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The Addition of Nitrile Oxides to C_{60}

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Abstract. The 1,3-dipolar cycloaddition of nitrile oxides to C_{60} is described. These reactions result in the formation of fullerene-fused isoxazoline heterocycles bearing a series of different substituents in 3-position. The preparation and spectroscopic characterization of these compounds are reported, as well as some investigations of the reactivity of these heterocycles. It is found that fullerene isoxazolines are less reactive than aliphatic isoxazolines. Copyright © 1996 Elsevier Science Ltd

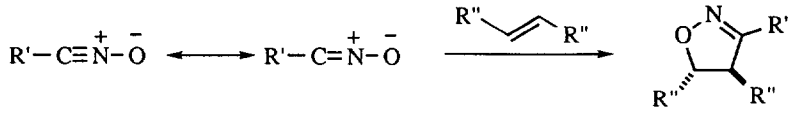
INTRODUCTION

Fullerenes have proven to be remarkably reactive species. Within the first years following the isolation of milligram quantities of these compounds, it was learned that they are reactive toward a number of different reagents, including nucleophiles, electrophiles, and dienes.[1] A major problem that arose early in the history of fullerene chemistry was the difficulty in controlling the extent of reaction and the regiochemistry of addition of nucleophiles to the fullerene nucleus. One of the first fullerene derivatives reported,[2] $C_{60}H_{36}$, can exist as a mixture of as many as $6x10^{14}$ isomers.[3] With some exceptions,[4,5] nucleophilic addition leads to mixtures of compounds $C_{60}(Nuc)_nH_n$ (Nuc = RNH, OR, H, others), also as a mixture of a number of isomers. Similar results have been reported in electrophilic aromatic substitution involving C_{60}.[6] The quest for methodology for the preparation of isomerically pure fullerene derivatives with well-defined levels of substitution began very early in fullerene chemistry, and cycloadditions have emerged as the premier techniques for derivatizing fullerenes.

Diels-Alder,[7] hetero-Diels-Alder,[8] [2+2],[9-15] [8+2],[16] and 1,3 dipolar cycloadditions have all produced new fullerene derivatives resulting from the addition of one equivalent of reagent to the fullerene. Of the latter, the addition of diazoalkanes[1,17] is the most studied, although the addition of alkyl or aryl azides,[18] sulfinimines,[19] azomethine ylids,[20-23] and nitrile oxides[24-26] have been accomplished. By the nature of cycloadditions, these reactions result in the formation of a single isomer of monoadduct, although multiple isomers can be formed in di- and higher adducts.[27,28]

We have reported the reaction of nitrile oxides with C_{60}[25] and with C_{70}.[24] The isoxazolines produced are 1,2-heterobifunctional derivatives of these fullerenes and have a great deal of potential as a general route to other novel derivatives. The reaction of nitrile oxides with alkenes, alkynes, and carbon-heteroatom multiple bonds has been exploited as a path to a variety of natural products.[29,30]

Nitrile oxides (**1**) undergo [4+2] cycloaddition with a wide variety of alkenes, alkynes, and even some carbon-heteroatom multiple bonds.[31] These cycloadditions are fairly insensitive to the structure of the dipolarophile, although there is a preference for electron deficient dipolarophiles. The addition is stereospecific, with the configuration of the alkene being preserved in the isoxazoline product **2**.

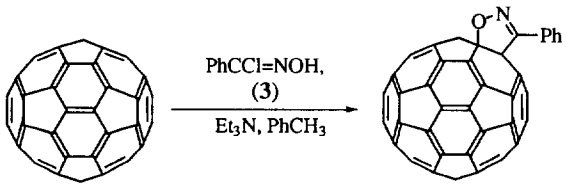


1 **2**

Most nitrile oxides are unstable toward dimerization, so they are not usually isolated and stored. They are commonly generated *in situ* by a variety of techniques, including dehydration of nitroalkanes, dehydrohalogenation of hydroximoyl halides (prepared from aldoximes), thermolysis of furoxan N-oxides, and others.[31] In the present work, we have used the dehydration of nitroalkanes and the dehydrochlorination of hydroximoyl chlorides, but other methods are likely to be successful as well.

NITRILE OXIDE CYCLOADDITIONS

Addition of 1 equivalent of triethylamine to a solution of C_{60} in toluene at room temperature containing 1.0 equivalents phenylhydroximoyl chloride (**3**) leads to the formation of isoxazoline **4** in 36% yield (45% after correction for recovered C_{60}) after purification by gel permeation chromatography (GPC).[32]



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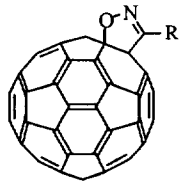
The GPC chromatographic system allows automated separation of mono-, di-, and tri-adducts from C_{60} using toluene as the mobile phase. Toluene enables fairly large injections (10 mL of saturated solution, ca. 2 mg/mL) and an isocratic system facilitates recovery and reuse of the mobile phase. All isomers of diadducts elute in one band under these conditions, the same holds for tri-adducts .

