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The Specific Acid-Catalyzed and Photochemical Isomerization of a Robust Fulleroid to a Methanofullerene

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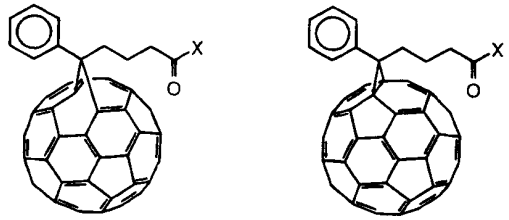
Recently we showed that fulleroids (structures **F**; methanoannulene analogs with 60*p* electrons) and methanofullerenes (structures **M**; cyclopropanofullerenes) carrying phenyl and butanecarboxylate groups on the 61st carbon (see **1**) are versatile fullerene derivatives for the study of biological and materials science properties.[1] In



F1 [5,6] **M1** [6,6]

order to prepare any conceivable ester or amide as well as other functional groups derivable from "C(O)X" (e.g., isocyanate, etc.), in the past, it was necessary to hydrolyze a methyl ester under relatively drastic conditions.[1]

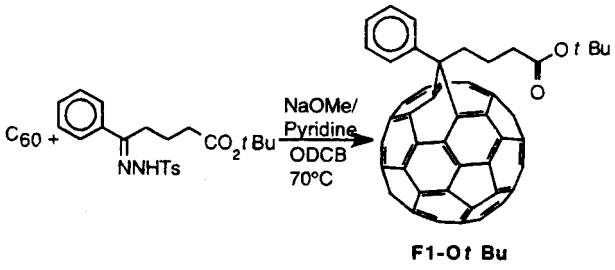
In this paper we report the first isolation and characterization of an isomerically pure fulleroid carboxylic acid **F1-OH** (X = OH). We additionally present an improvement in the preparation of **M1-OH** (X = OH), the immediate precursor to the important acid chloride intermediate (**M1-Cl**, X = Cl). We also report on the subtle interplay between acid strength and either the hydrolysis of a carboxylate ester or a fulleroid-methanofullerene rearrangement. Finally, we describe the preparative[2] scale photochemical fulleroid-methanofullerene rearrangement.

Results

The diazoalkane addition to fullerene C_{60} is the only known method for the synthesis of fulleroids.[3] Most fulleroids are quite labile and isomerize to methanofullerenes thermally (as low as 80 °C). So far, only [5,6]-$C_{61}H_2$ is the only fulleroid which is not convertible to the [6,6] isomer. The esters described within are, next to [5,6]-$C_{61}H_2$, the most stable fulleroids we encountered.

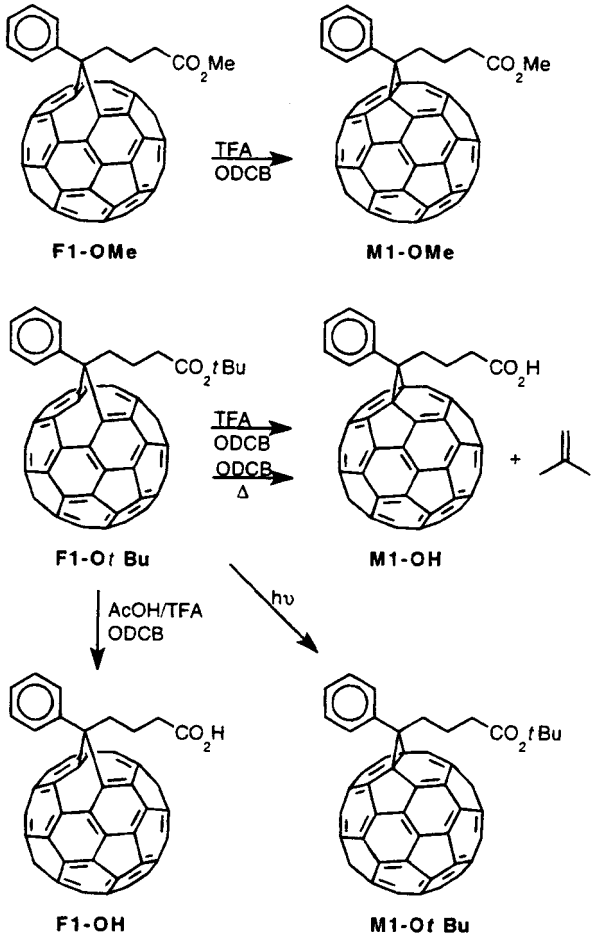
The fulleroid *tert*-butyl ester (**F1-O*t*-Bu**) was prepared according to Scheme 1. The *tert*-butyl 4-benzoylbutyrate tosylhydrazone was prepared in the usual way as described previously for the methyl ester.[1] In this method, the requisite diazoalkane was generated *in situ* in a "one-pot reaction". The fulleroid ester was isolated by chromatography in 30% yield (ca. 60% based on recovered C_{60}) and was found to be essentially pure (95%) [5,6] with the

