

Proposal II:

**Manipulating the Triplet State Lifetime of
Fullerene-C60 Derivatives with Heterocycles**

**Sean O. Clancy
Advisor: Aaron W. Harper
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The derivatization of fullerene-C60 through cycloaddition reactions has been the focus of intense study in recent years.^{1,2,3,4} One of the features of fullerene that has been discovered is that it has a long-lived triplet excited state and can transfer energy to molecular oxygen very efficiently to form singlet oxygen.⁵ The goal of this proposal is to develop a persistent triplet state in fullerene C60 derivatives, in order to get high and persistent singlet oxygen concentrations. The efficient production of singlet oxygen from C60 derivatives can have many applications ranging from materials^{6,7,8,9} to medicinal.¹⁰ To accomplish this proposal's goal, a series of fullerene monoadduct analogs with different heteroatoms are to be synthesized, characterized, and studied photophysically.

The photophysical properties of fullerene-C60 are what has sparked such a keen interest from many in the sciences. The ground state absorption of C60 features intense absorptions in the ultraviolet region with weaker bands that extended through the visible wavelengths to 700 nm. When C60 is irradiated, it is excited to a short-lived singlet state, which converts with nearly quantitatively to a longer-lived triplet state. These lifetimes are in the low nanoseconds for the S₁-singlet excited state, and in the range of tens to hundreds of microseconds for the T₁-triplet excited state.^{11,12} The triplet state then transfers energy very efficiently to molecular oxygen, which generates singlet oxygen with almost unit yield.¹³ The S₁ and the T₁ excited states of fullerene-C60 have transient absorptions in the near-IR with maxima around 900 nm for the S₁→S₂ transition, and 700 nm for the T₁→T₂ transition. An energy level diagram for fullerene-C60 is depicted in Figure 1.

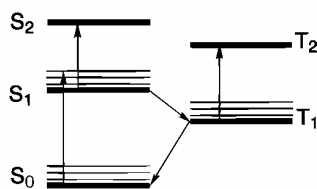


Figure 1. Ground and excited states of fullerenes.¹⁴

In terms of structural features, fullerene-C60 has 30 double bonds with similar reactivity. The 6-6 double bonds, located in the junctions of the hexagons in C60, are dienophilic,¹⁵ which enables it to undergo a variety of [4 + 2] Diels-Alder reactions.¹⁶ One such reaction is that of isobenzofuran with C60,¹⁷ as shown in Scheme 1. The adduct is stabilized by the aromatization of the benzene ring, which must be overcome for cycloreversion to occur. In a recent computational study,¹⁸ Geerlings *et al.* found that in the addition of a series of *o*-quinodimethanes (QDMs, Figure 2) to C60, the efficiency of fullerenes toward Diels-Alder reactions can be related to the effect of aromaticity. The nucleophilic QDMs transmit their gained aromaticity to the electrophilic and aromatic fullerene, thereby strengthening the overall aromaticity of the coupled product.

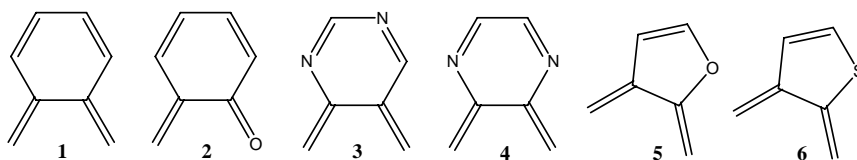


Figure 2. Series of *o*-quinodimethanes.

In a series of QDM adducts studied by Nakamura *et al.*,¹⁹ the presence of alkoxy or hydroxyl groups on the far end of the QDM made little to no difference in the adducts' photophysical properties. Nagano *et al.*²⁰ also noticed that functionalization of the fullerene core reduced its photodynamic activity and was not significantly dependent upon the kind of addend, which in their case was either oxygen or diethyl malonate. In

both studies, as well as in several others,^{21,22} it was noted that adding more than one addend reduces the fullerene's photophysical properties.

The lack of sensitivity to molecular architecture beyond two or three atoms away led to the idea of using analogs of isobenzofuran, with atoms other than oxygen in the heterocycle. In doing so, changes in the lifetime of the fullerene can be manipulated through the use of heteroatoms, which would be separated from fullerene by only one carbon unit. The heteroatoms in close proximity can then exert an internal heavy atom effect on the lifetime of the excited state of the fullerene.