The structural assignment is based on the ^{13}C NMR spectrum. The aliphatic region shows resonances for C4 and C5 at 79 ppm and 104 ppm, respectively. A single intensity line at 153 ppm is assigned to isoxazoline C3. Resonances from the phenyl group appear at 128, 129, 130, and 143 ppm. The remaining lines are due to fullerene sp^2 carbons; 2 of single intensity, 24 of double intensity, and 2 of quadruple intensity. This is consistent with a C_s symmetrical fullerene derivative where four carbons (resonances at 78.91, 103.84, 146.92, and 147.42 ppm) lie on the symmetry plane and are of single intensity. All other fullerene carbons have mirror-image partners and appear as double intensity lines, except for coincident lines (142.13 and 142.51 ppm) of quadruple intensity. The C5 shift of 103.81 ppm is quite close to that of the epoxide carbons in $C_{60}O$ and the C4 shift of 78.91 ppm is typical for isoxazolines.

Using this methodology, we have prepared a variety of fullerene isoxazolines, including **5** - **11**.



R = Ph (**5**), CH_3 (**6**), CH_2CH_3 (**7**), 4-$C_6H_4OCH_3$ (**8**), 4-C_6H_4CHO (**9**), CO_2Et (**10**), $(CH_2)_4CO_2CH_3$ (**11**)

Results from different methods of producing the nitrile oxide is shown below (Table 1). It is clear that optimum amount of nitrile oxide depends somewhat on the technique used for its generation. For the dehydration of nitroalkanes (Method A), the best yields are obtained when an excess of nitroalkane is used, and for the dehydrohalogenation of hydroximoyl chlorides (Method B), one equivalent is most effective. The difference here is probably due to the different rates of the nitrile oxide forming reaction. The dehydro-

halogenation of hydroximoyl chlorides is faster than the dehydration of nitroalkanes, and therefore a higher concentration of nitrile oxide is achieved. With multiple equivalents of nitrile oxide, the yield of monoadduct declines as larger quantities of higher adducts are formed.

Table 1. Typical yields of monoadduct as a function of amount of nitrile oxide precursor present and the method of nitrile oxide production.

R	Method	Ratio	Time	Yield ()[a]
CH_3	A	1:8	Overnight	35% (63%)
CH_3	B	1:2	10 min	33% (44%)
C_2H_5	A	1:2	Overnight	15%
C_2H_5	A	1:8	Overnight	29% (63%)
C_2H_5	A	1:10	Overnight	34% (61%)
C_6H_5	B	1:1	10 min	36% (45%)
p-CH_3OPh	B	1:1	10 min	32%
p-CH_3OPh	B	1:2	10 min	16%
p-CF_3OPh	B	1:1	10 min	13%
$CO_2C_2H_5$	B	1:1	30 min	34% (46%)
$(CH_2)_4CO_2CH_3$	A	1:10	Overnight	19%
Ph-4-CHO	B	1:1	10 min	40% (63%)

[a]Yield adjusted for the amount of C_{60} recovered from the reaction mixture.

Addition of nitrile oxides to C_{70} proceeds in similar yields, although competition experiments involving addition of acetonitrile oxide to a 1:1 mixture of C_{60} and C_{70} indicate that the rate of addition to C_{70} is about 50% of the rate of addition to C_{60}. The lower symmetry of C_{70} leads to the possibility of isomeric monoadducts, and we have isolated three by means of chromatography on a Buckyclutcher column in toluene/hexane. Two of the isomers result from addition to the 1,9 bond (in different orientations) and one results from addition to the 7,8 bond.[24]

The ratio of these adducts is close to 1:1:1. The addition of diazomethane to C_{70} is more selective for addition to the 1,9 bond, (13:2 over addition to the 7,8 bond) and one orientation of addition to the 1,9 bond is highly dominant over the other (12:1 ratio).[33] The difference in regioselectivity in these two 1,3-dipolar additions may be due to inherently lower selectivity in the nitrile oxide case. Alternatively, the difference in selectivity may result from a true kinetic distribution of isomers being formed in the diazomethane case,[33] and in nitrile oxide reactions we are observing an isoxazoline mixture that is shaped by at least partial equilibration to a thermodynamic mixture.

Fullerene isoxazolines undergo 1,3-dipolar cycloreversion upon thermolysis, resulting in the formation of C_{60} and a nitrile oxide. Thermal gravimetric analysis (TGA) indicates that this process begins at about 280 °C and is complete by 400 °C, and the mass loss is quite close that predicted for loss of the nitrile oxide moiety (12.3% observed as compared to 13.8% calculated for the example shown in Figure 1). When **5** is heated in a stilbene melt at 280 °C for several hours, cycloreversion generates the nitrile oxide which is then trapped by stilbene. The resulting adduct can be isolated in 50% yield and there is virtually no surviving **5**.[34] This experiment lends support to the notion that the distribution of 1,9 and 7,8 isomers in the C_{70} series is due to equilibration.

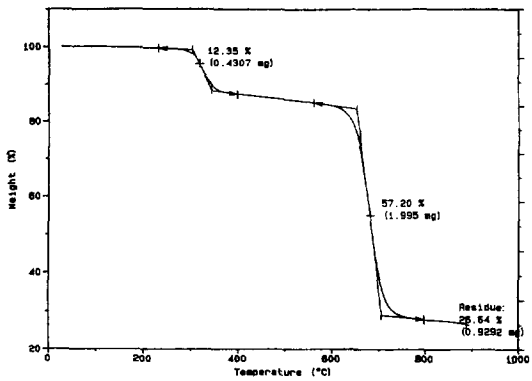


Figure 1. Thermal Gravimetric Analysis Of **10**.

