Addition of Nitrile Oxides to C_{60}: Formation of Isoxazoline Derivatives of Fullerenes

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Summary: Nitrile oxides add to C_{60} in a 1,3-dipolar fashion. The nitrile oxides were generated *in situ*, and the products were isolated by gel permeation chromatography. Products with C_s symmetry are indicated by the ^{13}C NMR spectra, suggesting that the addition takes place across a 6,6 ring fusion.

Investigation of the fundamental chemical reactivity of fullerenes is rapidly producing methods for the preparation of derivatized fullerenes. Cycloadditions have proven to be highly successful. C_{60} undergoes cycloaddition with a variety of reagents, including Diels–Alder reactions with cyclopentadiene[1] and *o*-quinodimethanes,[2,3] 1,3-dipolar addition with diazoalkanes[4–7] and azides,[8,9] [2 + 2] cycloaddition of singlet oxygen[9] and benzyne,[10] and addition of 1,3-diyls.[11] The addition of diazoalkanes has become a highly versatile method for the preparation of "fulleroids"—fullerenes with a $-CR_2-$ unit inserted into the structure. 1,3-Dipolar addition of diazomethane to C_{60} initially results in the formation of a pyrazoline intermediate which has been isolated and characterized.[4] This material loses N_2 on heating, rearranging to the final product fulleroid.

We are interested in the potential synthetic utility of 1,3-dipolar adducts of C_{60}. The dipolar addition of nitrile oxides to C_{60} appears to be a particularly promising route to functionalized fullerenes. The isoxazolines formed by the addition of nitrile oxides to alkenes can be elaborated to a variety of different functional groups and have been used as the key step in numerous syntheses of highly functionalized natural products. 1,3-Dipolar addition of nitrile oxides to C_{60} may provide access to functionalized fullerenes that would be challenging to produce by other methods.

Treatment of C_{60} with propionitrile oxide, generated *in situ* from nitropropane, phenylisocyanate, and triethylamine, results in the formation of a brown color. Analysis of the crude reaction mixture by analytical gel-permeation chromatography (GPC) or by reversed-phase HPLC indicates the formation of a new compound (2) that elutes at shorter retention times than C_{60}. This adduct was separated from unreacted C_{60} by preparative gel-permeation chromatography.[12,13] Unreacted C_{60} was the major fullerene-containing impurity in the crude mixture, although several other compounds, presumably nitrile oxide decomposition products, are formed as well. The adduct was obtained in 29% yield (63% based on unrecovered C_{60}, unoptimized) as a brown-black powder. The ^1H NMR spectrum of the crude reaction mixture exhibited a single set of ethyl resonances suggesting that the product is a single cycloadduct. The ^{13}C NMR spectrum (Figure 2) of pure 2 confirms that a C_s isomer is obtained, resulting from addition across a 6,6-ring fusion. This structure (2) is analogous to the adduct formed between C_{60} and diazomethane.[4]

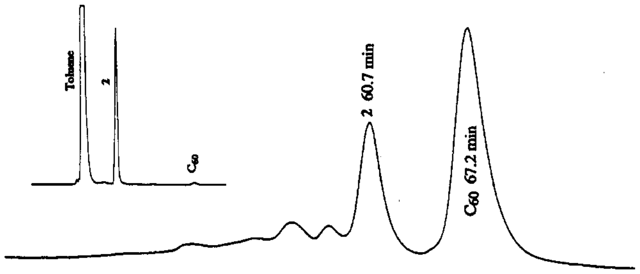
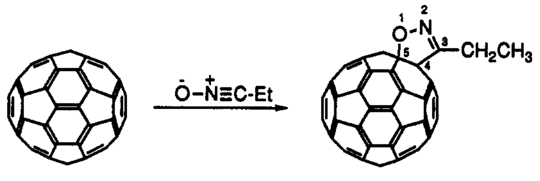


Figure 1. Gel permeation chromatogram of the crude reaction mixture. Inset: C_{18} reversed-phase HPLC chromatogram of purified 2 (30% MeCN/70% CH_2Cl_2 mobile phase, 1 mL/min).



1 2

The ^{13}C NMR spectrum[14] shows a total of 33 lines, of which 26 are in the fullerene sp^2 region between 135 and 148 ppm. The proposed structure of 2 has a plane of symmetry, with four fullerene carbons situated on the plane. Therefore, four fullerene carbon lines are expected

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(14) ^1H NMR data (200 MHz, $CDCl_3/CS_2$): δ 1.67 (*t*, CH_3, 3H, $J = 7.3$ Hz), δ 3.11 (q, 2H, CH_2, $J = 7.3$ Hz). ^{13}C NMR data: (100 MHz, $CS_2/CDCl_3 + Cr(acac)_3$): 11.26 (CH_3), 22.23 (CH_2), 80.03 (isoxazoline C-4, 1), 101.77 (isoxazoline C-5, 1), 136.15 (2), 136.49 (2), 139.74 (2), 140.31 (2), 141.38 (2), 141.76 (2), 141.81 (2), 141.88 (2), 141.99 (4), 142.38 (4), 142.57 (2), 143.68 (2), 143.96 (2), 144.47 (2), 144.60 (2), 144.68 (2), 144.69 (2), 144.76 (2), 144.86 (2), 145.04 (2), 145.19 (2), 145.44 (2), 145.56 (2), 145.75 (2), 145.81 (2), 145.92 (2), 146.78 (1), 147.31 (1), 154.80 (isoxazoline C-3). A small peak, believed to be a trace amount of either acetone or free Hacac, appears at 29 ppm.