Scheme 1



F1-O*t* Bu

Scheme 2



F1-OMe **M1-OMe**

F1-O*t* Bu **M1-OH**

F1-OH **M1-O*t* Bu**

phenyl over a former pentagon. The remaining resonances in the ^{1}H NMR were due to the fulleroid isomer with the phenyl ring over a former hexagon and due to the methanofullerene isomer.

In an attempt to hydrolyze the methyl ester (**F1-OMe**)[1] using trifluoroacetic acid in 1,2-dichlorobenzene (ODCB), we discovered that the fulleroid *isomerized to the methanofullerene* (**M1-OMe**) *without hydrolysis.* On the other hand hydrolysis *without rearrangement* was effected on **F1-O*t*-Bu** by the use of 40% (v/v) acetic acid in trifluoroacetic acid with ODCB as solvent yielding **F1-OH**. These observations are summarized in Scheme 2.

This procedure allowed the manipulation, for the first time, of a functional derivative of a fulleroid. To obtain the carboxylic acid of the methanofullerene, three avenues were available: (1) TFA in ODCB for the *t*-Bu ester, (2) heat,[4] and (3) photolysis. In the course of establishing the conditions for the thermal isomerization, we discovered that thermolysis of **F1-O*t*-Bu**, afforded,

(1) Hummelen, J. C.; Knight, B. W.; LePeq, F.; Wudl, F.; Yao, J.; Wilkins, C. L. *J. Org. Chem.* **1995**, *60*, 532-538.

(2) Janssen, R. A. J.; Hummelen, J. C.; Wudl, F. *J. Am. Chem. Soc.* **1995**, *117*, 544-545.

(3) Hirsch, A. *The Chemistry of the Fullerenes*; Thieme: Stuttgart, 1994.

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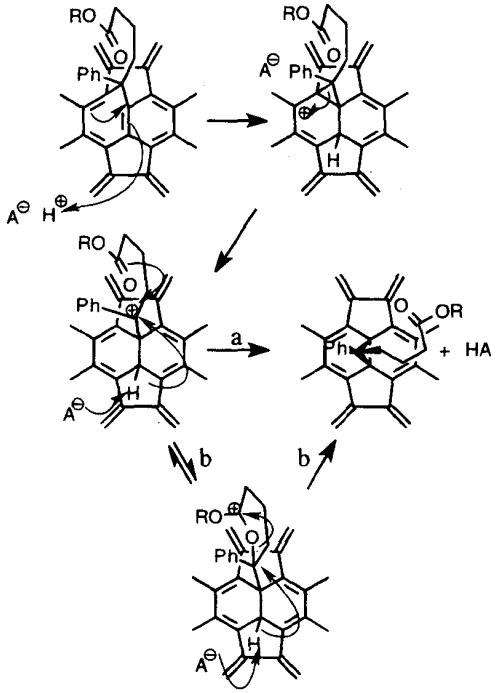
Scheme 3



in one step, the isomerization *and* "hydrolysis" (loss of isobutylene, see Scheme 2).

The **M1-O*t*-Bu** ester could be obtained cleanly by photolysis of **F1-O*t*-Bu**. By a combination of reactions depicted in Scheme 2 we were able to easily obtain and fully characterize the **F1** and **M1** carboxylic acids and *tert*-butyl esters.

A possible explanation of the processes occurring in Scheme 2 hinges on the difference in nucleophilicity between acetate and trifluoroacetate as well as the difference in polarity of the medium between TFA/ODCB and TFA/AcOH/ODCB. In the former, upon protonation of the carbonyl, we expect ionization of the *tert*-Bu group as well as competitive protonation of a fulleroid double bond. A possible mechanism for the acid-catalyzed fulleroid-methanofullerene isomerization is shown in Scheme 3 (path a). In TFA/AcOH/ODCB, the lower acidity of the medium is apparently insufficient to protonate a fulleroid double bond. Alternately, the protonated carbonyl, in TFA/ODCB, could act as a conduit for the delivery of a proton to a fulleroid double bond and initiate the isomerization to the methanofullerene.[5] The ester carbonyl can also help in the process by temporary trapping of the intermediate carbocation as shown in Scheme 3 (path b).