The reversibility of nitrile oxide dipolar addition to fullerenes has ramifications on the distribution of isomers of di- and higher adducts. When we conduct the addition of benzonitrile oxide to C_{60} at low temperatures (-78 °C), we obtain a different distribution of diadduct isomers when the addition is performed at high temperatures (110 °C). We have been able to isolate the major isomers in each case by using a combination of GPC and HPLC, and are currently working on structural characterization of these compounds.[35]

THE REACTIVITY OF FULLERENE ISOXAZOLINES

One of the primary reasons for interest in nitrile oxide cycloadditions to C_{60} is the potential for production of a wide variety of regiochemically-defined 1,2-heterobifunctional derivatives from fullerene isoxazolines. The elaboration of isoxazolines into a number of different functional groups is responsible for the utility of alkene-nitrile oxide cycloadditions in natural product synthesis.[29,30]

Opening an isoxazoline involves N-O bond reduction and often C=N bond reduction as well. Some of the most common transformations are shown in Figure 2 below. The reductive opening of isoxazolines is an excellent method for converting an alkene to α-hydroxy ketones, α-amino alcohols, and other functional groups. A wide variety of reagents are capable of accomplishing the reduction of simple aliphatic isoxazolines, but we have found that fullerene isoxazolines tend to be less reactive.

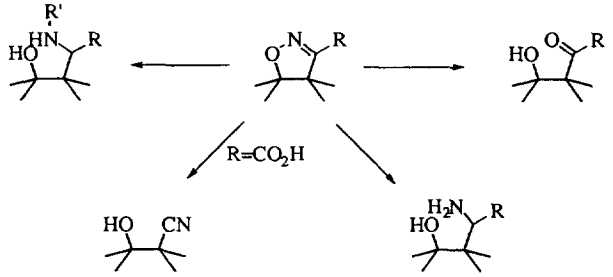


Figure 2. Some Typical Transformations Of Isoxazolines.

The reduction of N-O bonds, or other functional groups on fullerenes, presents a potential problem since fullerenes themselves are very easy to reduce[36] and are likely to reduce faster than (or competitively with) the isoxazoline moiety. Cyclic voltammetry of isoxazoline **10** in toluene/acetonitrile solution at high scan rates

(Figure 3) reveals that the reduction potentials for fullerene isoxazolines are very similar to the reduction potentials for C_{60} itself.[37] It is likely that these reduction waves are fullerene-based reductions, rather than isoxazoline-based. The reduction waves become significantly less reversible at lower scan rates. This suggests that chemical steps occur soon after reduction, possibly involving N-O bond cleavage.

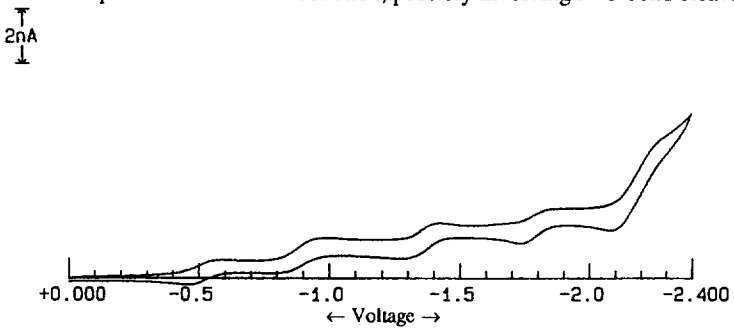


Figure 3. Cyclic Voltammogram Of **10** In 80% Toluene/20% MeCN. Scan rate 5000 mV/sec, 10 micron Pt electrode, Ag^+/Ag reference.

Attempts to Reduce the Isoxazoline Moiety

Initial chemical reduction experiments were conducted with $TiCl_3$. Typical reaction conditions for the $TiCl_3$ reduction of isoxazolines involves a few hours of reaction at room temperature in methanol solution. Isoxazoline **5** proved resistant to these conditions, and more forcing conditions were unsuccessful as well. Stirring a solution of $TiCl_3$ and **8** in MeOH/toluene solution at room temperature for 18 hours, then at reflux for 6 hours also produced no reaction that could be observed by HPLC.

Reductive cleavage of isoxazolines can also be accomplished with diisobutyl aluminum hydride (DIBAL). However, treatment of **5** with 1 equivalent of DIBAL did not produce the desired N-O bond reduction, and only resulted in a small amount (3%) of C_{60} being formed. Addition of a second equivalent of DIBAL led to another 3% of C_{60} to be formed, but no reduction of the isoxazoline (or the C_{60}) was observed, even after long reaction times. These results suggest that the apparent cycloreversion is caused by a minor component of the commercial DIBAL mixture rather than by DIBAL itself.

Reduction of isoxazolines with hydrogen and Raney nickel is another approach to N-O bond reduction. Treatment of isoxazoline **8** with Raney nickel lead to the formation of a black precipitate that left a nearly colorless supernatant solution. Attempts to solubilize or to analyze this material have not been successful. A similar material was formed upon treatment of C_{60} itself with Raney nickel, so it appears that this common route for reductive cleavage of the O-N bond is not applicable to fullerenes. A similar results were obtained from the reaction of **7** with Red-Al.®

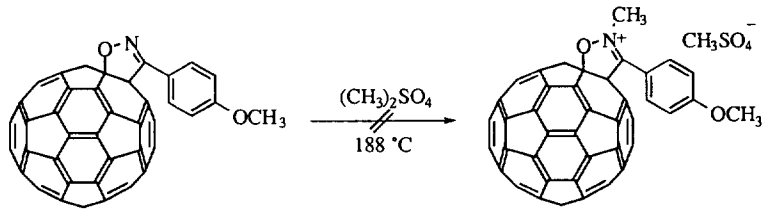
Lithium aluminum hydride is known to attack the fullerene nucleus and, not unexpectedly, it reacts rapidly with **10**, producing an insoluble material. Treatment of **5** with $NaBH_4$ in toluene/TFA resulted in minimal reaction.

