Pergamon

Tetrahedron Letters, Vol. 35, No. 51, pp. 9529-9532, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)02208-9

Cyclopropanation of C_{60} Via a Fischer Carbene Complex

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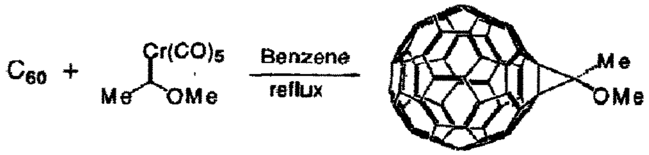
Abstract: *A new method for the preparation of methanofullerenes is demonstrated by the formation of 1,2-methyl(methoxymethano)fullerene-C_{60} by the thermal reaction of C_{60} with [methyl(methoxymethylene)]pentacarbonylchromium.*

In the quest to prepare and study derivatives of C_{60}, the methanofullerenes have become the most studied class of C_{60}-derived compounds.[1] The methanofullerenes are quite stable and have shown promise in applications in fields as diverse as material science and medicine. Wudl reported the synthesis of precursors to "pearl-necklace" polymers[2] and Rubin recently synthesized ethynyl-substituted methanofullerenes for use in the preparation of macrocyclic and polymeric carbon allotropes.[3] Interest in the potential medical applications of fullerenes has spurred research into the preparation of water soluble methanofullerene derivatives. A water soluble methanofullerene prepared by Wudl and coworkers has been shown to inhibit HIV-1 protease.[4] There are several methods for the preparation of methanofullerenes. The most common is via a [3+2] cycloaddition of diazo compounds with C_{60} to yield intermediate pyrazolines which thermally extrude nitrogen to produce the methanofullerenes[5] and has been used to synthesize a series of aryl- and ester-substituted derivatives.[2,6] Strategies involving generation of free carbenes have also been employed in the synthesis of methanofullerenes. Thermal decomposition of diazirines in the presence of C_{60} has been utilized to prepare a glucose-derived methanofullerene[7] and a chloro-substituted methanofullerene.[8] Dichloromethanofullerene[9] and dimethoxymethanofullerene[10] have also been prepared by the addition of free carbenes. A "carbene-free" methodology for the preparation of methanofullerenes involves the addition of bromomalonate anions to C_{60} followed by intramolecular substitution of the bromide, but this method is limited in scope.[11]

We envisioned a new route to methanofullerenes using the well-documented cyclopropanation chemistry of Fischer carbene complexes.[12] Cyclopropanation of electron-deficient olefins by chromium carbenes is sensitive to the steric environment about the alkene and is generally only effective for mono-substituted substrates. However, the steric effects of the tetrasubstituted double bonds in C_{60} were expected to be countred by the pyramidalized nature of the double bonds combined with the high electrophilicity, and hence π-acidity, of C_{60}.[13] We report herein successful cyclopropanation of C_{60} by a chromium carbene complex which provides another route to methanofullerenes which excludes free carbene intermediates.

Much of the reported chromium carbene-mediated cyclopropanation chemistry has used [phenyl-(methoxymethylene)]pentacarbonylchromium and [methyl(methoxymethylene)]pentacarbonylchromium, so these compounds were tested for C_{60} cyclopropanation.[14,15] While the phenyl methoxy carbene complex did not react with C_{60} under a variety of thermal conditions, the more reactive methyl methoxy carbene complex reacted successfully. Reaction of two equivalents of methyl methoxy carbene complex with C_{60} in vigorously refluxing benzene for 72 h with subsequent purification by flash chromatography (98:2 hexane/ethyl acetate) gave the desired 1,2-dihydro-1,2-methyl(methoxymethano)-fullerene-C_{60} as a brown solid (equation). The methanofullerene product was obtained as a single isomer resulting from cyclopropanation of a 6,6 ring junction. The presence of 26 signals (3 of greater intensity) in the fullerene region of the ^{13}C NMR confirmed the C_s symmetry of the product (see Figure).[16] The C_{60}-sp^3 carbon resonance is at 83 ppm, the methano-bridge carbon is observed at 73 ppm and the methyl and methoxy carbons are observed at 14 and 55 ppm, respectively. Two singlets in the ^1H NMR at 3.65 and 2.28 ppm correspond to the methoxy and methyl protons. The methanofullerene product can be consistently obtained in 20% yield, however this yield is not optimized and yields above 50% were achieved on multiple occasions.



Carbene derivatives of C_{60} can exist as isomeric methanofullerene 6,6 ring junction adducts and fulleroid (methanoannulene) 5,6 ring junction adducts.[17] For the unsubstituted derivative, $C_{61}H_2$, the fulleroid structure is predicted to be the more stable isomer by 0.34 kcal/mol,[6a] and equilibration studies confirm this prediction.[18] However, for substituted derivatives, PM3 calculations predict that the methanofullerene structure is the more stable isomer. These findings are in excellent agreement with the observation that the substituted fulleroid isomers can be converted to methanofullerene isomers under thermal conditions.[6a,6b,17] The methanofullerene and the fulleroid isomers are easily distinguished by the ^{13}C NMR shifts of the carbons directly attached to the methano-bridge.[6b] The sp^3 hybridized carbons of the methanofullerene isomers are observed between 70 and 90 ppm while the sp^2 carbons attached to the methano-bridge in the fulleroid isomers are observed between 130 and 150 ppm. The observation of a signal at 83 ppm in the ^{13}C NMR assigned to the C_{60}-sp^3 carbons definitively identifies the methyl(methoxymethano)fullerene as a methanofullerene. This result is in accord with the experimentally observed preference for substituted derivatives to exist as the methanofullerene isomer rather than the fulleroid isomer.[6a,6b] Although the fulleroid isomer is not observed, it may have been formed during the course of the reaction since the reaction conditions are sufficient to induce its isomerization to the more stable methanofullerene isomer.