Experimental Section[6]

4-Benzoylbutyric Acid *tert*-Butyl Ester. To a stirred solution of 4-benzoylbutyric acid (9.6 g, 50 mmol) in 200 mL distilled CH_2Cl_2 was added 2 mL of concd H_2SO_4. Isobutylene (75 mL) was bubbled into the solution over a period of 10 min. The resulting solution was stirred for 21 h at ambient temperature. The solution was poured on 400 mL aqueous Na_2CO_3 and the organic layer was shaken with water and dried with $MgSO_4$/Na_2CO_3 and a pinch of charcoal. Filtration over a small amount of silica gel (to remove traces of starting material) and concentration *in vacuo* gave the ester as a colorless oil: yield 9.8 g (80%). Kugelrohr distillation (oven temperature 150 °C/3 mmHg) afforded analytically pure material. ^{1}H NMR ($CDCl_3$/TMS, 500MHz): 7.95 (d, J = 7.5 Hz, 2H), 7.53 (m, 1H), 7.44 (m, 2H), 3.02 (t, J = 7 Hz, 2H), 2.34 (t, J = 7.5 Hz, 2H), 2.03 (m, 2H), 1.44 (s, 9H) ppm. ^{13}C NMR ($CDCl_3$/TMS, 50 MHz): 199.43, 172.59, 136.86, 133.01, 128.58, 128.03 , 80.20, 37.46, 34.62, 28.09, 19.62 ppm. FTIR (KBr): 2978 s, 1727 s, 1687 s, 1367 s, 1147 s cm^{-1}. MS: m / z 249(M + H)$^+$, 193, 175, 147, 105, 77. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.28; H, 7.99.

4-Benzoylbutyric Acid *tert*-Butyl Ester Tosyl Hydrazone. A solution of 4-benzoylbutyric acid *tert*-butyl ester (5.0 g) and *p*-toluenesulfonyl hydrazide (4.65 g, 1.25 equiv) in 15 mL MeOH was stirred at reflux temperature for 6 h. The mixture was concentrated *in vacuo* and left to allow crystallization of the hydrazone. The solid was collected by filtration, washed with EtOH, and dried. Yield: 5.4 g (64%) white crystals. Mp: 118-120 °C. ^{1}H NMR ($CDCl_3$/TMS, 200 MHz): 9.52 (s, 1H), 7.91 (d, J = 8.5 Hz, 2H), 7.64 (m, 2H), 7.32 (m, 3H), 7.28 (d, J = 8.5 Hz, 2H), 2.62 (t, J = 8 Hz, 2H), 2.38 (s, 3H), 2.19 (t, J = 8 Hz, 2H), 1.60 (m, 2H), 1.50 (s, 9H) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): 174.02, 153.88, 143.51, 136.22, 129.40, 128.35, 127.91, 126.21, 81.81, 33.30, 28.05, 25.91, 21.50, 21.22 ppm. FTIR (KBr): 3125 s, 1699 s, 1374 s, 1366 s, 1350 s, 1333 s, 1325 s, 1242 s, 1181 s, 1169 s, 817 s, 759 m, 688 m, 560 m,551 s cm^{-1}. MS: m/z 416 (M)$^+$, 360, 343, 205, 176, 117 (100), 91. Exact mass: calcd. For $C_{22}H_{28}N_2O_4S$ 416.1773; found 416.1770. Anal. Calcd for $C_{22}H_{28}N_2O_4S$: C, 63.44; H, 6.78; N, 6.73; S, 7.70. Found: C, 63.23; H, 6.84; N, 6.73; S, 7.76.