Birch reduction (Li, NH_3, tBuOH) of C_{60} results in a mixture of highly hydrogenated species with molecular formula $C_{60}H_{36}$.[2,38] Reduction of so many of the double bonds dramatically changes the electronic nature of the fullerene nucleus, and we reasoned that this change may then enable us to perform transformations on the isoxazoline moiety. Reoxidation with DDQ, a reagent that is known to convert $C_{60}H_{36}$ back to C_{60},[2] would then regenerate the parent fullerene. Accordingly, **7** was added to a solution of lithium in ammonia containing t-butanol at -35 °C, then evaporated and the residue was reoxidized with DDQ. HPLC analysis of the resulting mixture indicated that the two fullerene containing materials present were unreacted **7** and C_{60}. We have attempted the same transformation with Zn/HCl and with Zn/HOAc, reducing systems with much less power than Li/NH_3, but strong enough to achieve partial reduction of C_{60}.[39] After reduction of **8** and subsequent reoxidation with DDQ, C_{60} and unreacted **8** were the only compounds detectable.

Protic acid is not responsible for this cycloreversion: **5** is stable for extended periods of time in toluene/wet trifluoroacetic acid solution. These results suggest that 1,3-dipolar cycloreversion is much more facile from a reduced fullerene, although it is unclear if the reactive species is the radical anion, a polyanion, or a hydrogenated fullerene. Further study of this phenomenon is underway.

Treatment of **5** with SmI_2 leads to the formation of a new product and no detectable C_{60}. The identity of the product has not been established at this time, but changes in the absorption spectrum of the new product suggest that the reduction takes place on the fullerene moiety rather than on the heterocycle. Similar results have been obtained with diimide. These results indicate that isoxazolines of hydrogenated fullerenes are stable compounds, and that the formal cycloreversion observed with the Li/NH_3 and Zn/HCl reductions may occur from anionic intermediates.

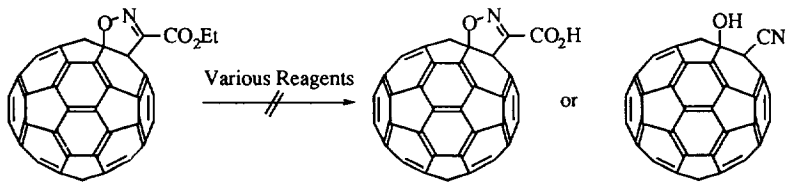
The alkylation of isoxazoline nitrogen, forming an iminium ion, should render the isoxazoline easier to reduce.[40] In general, the alkylation is accomplished by treatment of the heterocycle with Me_2SO_4 at room temperature, but no reaction between **5** and Me_2SO_4 could be detected by HPLC after one week. Treatment of **8** with an excess of Me_2SO_4 in refluxing toluene did not lead to the formation of the desired iminium salt **12**. Heating a mixture of **8** in neat Me_2SO_4 at reflux (188 °C) for 18 hours produces no observable reaction. Methyl iodide is equally ineffective. The reasons why these compounds are deactivated toward both reducing agents and alkylating agents is unclear at this time.



8 **12**

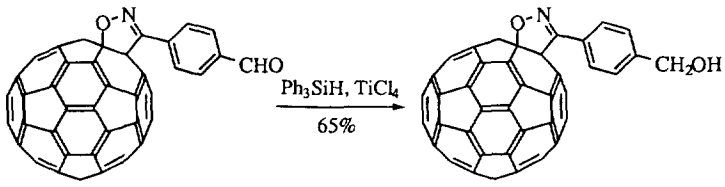
Sidechain Manipulation

3-Carboxyisoxazolines suffer decarboxylation upon heating to produce 2-cyano alcohols, offering a different route to N-O bond cleavage under non-reductive conditions.[41] Dehydrohalogenation of ethyl chlorohydroximidoacetate[41] in the presence of C_{60} produces ester **10** in 34% yield. This ester proved to be highly resistant to acid hydrolysis. Treatment of **10** with TFA in toluene/water or with CF_3SO_3H/ dioxane/ water/toluene failed to produce acid **13** or the fragmentation product **14**, even after extended reaction times. Heating **10** in collidine containing lithium iodide also failed to produce **13**. This resistance to hydrolysis is very similar to results from Wudl's group, who reported similar behavior in a methanofullerene ester.[42] The reasons for this lack of reactivity are not clear.



10 **13** **14**

Aldehyde **9** is sufficiently insulated from the fullerene moiety to allow reduction. Treatment with triphenylsilane and $TiCl_4$ produced benzylic alcohol **15** in 65% yield.



9 **15**

CONCLUSIONS

C_{60} and C_{70} react with a variety of nitrile oxides, forming a new carbon-carbon and a new carbon-heteroatom bond, providing access to an array of fullerene-fused heterocycles bearing different substituents. Both electron rich (alkyl) and electron deficient (carboxyethyl) nitrile oxides participate in this reaction, and the reaction proceeds at a 6,6 ring fusion in all cases. The cycloaddition is reversible at elevated temperatures (>250 °C). It is clear that the presence of a fullerene moiety causes a significant reduction in the reactivity of the isoxazoline ring relative to non-fullerene isoxazolines. The nucleophilicity of the ring nitrogen is diminished, yet at the same time the heterocycle is less susceptible to reduction than typical isoxazolines.