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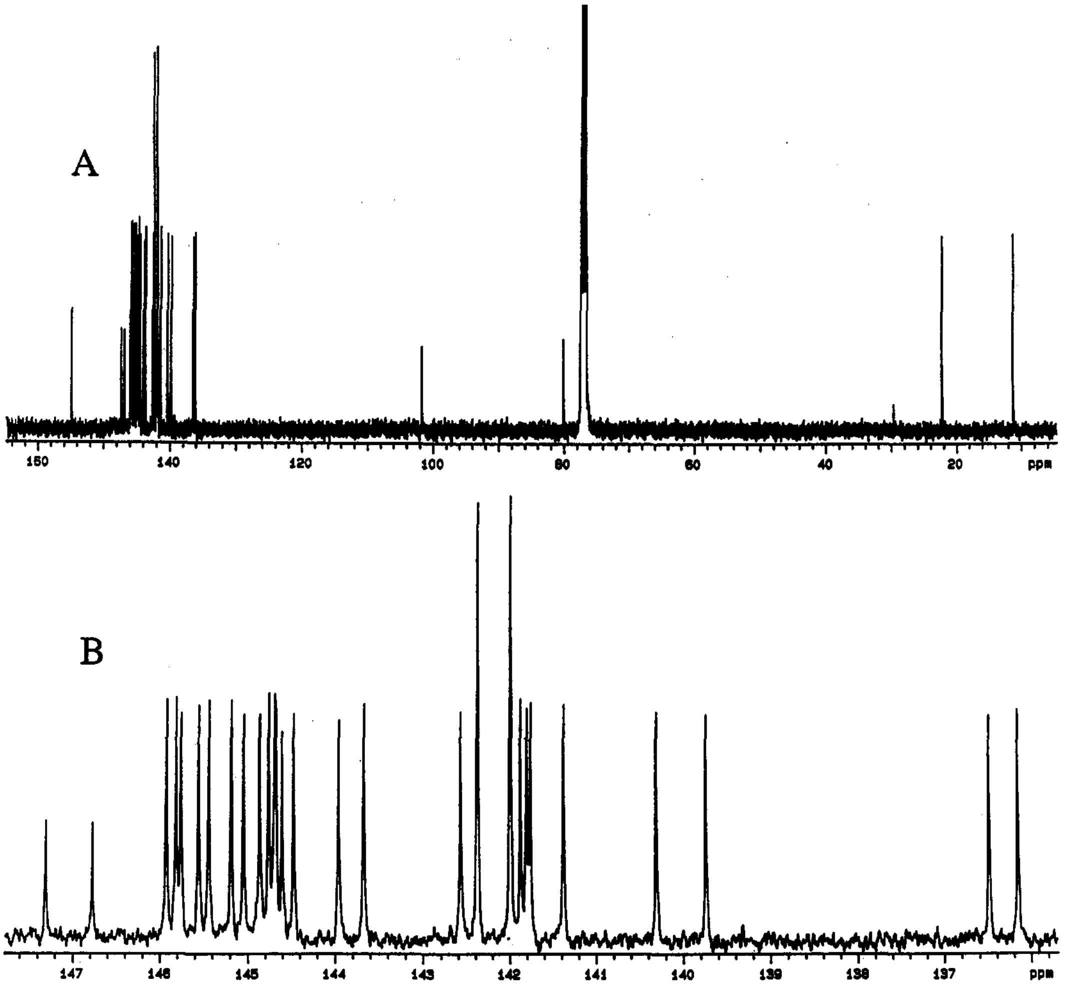


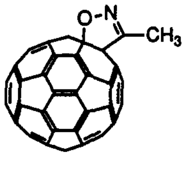
Figure 2. (A) ^{13}C NMR spectrum of 2 ($CDCl_3/CS_2$ with 0.02 M $Cr(acac)_3$, 53 248 transients). (B) Expanded view of the sp^2 carbon region.

to be of single intensity and 28 of double intensity. In the measured spectrum (Figure 2), single intensity lines corresponding to the isoxazoline C-4 and C-5 appear at 80.0 and 101.8 ppm. Two other fullerene lines (146.78, 147.31 ppm) are of single intensity, and 24 fullerene lines are of double intensity. Two (141.99 and 142.38 ppm) are of quadruple intensity, due to accidental overlap. This leads to a total of 32 fullerene lines, consistent with the C_s-symmetry of 2. A carbon line at 154 ppm is assigned to the isoxazoline C-3, and the two side-chain carbons appear at 11 and 22 ppm.

Mass spectrometric analysis of this sample was plagued by substantial amounts of fragmentation, a problem that is very common with fullerene derivatives. A mass line at *m/e* 791, corresponding to 2, appears in the negative-ion FABS spectrum, but the base peak is at *m/e* 720, corresponding to C_{60}. A number of other fragments were observed as well.

The addition of acetonitrile oxide to C_{60} was also successful, leading to isoxazoline 3. Purification of this compound was performed in the manner described above, and the overall yield (35%, 63% based on unreacted starting material) is comparable to that obtained with propionitrile oxide. The absorption spectra of 2 and 3 are virtually superimposable, and the NMR spectra of the adduct are consistent with the C_s structure 3.

The observation of apparent C_s symmetry in these reactions indicates a typical [4 + 2] mode of addition across a fulvalene-like double bond. The addition of benzonitrile oxide to 6,6-dimethylfulvene takes place in a [4 + 2] manner across an endocyclic double bond, but a [6 + 4] addition occurs in electron-rich fulvenes such as 6-(dimethylamino)fulvene.[15] A [6 + 4] addition to C_{60} would produce a product with low symmetry and therefore a much more complex ^{13}C NMR spectrum than we observe.



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Supplementary Material Available: Experimental procedures and spectral data for compounds 2 and 3 (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered by the ACS; see any current masthead page for ordering information.

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