{6}-1-[3-(*tert*-Butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61} (F1-O*t*-Bu). Sodium methoxide (225 mg, 4.16 mmol) was added to a solution of *tert*-butyl 4-benzoylbutyrate *p*-tosylhydrazone (1.66 g, 4 mmol) in 30 mL of dry pyridine under nitrogen and the mixture was stirred for 15 min. A solution of C_{60} (1.44 g, 2 mmol) in 100 mL of HPLC grade 1,2-dichlorobenzene was added and the reaction mixture was stirred at 65-70 °C for 30 h. The solvent was removed *in vacuo*, and the product was purified by column chromatography (SiO_2, toluene). It was eluted first with 200 mL of chlorobenzene and then with toluene. The fraction containing the product was collected, solvents were removed *in vacuo* and the product was precipitated with methanol from a toluene/methanol solution. The precipitate was centrifuged, washed with methanol, centrifuged twice more, and finally dried *in vacuo*. Yield: 576 mg (30%, 61% based on consumed C_{60}).^{1}H NMR (CS_2, 500 MHz): [major isomer (95%)] 7.88 (d, J = 7.5 Hz, 2H), 7.49 (m, 2H), 7.37 (m, 1H), 1.91 (t, J = 7.5 Hz, 2H), 1.55 (m, 2H), 1.30 (m, 2H), 1.31 (s, 9H) ppm; [minor isomer (5%)] 7.10-7.25 (m, 5H), 3.77 (m, 2H), 2.48 (t, J = 7.5 Hz, 2H), 1.85 (m, 2H), 1.34 (s, 9H) ppm. ^{13}C NMR (CS_2, 75 MHz): 170.2, 147.2, 146.2, 144.9, 144.6, 144.3, 144.0, 143.8, 143.6, 143.5, 143.4, 143.0, 142.9, 142.8, 142.6, 142.5, 142.3, 141.9, 141.8, 141.7, 141.1, 140.8, 140.3, 139.5, 138.6, 138.0, 137.7, 136.4, 134.8, 130.5, 128.6, 127.6, 78.8, 60.8, 35.5, 34.9, 27.9, 20.0 ppm. FTIR (KBr): 1724 m, 1445 m, 1363 m, 1171 m, 1146 m, 753 m, 699 m, 644 m, 616 w, 588 w, 583 w, 579 w, 572 m, 559 w, 554 w, 550 w, 546 w, 542 m, 529 s, 527 s, 521 s, 512 m cm^{-1}. UV-Vis (toluene) l_{max} (nm): 344, 426, 538. FABMS (toluene/NBA): m / z 953 (M + H)$^+$. Anal. Calcd for $C_{75}H_{20}O_2$: C, 94.54; H, 2.10. Found: C, 92.91; H, 2.07.

1-[3-*tert*-Butoxycarbonyl)propyl]-1-phenyl-[6.6]-C_{61} (M1-O*t*-Bu)(Photochemical Isomerization). {6}-1-[3-*tert*-Butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61} (75 mg, 0.079 mmol) was dissolved in 100 mL of toluene under nitrogen, and the solution was irradiated for 30 min with a 500 W flood lamp. Toluene was removed *in vacuo*, and the product was precipitated with methanol from a toluene/methanol solution. The precipitate was centrifuged, washed with methanols and centrifuged twice more, and finally dried *in vacuo*. Yield: 72 mg (96%). ^{1}H NMR (CS_2, 500 MHz): 7.84 (d, J = 7.5 Hz, 2H), 7.48 (m, 2H), 7.42 (m, 1H), 2.83 (m, 2H), 2.32 (t, J = 7.5 Hz, 2H), 2.06 (m, 2H), 1.39 (s, 9H) ppm. ^{13}C NMR (CS_2, 125 MHz): 170.5, 148.6, 147.7, 145.8, 145.2, 145.0, 144.8, 144.7, 144.6,144.5,144.1,143.7,143.1, 143.0,

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(5) The rearrangement could be considered a Berson-Wilcott rearrangement[7] which was recently invoked in a related transformation of an 11-carboxyl-1,6-methano[10]annulene.[8] Unlike the latter, in our fulleroid, the carbonyl carbon is too far away to have a substantial effect, upon protonation, on the electronegativity of the bridge carbon atom.

(6) In the nomenclature below {n} means the moiety over a former pentagon (n = 5) or hexagon (n = 6).

(7) Berson, J. *Acc. Chem. Res.* **1968**, *1*, 152.

(8) Barret, D. G.; Gellman, S. H. *Tetrahedron Lett.* **1994**, *35*, 2299.

142.9, 142.2, 142.1, 142.0, 141.1, 140.8, 138.2, 137.7, 136.7, 132.1, 128.5, 128.3, 79.7, 79.2, 52.0, 35.1, 33.8, 28.1, 22.8 ppm. FTIR (KBr): 1728 s, 1445 m, 1428 m, 1364 m, 1187 m, 698 m, 585 m, 572 m, 564 w, 558 w, 554 w, 550 m, 527 s, 523 s cm^{-1}. UV-Vis (toluene) l_{max} (nm): 332, 434, 492, 696. FABMS (toluene/NBA): *m / z* 953 $(M + H)^+$, 720 $(C_{60})^+$. Anal. Calcd for $C_{75}H_{20}O_2$: C, 94.54; H, 2.10. Found: C, 92.14; H, 2.6.