EXPERIMENTAL

Buckminsterfullerene (C_{60}) was obtained by GPC purification of fullerene extract, obtained by toluene extraction of soot obtained from various sources. The GPC methodology and equipment used in this study has been described in detail.[24,32] THF was distilled from sodium benzophenone ketyl under nitrogen. Toluene was distilled from sodium under argon. All reactions were performed under an inert atmosphere.

Samples for FAB mass spectra were prepared in toluene/m-nitrobenzylalcohol matrices. Electrochemistry was performed using a Bioanalytical Systems 100A and a BAS low current module. The working electrodes were Pt microelectrodes of 5 micron diameter, the counter electrode was a Pt wire, and BAS SCE microreference electrodes were used. Compounds **6** and **7** have been reported in the past.[25]

Sample experimental procedure A: Preparation of **3**: To a solution of C_{60} (72 mg, 0.1 mmole) in 60 mL toluene was added phenylhydroximoyl chloride (15.6 mg, 0.1 mmole) in 1 mL of toluene. Triethylamine (10.1 mg, 0.1 mmole) was added and the reaction mixture changed from magenta to brown in color over a 10 minute period. The mixture was washed with water, then dried over $Mg(SO_4)$, then concentrated *in vacuo* to a final volume of 10 mL. This solution was filtered (0.2 μ nylon) then purified by gel permeation chromatography. The monoadduct band was isolated and evaporated to dryness to produce **3** as a dark brown-black powder (30 mg, 36% yield, 45% yield based on unrecovered C_{60}). ^1H NMR (200 MHz, $CDCl_3/CS_2$): δ 7.53 (m, 3H), 8.15 (m, 2H). ^{13}C NMR : (100 MHz, $CDCl_3/CS_2$ + $Cr(acac)_3$): δ 78.91 (isoxazoline C-4, 1), 103.84 (isoxazoline C-5, 1), 128.56 (phenyl), 128.74 (phenyl), 130.34 (phenyl), 136.34 (2), 136.69 (2), 139.96 (2), 140.00 (2), 141.37 (2), 141.75 (2), 141.95 (2), 141.98 (2), 142.13 (4), 142.51 (4), 142.65 (2), 142.75 (phenyl), 143.74 (2), 144.06 (2), 144.11 (2), 144.37 (2), 144.43 (2), 144.80 (2), 144.88 (2), 145.06 (2), 145.28 (2), 145.49 (2), 145.59 (2), 145.65 (2), 145.90 (2), 145.92 (2), 146.05 (2), 146.92 (1), 147.42 (1), 153.12 (isoxazoline C-3, 1). FAB MS *m/e* 840.2 (MH^+).

Sample experimental procedure B: Preparation of **11**: A solution of C_{60} (144 mg, 0.20 mmoles) and methyl 5-nitrohexanoate (prepared from 2-nitrocyclohexanone)[43] (350 mg, 2 mmoles) in 120 mL of toluene was heated to reflux and phenylisocyanate (476 mg, 4 mmoles) was added over 10 minutes. The resulting solution was maintained at reflux for 4 hours, then cooled to room temperature. The brown solution was washed with water, dried ($MgSO_4$), and concentrated *in vacuo* to a final volume of 10 mL. This solution was filtered (0.2 μ nylon) then purified by gel permeation chromatography to produce **11** (33 mg, 19%). ^1H NMR (200 MHz, $CDCl_3/CS_2$): δ 1.87-2.02 (m, CH_2,2H), 2.08-2.23 (m, CH_2, 2H), 2.46 (t, CH_2, 2H), 3.07 (t, CH_2, 2H), 3.67 (s, CH_3, 3H). ^{13}C NMR (100 MHz, $CDCl_3/CS_2$ + $Cr(acac)_3$): δ 24.54 (CH_2), 25.87 (CH_2), 27.94 (CH_2), 33.23

(CH_2), 50.82 (OCH_3), 79.96 (isoxazoline C-4, 1), 101.60 (isoxazoline C-5, 1), 136.05 (2), 136.42 (2), 139.66 (2), 140.24 (2), 141.31 (2), 141.68 (2), 141.72 (2), 141.79 (2), 141.90 (2), 141.91 (2), 142.30 (4), 142.49 (2), 143.59 (2), 143.87 (2), 144.36 (2), 144.40 (4), 144.60 (2), 144.68 (2), 144.77 (2), 144.91 (2), 145.12 (2), 145.36 (2), 145.48 (2), 145.68 (2), 145.73 (2), 145.85 (2), 146.69 (1), 147.23 (1), 153.20 (isoxazoline C-3, 1), 172.05 (C=O). FAB MS *m/e* 878.3 (MH^+).