The heteroatoms chosen include nitrogen in the form of N-methyl, as well as those that also are members of oxygen's chalcogen family (group VI.A.): sulfur, selenium, and tellurium. By reacting these heterocycles (Figure 3) with fullerene,

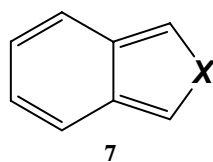
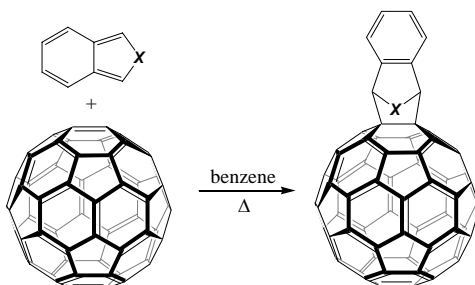


Figure 3. Structure of heterocyclic diene, where $X = \text{N-CH}_3, \text{O, S, Se, Te}$.

products will be formed that incorporate various atoms within two atom units to the fullerene core, as shown in Scheme 1. By changing out the heteroatoms in the molecule that is reacted with fullerene, an internal heavy atom effect should be observed.



Scheme 1. [4 + 2] Diels-Alder reaction of heterocyclic diene with fullerene (C60), again where $X = \text{N-CH}_3, \text{O, S, Se, Te}$.

The heavy atom effect is an important perturbation method for enhancing ground state singlet to excited state triplet ($S_0 \rightarrow T_1$) absorption in aromatic hydrocarbons. The heavy atom may be located in the solvent, which is the case for the *external* heavy atom effect, or it may be affixed to the molecule being studied, which is the *internal* heavy atom effect.²³ The increased atomic mass of the heavy atom perturbs the magnetic field near the nucleus and allows for mixing of pure singlet and pure triplet states. Since the states are no longer ideal, the spin multiplicity rules are not as stringent,²⁴ which means the rate for intersystem crossing (ISC) from the excited state singlet to excited state triplet ($S_1 \rightarrow T_1$) should increase. One applicable example was when the rate for ISC increased for Krieg *et al.*,²⁵ when they replaced the sulfur for selenium in dialkylcarbocyanine dyes they studied (Figure 4).

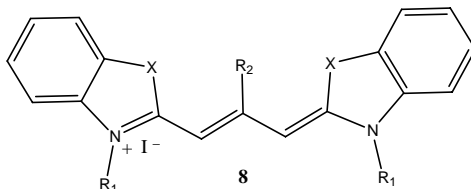
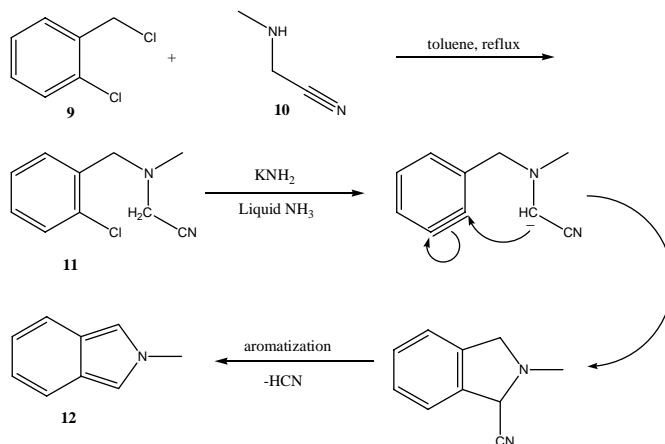


Figure 4. Dialkylcarbocyanine dyes, where X = S, Se; R₁ = Et, Hex, Octodecyl; R₂ = Me, Et, Ph.

The syntheses of the derivatives are done by a Diels-Alder [4+2] cycloaddition to a fullerene. The heteroatom functionality is added by the addition of: 2-methylisindole (or N-methylbenzo[c]pyrrole); isobenzofuran (or benzo[c]furan); benzo[c]thiophene; benzo[c]selenophene; and benzo[c]tellurophene. The syntheses of these compounds are as follows.