Successful cyclopropanation of C_{60} required a vigorous benzene reflux for 3 to 4 days. When compared to the conditions necessary for the reaction of chromium carbenes with activated, sterically unencumbered alkenes (80°C, 3-6 h)[14] and with more substituted, activated alkenes (100-110°C, 10-24 h),[15] it becomes apparent that C_{60} is a sluggish substrate. The low reactivity of the unactivated tetrasubstituted double bonds of C_{60} is only partially countered by the pyramidalized nature of the double bonds as well as the high electron-affinity of C_{60}, which accounts for the modest yield in the C_{60} cyclopropanation reaction.

The mechanism of the cyclopropanation of C_{60} is believed to be analogous to that proposed for electron-deficient alkenes and does not involve free carbenes.[12,19] Thermally-induced loss of a CO with subsequent coordination of C_{60} generates an η^2-C_{60} chromium complex. This step is sensitive to the steric and electronic nature of the alkene substrate, but C_{60} is an excellent π-acceptor, as is well-documented by its organometallic coordination chemistry,[20] and this electronic effect is potentially crucial to the success of the cyclopropanation reaction. Formal [2+2] cycloaddition produces a metallacyclobutane from which reductive elimination yields the methanofullerene.

In conclusion, the cyclopropanation of C_{60} by a Fischer chromium carbene complex has been realized as a potentially general route to methanofullerenes. Overall, the oxygen stabilized carbene complexes are likely to be of specific interest due to their ease of preparation and the presence of the ether functionality which provides a handle for further functionalization of the methanofullerenes. Other Fischer carbene complexes such as the more reactive molybdenum and non-heteroatom stabilized carbene complexes are expected to react readily with C_{60}.[21] Studies on these fronts are in progress.

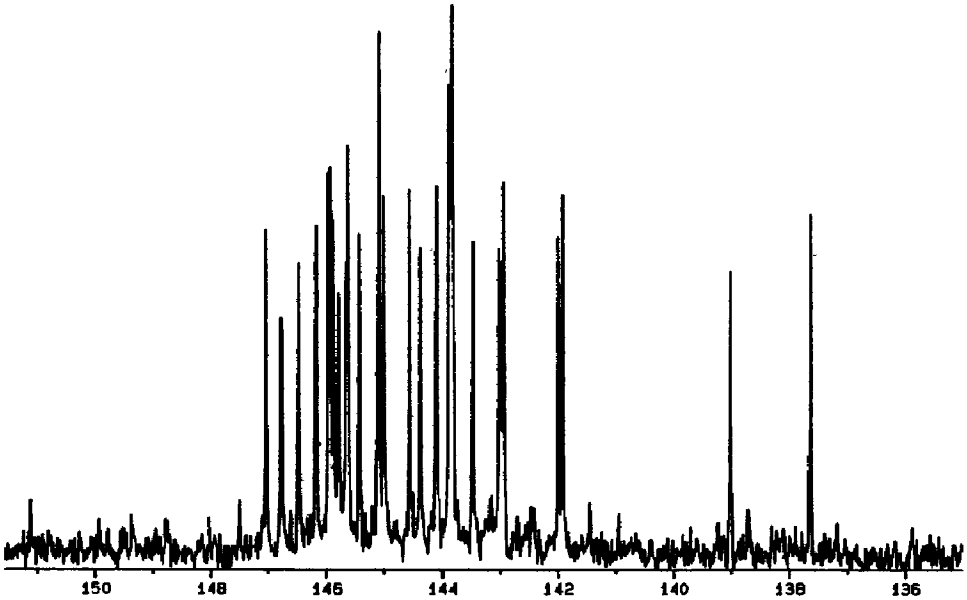


Figure. Fullerene region of the ^{13}C NMR of 1,2-methyl(methoxymethano)fullerene-C_{60}

Acknowledgement: We thank the National Science Foundation (CHE-9257081) for support of this research.

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16. IR (KBr pellet): 2962, 2929, 2850, 1736, 1504, 1458, 1425, 1378, 1259, 1219, 1160, 1099, 1073, 1034, 801, 523, 430, 420. ^{1}H NMR (360 MHz, CS_2/C_6D_6) δ: 2.28 (1H, s), 3.65 (1H, s). ^{13}C NMR (90.6 MHz, CS_2/C_6D_6, 0.01 M $Cr(acac)_3$) δ: 146.45, 146.19, 145.90, 145.60, 145.38, 145.34, 145.30, 145.22, 145.08, 145.06, 144.85, 144.52, 144.43, 143.98, 143.80, 143.53, 143.29, 143.24, 142.89, 142.44, 142.40, 142.36, 141.42, 141.35, 138.44, 137.06, 83.02, 73.81, 55.83, 14.47. MS (FAB): 779 (50, M+1), 763(28, M-CH_3), 747(28, M-OCH_3), 721(62, C_{60}+1).
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(*Received in USA* 6 *October* 1994; *accepted* 3 *November* 1994)