C_{60} p-CH_3O-C_6H_4-isoxazoline: (8)
^1H NMR (200 MHz, $CDCl_3/CS_2$): δ 3.86 (s, OMe, 3H), 7.00-7.05, 8.10-8.15 (AA'BB' phenyl ring, 4H). ^{13}C NMR (100 MHz, $CDCl_3/CS_2$ + $Cr(acac)_3$): δ 54.91 (OMe), 78.85 (isoxazoline C-4, 1), 103.66 (isoxazoline C-5, 1), 114.25 (phenyl), 121.14 (phenyl), 130.08 (phenyl), 136.34 (2), 136.71 (2), 140.00 (4), 141.40 (2), 141.83 (2), 142.00 (2), 142.06 (2), 142.19 (4), 142.56 (4), 142.70 (2), 143.80 (2), 144.14 (2), 144.52 (4), 144.70 (2), 144.84 (2), 144.92 (2), 145.12 (2), 145.30 (2), 145.62 (4), 145.68 (2), 145.93 (4), 146.09 (2), 146.95 (1), 147.31 (1), 152.01 (isoxazoline C-3, 1), 161.07 (phenyl). FAB MS *m/e* 870.2 (MH^+).

C_{60} p-CHO-C_6H_4-isoxazoline (9):
^1H NMR (200 MHz, $CDCl_3/CS_2$): δ 8.03-8.08, 8.39-8.44 (AA'BB' phenyl ring, 4H), 10.12 (CHO, 1H). ^{13}C NMR (100 MHz, $CDCl_3/CS_2$+$Cr(acac)_3$): δ 78.40 (isoxazoline C-4, 1), 104.62 (isoxazoline C-5, 1), 129.23 (phenyl), 129.91 (phenyl), 134.40 (phenyl), 136.47 (2), 136.98 (2), 137.35 (1), 137.36 (1), 140.14 (2), 140.20 (2), 141.51 (2), 141.78 (2), 142.04 (4), 142.25 (2), 142.27 (2), 142.67 (2), 142.68 (2), 142.80 (2), 143.68 (1), 143.69 (1), 143.79 (phenyl), 143.82 (2), 144.18 (2), 144.41 (2), 144.95 (2), 145.01 (2), 145.12 (2), 145.27 (2), 145.47 (2), 145.76 (2), 145.82 (2), 146.07 (2), 146.09 (2), 146.21 (2), 147.09 (1), 147.58 (1), 152.72 (isoxazoline C-3, 1), 190.68 (CHO).

C_{60} CO_2Et-isoxazoline (10):
^1H NMR (200 MHz, $CDCl_3/CS_2$): δ1.50 (t, 3H, J = 7 Hz), 4.54 (q, 2H, J = 7 Hz). ^{13}C NMR (100 MHz, $CDCl_3/CS_2$+$Cr(acac)_3$): δ 14.04 (CH3), 62.86 (CH_2), 75.35 (isoxazoline C-4, 1), 105.99 (isoxazoline C-5, 1), 136.30 (2), 136.77 (2), 140.00 (2), 140.02 (2), 141.54 (2), 141.57 (2), 141.91 (2), 142.15 (2), 142.23 (4), 142.26 (2), 142.59 (2), 142.63 (4), 143.29 (1), 143.93 (2), 143.95 (2), 144.31 (2), 144.95 (2), 144.97 (2), 145.06 (2), 145.48 (2), 145.76 (4), 146.10 (2), 146.12 (2), 146.15 (2), 146.58 (2), 146.93 (1), 146.98 (1), 147.59 (1), 159.55 (isoxazoline C-3,1), 179.74 (C=O). FAB MS *m/e* 836.2 (MH^+).

Reduction of Ph-4-CHO (9) to Ph-4-CH_2OH (15): A solution of isoxazoline **9** (66 mg, 0.067 mmoles) in 25 mL CH_2Cl_2 was cooled to -65 °C. A solution of Et_3SiH (126 μL, 106 mg, 0.913 mmoles) and $TiCl_4$ (274 μL of 1 M solution of CH_2Cl_2) in CH_2Cl_2 was added, and the resulting mixture was stirred at -65 °C for 4 hours, then overnight at room temperature. Water (75 mL) was added, and the CH_2Cl_2 layer was separated, dried ($MgSO_4$) and evaporated to dryness to produce **12** (43 mg, 65%). ^1H NMR (200 MHz, $CDCl_3/CS_2$): δ 1.63 (broad t, OH, 1H, J=4.5Hz), 1.78 (d, CH_2, J=4.5Hz, 2H), 7.49-7.53, 8.13-8.17 (AA'BB' phenyl ring, 4H). ^{13}C NMR (100 MHz, $CDCl_3/CS_2$ + $Cr(acac)_3$): δ 64.71 (CH_2), 78.79 (isoxazoline C-4, 1), 103.76 (isoxazoline C-5, 1), 126.99 (phenyl), 127.76 (phenyl), 128.70 (phenyl), 136.26 (2), 136.63 (2), 139.90 (2), 139.93 (2), 141.31 (2), 141.69 (2), 141.87 (2), 141.92 (2), 142.07 (2), 142.45 (2), 142.59 (2), 142.68 (4), 143.38 (phenyl), 143.67 (2), 144.00 (2), 144.04 (2), 144.27 (2), 144.36 (2), 144.74 (2), 144.82 (2), 144.99 (2), 145.21 (2), 145.41 (2), 145.53 (2), 145.58 (2), 145.84 (2), 145.86 (2), 145.99 (2), 146.85 (1), 147.35 (1), 152.78 (isoxazoline, C-3, 1). FAB MS *m/e* 870.1 (MH^+).