{6}-1-(3-Carboxypropyl)-{5}-1-phenyl-[5.6]-C_{61} (F1-OH) (Hydrolysis without Isomerization). To a solution of {6}-1-[3-*tert*-butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61} (40 mg, 0.042 mmol) in 4 mL of 1,2-dichlorobenzene was added 1.6 mL of acetic acid and 2.4 mL of trifluoroacetic acid. The mixture was stirred at room temperature for 6 h. Solvents were removed *in vacuo*, and the product was washed with ether. The precipitate was centrifuged, washed with ether, centrifuged twice more, and finally dried *in vacuo*. Yield: 35 mg (93%). ^{1}H NMR (CS_2/formic acid-d_2, 500 MHz): 7.89 (d, *J* = 7.5 Hz, 2H), 7.50 (m, 2H), 7.38 (m, 1H), 2.12 (t, *J* = 7.5 Hz, 2H), 1.62 (m, 2H), 1.44 (m, 2H) ppm. ^{13}C NMR (CS_2/formic acid-d_2, 125 MHz): 179.2, 147.3, 146.2, 145.1, 144.8, 144.5, 144.2, 143.9, 143.7, 143.6, 143.2, 143.1, 143.0, 142.7, 142.4, 142.2, 141.9, 141.3, 141.0, 140.5, 139.6, 139.4, 138.8, 138.3, 138.1, 137.9, 136.6, 130.6, 128.9, 127.9, 123.0, 60.7, 35.4, 33.8, 19.9 ppm. FTIR (KBr): 1703 s, 1436 m, 1171 m, 697 m, 688 w, 682 w, 597 w, 572 m, 559 w, 545 w, 542 m, 529 s, 526 s, 521 s, 517 s, 512 m cm^{-1}. UV-Vis (pyridine) l_{max} (nm): 336, 428, 538. Anal. Calcd for $C_{71}H_{12}O_2$: C, 95.09; H, 1.34. Found: C, 92.08; H, 1.53.

1-(3-Carboxypropyl)-1-phenyl-[6.6]-C_{61} (M1-OH) (From {6}-1-[3-*t*-Butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61}) (Thermal Isomerization and Hydrolysis). A solution of {6}-1-(3-(*tert*-butoxycarbonyl)propyl)-{5}-1-phenyl-[5.6]-C_{61} (100 mg, 0.105 mmol) in 1,2-dichlorobenzene (10 mL) was refluxed overnight. Solvent was removed *in vacuo* and the product was washed with methanol. The precipitate was centrifuged, washed with methanol, centrifuged twice more, and finally dried *in vacuo*. Yield: 90 mg (95%). Spectral data are identical to those of the compound obtained from **M1-OMe**.[1]

1-(3-Carboxypropyl)-1-phenyl-[6.6]-C_{61} (M1-OH) (From {6}-1-[3-(*tert*-Butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61}) (Acid-Assisted Isomerization and Hydrolysis). Trifluoroacetic acid (0.5 mL) was added to a solution of {6}-1-[3-(*tert*-butoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61} (10 mg, 0.01 mmol) in 1,2-dichlorobenzene (1 mL) and the mixture was stirred at room temperature overnight. The solvent was removed *in vacuo*, and the product was washed with ether. The precipitate was centrifuged, washed with ether, centrifuged twice more, and finally dried *in vacuo*. Yield: 9 mg (95%). (See above.[1])

1-[3-(Methoxycarbonyl)propyl]-1-phenyl-[6.6]-C_{61} (M1-OMe) (Acid-Assisted Isomerization without Hydrolysis). To a solution of {6}-1-[3-(methoxycarbonyl)propyl]-{5}-1-phenyl-[5.6]-C_{61} (10 mg, 0.011 mmol) in 1 mL of 1,2-dichlorobenzene was added trifluoroacetic acid (0.5 mL), and the mixture was stirred at room temperature for 3 h. The purple solution became brown. Solvents were removed *in vacuo* and the product was precipitated with methanol from a toluene/methanol solution. The precipitate was centrifuged, washed with methanol, centrifuged twice more, and finally dried *in vacuo*. Yield: 9 mg (90%). Spectral data identical to those of compound obtained from **F1-OMe** by thermal isomerization.[1]

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