to addition of a zinc enolate. If two-electron transfer from Zn to C_{70} occurs and is followed by alkylation and protonation steps, the same outcome should be observed regardless of the method used to generate the anion. However, we knew that $PhCH_2Br$ alkylation of C_{70}^{2-} formed by deprotonation of $C_{70}H_2$ resulted in a set of isomeric dialkylated species, with the major product resulting from dialkylation near the equator.[2g]

In an effort to determine if the specific alkyl halide determined the regiochemistry of alkylation, we generated C_{70}^{2-} by deprotonation of 1,2-$C_{70}H_2$ (**3**) and then added methyl bromoacetate. Under these conditions we obtain the C1-monoalkylated product **4** (29% absolute yield, 37% based on consumed C_{70}), with only trace quantities (~1% yield) of the C2-monoalkylated isomer **1** (Scheme 2). This regiochemistry is the opposite of that obtained in the Zn/RX reaction (Scheme 1) and quite unlike the course that the reaction takes when $C_{70}H_2$ is treated with excess base and excess $PhCH_2Br$.

The regiochemistry of alkylation in **1**, **2**, and **4** was established by comparison of the absorption spectra with those of previously reported 1,2-adducts (Figure 1).

The specific orientation of alkylation at the C1−C2 bond in **1** and **4** was established by comparison of ^1H chemical shifts of the CH_2 groups. It is known that groups held over the pole of C_{70} exhibit resonances that are shifted downfield relative to the resonances of groups

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(2) For examples, see: (a) Caron, C.; Subramanian, R.; D'Souza, F.; Kim, J.; Kutner, W.; Jones, M. T.; Kadish, K. M. *J. Am. Chem. Soc.* **1993**, *115*, 8505−8506. (b) Chen, J.; Cai, R.-F.; Huang, Z.-E.; Wu, H.-M.; Jiang, S.-K.; Shao, Q.-F. *J. Chem. Soc., Chem. Commun.* **1995**, 1553−1554. (c) Fukuzumi, S.; Suenobu, T.; Hirasaka, T.; Arakawa, R.; Kadish, K. M. *J. Am. Chem. Soc.* **1998**, *120*, 9220−9227. (d) Kadish, K. M.; Gao, X.; Caemelbecke, E. V.; Hirasaka, T.; Suenobbu, T.; Fukuzumi, S. *J. Phys. Chem. A* **1998**, *102*, 3898−3906. (e) Fukuzumi, S.; Suenobu, T.; Hirasaka, T.; Arakawa, R.; Kadish, K. M. *J. Am. Chem. Soc.* **1998**, *120*, 9220−9227. (f) Allard, E.; Delaunay, J.; Cheng, F.; Cousseau, J.; Ordúnam, J.; Garín, J. *Org. Lett.* **2001**, *3*, 3503−3506. (g) Meier, M. S.; Bergosh, R. G.; Gallagher, M. E.; Spielmann, H. P.; Wang, Z. *J. Org. Chem.* **2002**, *67*, 5946−5952.
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(4) (a) Chen, J.; Cai, R.-F.; Huang, Z.-E.; Wu, H.-M.; Jiang, S.-K.; Shao, Q.-F. *J. Chem. Soc., Chem. Commun.* **1995**, 1553−1554. (b) Wang, Z.; Meier, M. S. *J. Org. Chem.* **2003**, *68*, 3042−3048. (c) Allard, E.; Delaunay, J.; Cousseau, J. *Org. Lett.* **2003**, *5*, 2239−2242.

(5) The numbering system used here is the "trivial" system described in Powell, W. H.; Cozzi, F.; Moss, G. P.; Thilgen, C.; Hwu, R. J.-R.; Yerin, A. *Pure Appl. Chem.* **2002**, *74*, 629−695.