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REFERENCES AND NOTES

1. Wudl, F.; Hirsch, A.; Khemani, K. C.; Suzuki, T.; Allemand, P.-M.; Koch, A.; Eckert, H.; Srdanov, G.; Webb, H. M. In *Fullerenes: Synthesis, Properties, and Chemistry of Large Carbon Clusters*; G. S. Hammond and V. J. Kuck, Ed.; ACS: Washington, DC, 1992; Vol. 481; pp 161-175.
2. Haufler, R. E.; Conceicao, J.; Chibante, L. P. F.; Chai, Y.; Byrne, N. E.; Flanagan, S.; Haley, M. M.; O'Brien, S. C.; Pan, C.; Xiao, Z.; Billups, W. E.; Ciufolini, M. A.; Hauge, R. H.; Margrave, J. L.; Wilson, L. J.; Curl, R. F.; Smalley, R. E. *J. Phys. Chem.* **1990**, *94*, 8634-6.
3. Balasubramanian, K. *Chem. Phys. Lett.* **1992**, *182*, 257-262.
4. Fagan, P. J.; Krusic, P. J.; Evans, D. H.; Lerke, S. A.; Johnston, E. *J. Am. Chem. Soc.* **1992**, *114*, 9697-9699.
5. Hirsch, A.; Soi, A.; Karfunkel, H. R. *Angew. Chem.* **1992**, *104*, 808-810.
6. Olah, G. A.; Bucsi, I.; Lambert, C.; Aniszfeld, R.; Trivedi, N. J.; Sensharma, D. K.; Prakash, G. K. S. *J. Am. Chem. Soc.* **1991**, *113*, 9387-9388.
7. Some representative examples include: An, Y.-Z.; Anderson, J. L.; Rubin, Y. *J. Org. Chem.* **1993**, *58*, 4799-4801; Khan, S. I.; Oliver, A. M.; Paddon-Row, M. N.; Rubin, Y. *J. Am. Chem. Soc.* **1993**, *115*, 4919-4920; Meidine, M. F.; Roers, R.; Langely, G. J.; Advent, A. G.; Darwish, A. D.; Firth, S.; Kroto, H. W.; Taylor, R.; Walton, D. R. M. *J. Chem. Soc., Chem. Commun.* **1993**, 1342-1344; Rubin, Y.; Khan, S.; Freedberg, D. I.; Yeretzian, C. *J. Am. Chem. Soc.* **1993**, *115*, 344-345; Wilson, S. R.; Lu, Q. *Tetrahedron Lett.* **1993**, *34*, 8043-8046; Bidell, W.; Douthwaite, R. E.; Green, M. L. H.; Stephens, A. H. H.; Turner, J. F. C. *J. Chem. Soc.; Chem. Commun.* **1994**, 1641-1642; Zhang, X.; Foote, C. S. *J. Org. Chem.* **1994**, *59*, 5235-5238; Linssen, T. G.; Dürr, K.; Hanack, M.; Hirsch, A. *J. Chem. Soc., Chem. Commun.* **1995**, 103-104; Gügel, A.; Kraus, A.; Spickermann, J.; Belik, P.; Müllen, K. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 559-561.
8. Ohno, M.; Kojima, S.; Eguchi, S. *J. Chem. Soc., Chem. Commun.* **1995**, 565-566.
9. Zhang, X.; Romero, A.; Foote, C. S. *J. Am. Chem. Soc.* **1993**, *115*, 11024-11025.
10. Yamago, S.; Takeichi, A.; Nakamura, E. *J. Am. Chem. Soc.* **1994**, *116*, 1123-1124.
11. Wilson, S. R.; Wu, Y.; Kaprinidis, N. A.; Schuster, D. I. *J. Org. Chem.* **1993**, *58*, 6548-6549.
12. Wilson, S. R.; Kaprinidis, N.; Wu, Y.; Schuster, D. I. *J. Am. Chem. Soc.* **1993**, *115*, 8495-8496.
13. Rao, A. M.; Zhou, P.; Wang, K.-A.; Hager, G. T.; Holden, J. M.; Wang, Y.; Lee, W.-T.; Bi, X.-X.; Eklund, P. C.; Cornett, D. S.; Duncan, M. A.; Amster, I. J. *Science* **1993**, *259*, 955-957.
14. Zhang, X.; Foote, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 4271-4275.
15. For an example of a photochemical [2+3] cycloaddition, see Akasaka, T.; Ando, W.; Kobayashi, K.; Nagase, S. *J. Am. Chem. Soc.* **1993**, *115*, 10366-10367.
16. Beer, E.; Feuerer, M.; Knorr, A.; Mirlach, A.; Daub, J. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1087-1089.
17. For examples, see Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, Ö. *Science* **1991**, *254*, 1186-1188; Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, Ö. *J. Am. Chem. Soc.* **1992**, *114*, 7300-7301; Shi, S.; Khemani, K. C.; Li, Q. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 10656-10657; Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F. *J. Am. Chem. Soc.* **1992**, *114*, 7301-7302; Sijbesma, R.; Srdanov, G.; Wudl, F.; Castoro, J. A.; Wilkins, C.; Friedman, S. H.; DeCamp, D. L.; Kenyon, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 6510-6512; Anderson, H. L.; Faust, R.; Rubin, Y.; Diederich, F. *Angew.*

Chem. Int. Ed. Engl. **1994**, *33*, 1366-1368; Smith, A. B. III; Strongin, R. M.; Brard, L.; Furst, G. T.; Romanow, W. J.; Owens, K. G.; King, R. C. *J. Am. Chem. Soc.* **1993**, *115*, 5829-5830.