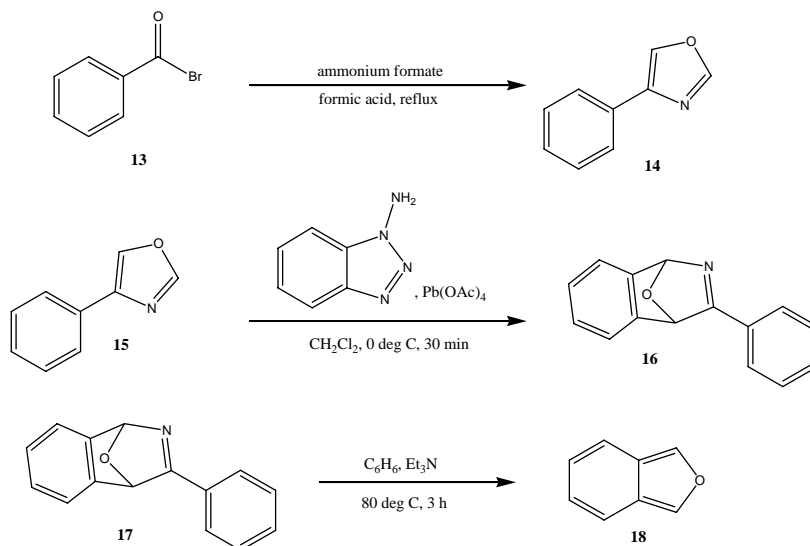
In Scheme 2, 2-chlorobenzyl chloride (**9**) and N-methylaminoacetonitrile (**10**) are refluxed together in toluene to give N-2-chlorobenzyl-N-methylaminoacetonitrile (**11**).

Compound **11** is converted to 2-methylisindole (**12**) via reaction with potassium amide and liquid ammonia.

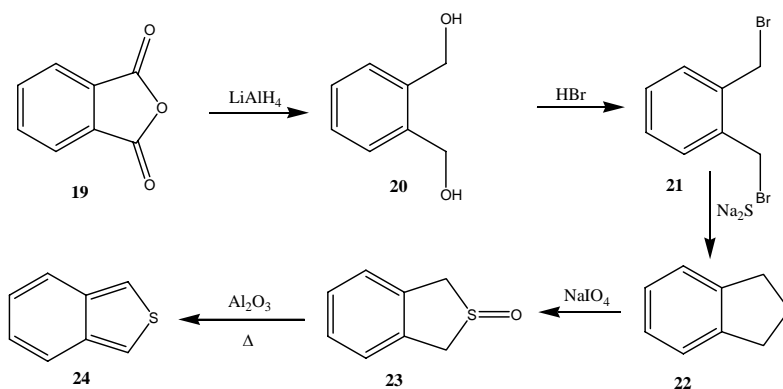


Scheme 2. Synthesis of 2-methylisindole.²⁶

In Scheme 3, phenacyl bromide (**13**) is treated with ammonium formate in formic acid to give 4-phenyloxazole (**14**). The simultaneous addition of 1-aminobenzotriazole and lead(IV) tetraacetate in dichloromethane gives the 1,4-dihydro-1,4-epoxy-3-phenylisoquinoline (**15**). Compound **15** is the precursor to isobenzofuran (**16**) which is generated *in situ* when it is added to the fullerene.