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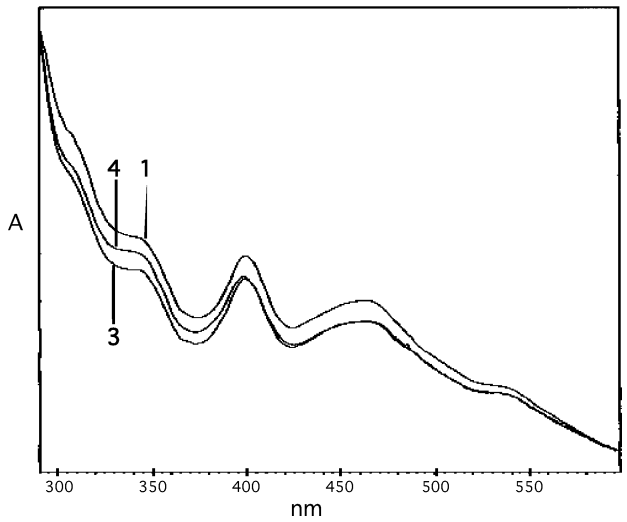

FIGURE 1. Absorption spectra of **1**, **3**, and **4**.

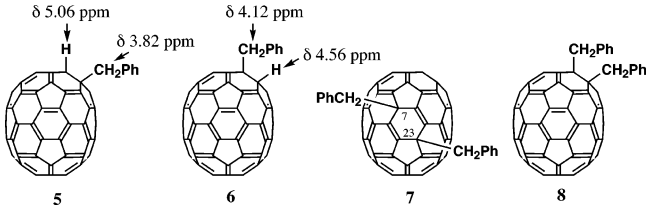

FIGURE 2. The products of the reaction of $PhCH_2Br$ with 1,2-$C_{70}H_2$ and limited amounts of base.

help over the side,[6] and we assign structure **4** on the basis of an absorption spectrum that is a very close match to that of **1** and **3**, a ^{13}C NMR spectrum consistent with the symmetry, a ^1H NMR shift of the fullerene C−H that is *downfield* of the corresponding resonance in **1**,[2g] and a ^1H NMR shift of the acetate CH_2 that is *upfield* of the corresponding resonance in **1** (Scheme 2).

We found that when $PhCH_2Br$ is used in place of $BrCH_2CO_2CH_3$, the outcome of the reaction is very dependent on the amount of base added. When 1.2 equiv of TBAOH and excess $PhCH_2Br$ are used, the C1 alkylated species **5** was the only product isolated (7% absolute yield, 22% yield based on unrecovered fullerene).[7] When 3.6 equiv of TBAOH was added, presumably furnishing more of the C_{70}^{2-} dianion, both of two possible mono 1,2-isomers (**5**, 20% based on unrecovered fullerene, and **6**, 2%) were produced, together with a 25% combined yield of the diadducts reported previously (Figure 2).[2g,8] The structures of **5** and **6** were assigned in the same manner used above. When stoichiometric amounts of $BrCH_2Ph$ were used with an excess of TBAOH, most of the starting material (**3**) was converted to C_{70} and only traces of monoalkylated products were observed in HPLC.

Monoalkylation at C1 with benzyl bromide is only observed when using limited amounts of base. This result suggests that the first deprotonation of **3** occurs preferentially at C1, leading to alkylation at that carbon. Some support for this notion is provided by calculations that have predicted that the C1 proton of **3** should be significantly more acidic than the C2 proton.[9] As the amount of base is increased, an increasing amount of C_{70}^{2-} is produced, dialkylation becomes increasingly important, and the product distribution resembles the dialkylation we observed previously. In the range of stoichiometry we investigated here we are able to observe both dialkylated and monoalkylated species. Interestingly, no C7-monoalkylated material was isolated, suggesting that 7-benzylC_{70}^- anion is more nucleophilic than either of the 1-benzylC_{70}^- or 2-benzylC_{70}^- anions.

This work provides a useful route to C1-monoalkylated C_{70} derivatives. In tandem with the Zn/RX method,[4b] it is possible to prepare either one of the two C1−C2 regioisomers. The results herein suggest that the Zn/RX method[2f] does not involve alkylation of the same discrete anions that are formed by deprotonation of hydrogenated fullerenes.