18. Representative examples include the following: Schinazi, R. F.; Sijbesma, R.; Srdanov, G.; Hill, C. L.; Wudl, F. *Antimicrob. Agents Chemother* **1993**, *37*, 1707-10; Wilson, S. R.; Wu, Y. *J. Chem. Soc., Chem. Commun* **1993**, *9*, 784-6; Hawker, C. J.; Wooley, K. L.; Fréchet, J. M. *J. Chem. Soc. Chem. Commun.* **1994**, 925-926; Hawker, C. J.; Saville, P. M.; White , J. W. *J. Org. Chem.* **1994**, *59*, 3503-3505; Yan, M.; Cai, S. X.; Keana, J. F. W. *J. Org. Chem.* **1994**, *59*, 5951-5954; Prato, M.; Li, Q. C.; Wudl, F.; Lucchini, V. *J. Am. Chem. Soc.* **1993**, *115*, 1148-1150.
19. Brizzolara, D.; Ahlemann, J. T.; Roesky, H. W.; Keller, K. *Bull. Soc. Chim. Fr.* **1993**, *130*, 745-747.
20. Maggini, M.; Karlsson, A.; Scorrano, G.; Sandonà, G.; Farnia, G.; Prato, M. *J. Chem. Soc., Chem. Commun.* **1994**, 589-590.
21. Maggini, M.; Scorrano, G.; Prato, M. *J. Am. Chem. Soc.* **1993**, *115*, 9798-9799.
22. Maggini, M.; Karlsson, A.; Pasimeni, L.; Scorrao, G.; Prato, M.; Valli, L. *Tetrahedron Lett.* **1994**, *35*, 2985-2988.
23. Zhang, X.; Willems, M.; Foote, C. S. *Tetrahedron Lett.* **1993**, *34*, 8187-8188.
24. Meier, M. S.; Poplawska, M.; Compton, A. L.; Shaw, J.; Selegue, J. P.; Guarr, T. F. *J. Am. Chem. Soc.* **1994**, *116*, 7044-7048.
25. Meier, M. S.; Poplawska, M. *J. Org. Chem.* **1993**, *58*, 4524-4525.
26. Irngartinger, H.; Köhler, C.-M.; Huber-Patz, U.; Krätschmer, W. *Chem. Ber.* **1994**, *127*, 581-584.
27. Hirsch, A.; Lamparth, I.; Karfunkel, H. R. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 437-438.
28. Meier, M. S.; Rice, D. J.; Thomas, C. J.; Majidi, V.; Pogue, R.; Poplawska, M. In *Science and Technology of Fullerene Materials*; Materials Research Society: Boston, MA, 1994; pp 369-372.
29. Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410-416.
30. Kanemasa, S.; Tsuge, O. *Heterocycles* **1990**, *30*, 719-736.
31. Caramella, P.; Grünanger, P. In *1,3-Dipolar Cycloaddition Chemistry*; A. Padwa, Ed.; Wiley: New York, 1984; Vol. 1; pp 291-380.
32. Meier, M. S.; Selegue, J. P. *J. Org. Chem.* **1992**, *57*, 1924-1926.
33. Smith, A. B. III.; Strongin, R. M.; Brard, L.; Furst, G. T.; Romanow, W. J.; Owens, K. G.; Goldschmidt, R. J. *J. Chem. Soc., Chem. Commun.* **1994**, 2187-2188.
34. Meier, M. S.; Pogue, R. T.; Thomas, C. J.; Majidi, V.; Poplawska, M. Submitted for publication.
35. Meier, M. S.; Rice, D. J. Presented at the 1995 National Meeting of the Electrochemical Society, Reno, Nevada, May, 1995.
36. Xie, Q.; Pérez-Cordero, E.; Echegoyen, L. *J. Am. Chem. Soc.* **1992**, *114*, 3978-3980.
37. Suzuki, T.; Maruyama, Y.; Akasaka, T.; Ando, W.; Kobayashi, K.; Nagase, S. *J. Am. Chem. Soc.* **1994**, *116*, 1359-1363.
38. Banks, M. R.; Dale, M. J.; Gosney, I.; Hodgson, P. K. G.; Jennings, R. C. K.; Jones, A. C.; Lecoultre, J.; Langridge-Smith, P. R. R.; Maier, J. P.; Scrivens, J. H.; Smith, M. J. C.; Smyth, C. J.; Taylor, A. T.; Thorburn, P.; Webster, A. S. *J. Chem. Soc., Chem. Commun.* **1993**, 1149-1152.
39. Meier, M. S.; Vance, V. K.; Corbin, P. K.; Clayton, M.; Mollman, M.; Poplawska, M. *Tetrahedron Lett.* **1994**, *35*, 5789-5792.
40. Kozikowski, A. P.; Chen, Y.-Y. *J. Org. Chem.* **1981**, *46*, 5248-5250.
41. Kozikowski, A. P.; Adamczyk, M. *J. Org. Chem.* **1983**, *48*, 366-372.
42. Win, W. W.; Kao, M.; Eiermann, M.; McNamara, J. J.; Wudl, F.; Pole, D. L.; Kassam, K.; Warkentin, J. *J. Org. Chem.* **1994**, *59*, 8571-8576.
43. Ballini, R.; Petrini, M. *Synth. Commun.* **1986**, *16*, 1781-1788.

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