Experimental Section

Methyl ([70]Fulleren-1(2*H*)-yl) Acetate (4). 1,2-$C_{70}H_2$ (**3**)[10] (86.0 mg, 0.102 mmol), methyl bromoacetate (1.52 g, 10.0 mmol), and benzonitrile (50 mL) were combined in a 100-mL Schlenk flask. TBAOH (2.0 mL, 1.0 M in methanol, 2.0 mmol) was placed in another 25-mL Schlenk flask, and most of the methanol was removed by evaporation. The two flasks were connected with a distillation head and deoxygenated for 10 FPT cycles. After warming to room temperature the contents of these two flasks were mixed thoroughly, and the mixture was stirred under Ar at room temperature for 5 days. Unreacted anions and base were quenched with 2 mL of acetic acid. Ammonium salts were removed by passing the solution through a silica plug and eluting with toluene. The solvents were evaporated under vacuum, and the resulting solid was dissolved in ∼15 mL of toluene and applied to a silica gel chromatography column. The column was eluted with toluene to produce a first fraction of recovered C_{70} (17.6 mg, 0.021 mmol)) and a second fraction containing the alkylated products. The second fraction was further purified with preparative HPLC (10 mm × 250 mm Cosmosil Buckyprep column, toluene as mobile phase, monitored at 310 nm), producing **4** (27.5 mg, 0.030 mmol, 29% yield (37% based on consumed C_{70})) and **1**[4] (1.2 mg, 0.0013 mmol, 1.3%). ^1H NMR: δ 3.50 (s, 2H), 3.91 (s, 3H), 5.17 (s, 1H). ^{13}C NMR: δ 46.79 (1C), 50.26 (1C), 52.38 (1C), 54.62 (1C), 131.51 (2C), 131.59 (2C), 131.80 (2C), 134.10 (2C), 134.32 (2C), 138.38 (2C), 140.15 (2C), 141.11 (2C), 143.08 (2C), 143.26 (2C), 143.40 (2C), 143.43 (2C), 145.38 (2C), 146.26 (2C), 146.49 (2C), 146.62 (2C), 147.18 (1C), 147.25 (2C), 147.28 (2C), 147.76 (2C), 149.06 (2C), 149.28 (2C), 149.73 (2C), 149.76 (2C), 150.16 (2C), 150.22 (2C), 150.29 (2C), 150.81 (2C), 150.88 (2C), 151.63 (2C), 151.70 (3C), 151.81 (2C), 156.73 (2C), 156.99 (2C), 169.95 (1C). MS: 914.0 (60%, calcd 914.0); 840.0 (100%).

Reactions of 1,2-$C_{70}H_2$ with Benzyl Bromide and TBAOH in PhCN. Reaction A (1.2 equiv of base, excess RX). $C_{70}H_2$ (**3**, 62.0 mg, 0.074 mmol), benzyl bromide (1.27 g, 7.4 mmol), and benzonitrile (50 mL) were combined in a 100-mL flask, TBAOH (9.0 mL, 0.01 M in methanol, 0.090 mmol, then vacuum evaporation of methanol), present in a separate 25-mL Schlenk flask, was connected through a distilling head and deoxygenated for 10 FPT cycles. The apparatus was then tipped to mix the reagents. After being stirred for 18 h, the mixture was worked up as with **4** (only without the silica gel column separation step). After being purified by preparative HPLC (10 mm × 250 mm Cosmosil Buckyprep column, toluene as mobile phase, monitored

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(7) Unreacted **3** (10%) and C_{70} (60%) were also recovered.
(8) Structures **7** and **8** were assigned earlier, and several additional isomeric dialkylated compounds (**9**, **10**) were isolated, but structures could not be definitively assigned. See ref 2g.
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at 310 nm), C_{70} (37.2 mg, 0.044 mmol, 60%) and **5** (4.7 mg, 0.0050 mmol, 6.8%, 22% based on unrecovered fullerene) were obtained, together with unreacted **3** (6.5 mg, 0.0077 mmol, 10%). **Reaction B (3.6 equiv of base, excess RX).** $C_{70}H_2$ (**3**, 93.0 mg, 0.110 mmol), benzyl bromide (1.95 g, 11.4 mmol), benzonitrile (60 mL), and TBAOH (40.1 mL, 0.01 M in methanol, 0.41 mmol, then vacuum evaporation of methanol) were employed as the similar procedure and workup as above. After being purified with preparative HPLC (10 mm × 250 mm Cosmosil Buckyprep column, toluene as mobile phase, monitored at 310 nm), C_{70} (37.2 mg, 0.044 mmol, 40%), **5** (12.2 mg, 0.013 mmol, 12% absolute yield, 20% based on unrecovered fullerene), **6** (1.2 mg, 0.0013 mmol, 1.9%), **7** ((7,23-$C_{70}Bn_2$), 6.1 mg, 0.0060 mmol, 10%), and two unidentified isomeric species **9** (6.8 mg, 11%) and **10** (2.6 mg, 4.4%) were produced. **Reaction C (28 equiv of base, excess RX).** $C_{70}H_2$ (**3**, 59.1 mg, 0.0702 mmol), benzyl bromide (0.85 g, 5.0 mmol), and benzonitrile (60 mL) and TBAOH (2.0 mL, 1.0 M in methanol, 2.0 mmol, then vacuum evaporation of methanol) were employed as the similar procedure and workup as above. After being purified with preparative HPLC (10 mm × 250 mm Cosmosil Buckyprep column, toluene as mobile phase, monitored at 310 nm), **7** (7.2 mg, 0.0070 mmol, 10%), **9** (7.1 mg, 10%), **10** (0.7 mg, 1%), and **8** (0.8 mg, 1%) were produced, along with C_{70} (4.1 mg, 0.0049 mmol, 7%) and unreacted **3** (1.5 mg, 0.0018 mmol, 2.5%).

1-Benzyl-1,2-dihydro[70]fullerene (5). ^{1}H NMR: δ 3.82 (s, 2H), 5.06 (s, 1H), 7.34−7.43 (m, 3H), 7.48−7.52 (m, 2H). ^{13}C NMR: δ 49.69 (1C), 50.57 (1C), 59.29 (1C), 128.11 (1C), 129.03 (2C), 131.41 (2C), 131.27 (2C), 131.64 (1C), 134.07 (2C), 134.13 (2C), 135.37 (2C), 137.71 (2C), 140.37 (2C), 141.18 (2C), 143.00 (2C), 143.18 (2C), 143.32 (2C), 143.37 (2C), 143.44 (2C), 145.39 (2C), 146.20 (2C), 146.54 (2C), 146.94 (2C), 147.13 (1C), 147.22 (2C), 147.30 (2C), 147.74 (2C), 149.04 (2C), 149.21 (2C), 149.64 (2C), 149.80 (2C), 149.98 (2C), 150.14 (2C), 150.24 (2C), 150.80 (2C), 150.87 (2C), 151.45 (2C), 151.67 (3C), 151.83 (2C), 156.74 (2C), 158.42 (2C); MS: 932.1 (30%, calcd 932.0); 840.0 (100%).

2-Benzyl-1,2-dihydro[70]fullerene (6). ^{1}H NMR: δ 4.12 (s, 2H), 4.56 (s, 1H), 7.45 (t, 1H), 7.53 (t, 2H), 7.70 (t, 2H). ^{13}C NMR: δ 52.13 (1C), 53.00 (1C), 57.95 (1C), 128.17 (1C), 129.23 (2C), 131.40 (2C), 131.51 (2C), 131.72 (2C), 134.20 (2C), 134.26 (1C), 135.73 (2C), 138.34 (2C), 140.65 (2C), 141.13 (2C), 142.88 (2C), 143.20 (2C), 143.27 (2C), 143.49 (2C), 145.77 (2C), 145.95 (2C), 146.23 (2C), 146.70 (2C), 147.05 (2C), 147.47 (2C), 147.64 (2C), 147.86 (2C), 149.19 (2C), 149.29 (2C), 149.51 (2C), 149.55 (1C), 149.79 (2C), 149.88 (2C), 150.03 (2C), 150.22 (2C), 151.02 (2C), 151.08 (2C), 151.49 (2C), 151.62 (3C), 151.67 (2C), 155.67 (2C), 158.78(2C); MS: 932.0 (25%, calcd 932.0); 840.0 (100%).

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Supporting Information Available: General experimental information and copies of the ^{13}C NMR spectra of **4**−**6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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