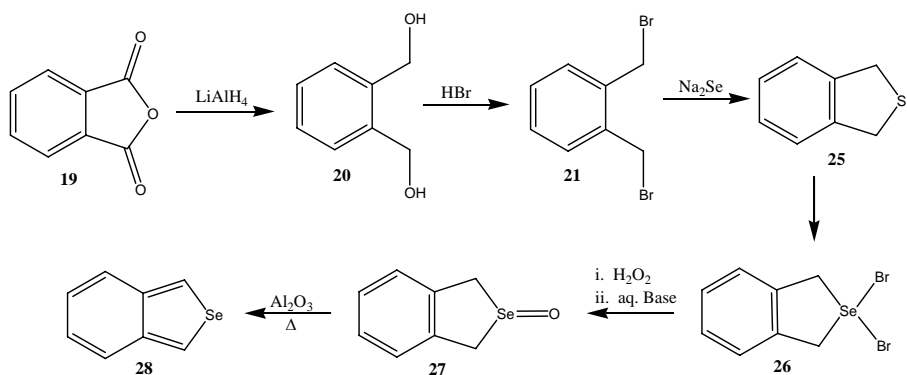


Scheme 3. Synthesis of isobenzofuran.²⁷



Scheme 4. Synthesis of benzo[c]thiophene.^{28, 29, 30}

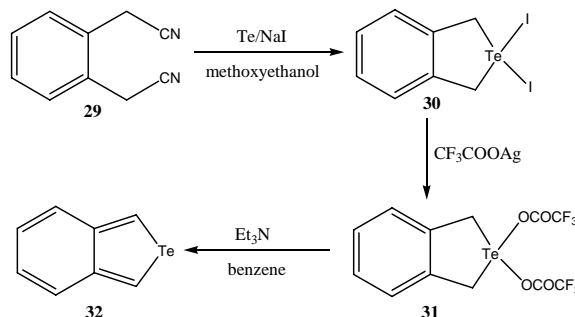
Phthalic anhydride (**19**) is converted to the 1,2-benzenedimethanol (**20**) and then to the 1,2-bis(bromomethyl)benzene (**21**). The dibromide is treated with sodium sulfide to give 1,3-dihydrobenzo[*c*]thiophene (**22**). It is oxidized with sodium periodate to the 1,3-dihydrobenzo[*c*]thiophen-2-oxide (**23**) and then converted to the benzo[*c*]thiophene (**24**) with aluminum oxide.



Scheme 5. Synthesis of benzo[*c*]selenophene.³¹

The synthesis of benzo[*c*]selenophene as shown in Scheme 5 is very similar to that of benzo[*c*]thiophene. In this case, 1,2-bis(bromomethyl)benzene (**21**) is reacted with sodium selenide to give 1,3-dihydrobenzo[*c*]selenophene (**25**). Compound **25** is then converted to 2,2-dibromo-1,2,2,3-tetrahydrobenzo[*c*]selenophene (**26**) so that it can

be made into 1,3-dihydrobenzo[*c*]selenophen-2-oxide (**27**). Upon treatment with aluminum oxide, the target, benzo[*c*]selenophene (**28**) is produced.



Scheme 6. Synthesis of benzo[*c*]tellurophene.

The synthesis of benzo[*c*]tellurophene³² is shown in Scheme 6. 1,2-bis(chloromethyl)-benzene (**29**) is reacted with tellurium and sodium iodide to give 1,3-dihydro-2,2-diiodobenzo[*c*]tellurophene (**30**). Compound **30** is then treated with silver(I) trifluoroacetate to give 1,3-dihydro-2,2-bis(trifluoroacetoxy)-benzo[*c*]tellurophene (**31**). This product was refluxed with triethylamine to give the target benzo[*c*]tellurophene (**32**).

When reacting with fullerene-C60, 2-methylisoindane, benzo[*c*]thiophene, and benzo[*c*]selenophene can individually be refluxed in benzene to get the Diels-Alder monoadduct (Scheme 1). For isobenzofuran, it is best to react its precursor, compound **17**, in the presence of triethylamine and fullerene in refluxing benzene.³³ In the case of benzo[*c*]tellurophene, extended heating will most likely lead to loss of tellurium from the adduct.³⁴ For this reason, heating for small periods of time, that is minutes instead of hours, in a microwave reactor will more likely give the desired product.

The monoadducts, with the exception of the one formed from isobenzofuran, are new compounds. As such, they will need to be characterized fully by: multinuclear NMR, e.g. ¹H, ¹³C, ¹⁵N, ⁷⁷Se, and ^{123/125}Te; mass spectrometry; elemental analyses; electrochemical measurements; UV-Vis absorption; fluorescence; phosphorescence; etc.

Triplet-triplet spectra, triplet-triplet extinction coefficients, triplet quantum yields, and triplet energies (using energy transfer) can be determined using a transient absorption setup.^{35,36} The excitation source is a Nd:YAG laser with 355 nm pulses of 6 – 7 ns width. A 75 W xenon arc lamp is used for a monitoring beam, and a photomultiplier tube is used to detect signals in the visible region. Energy-transfer experiments to observe quenching of the triplet state of the fullerene and singlet oxygen quantum yields can be performed with the same setup, but with a germanium photodiode near-IR detector.³⁷

Another method for $^1\text{O}_2$ detection is by monitoring the near-infrared emission spectra that corresponds to $\text{O}_2 (^1\Delta_g) \rightarrow \text{O}_2 (^3\Sigma_g^-)$ transition at 1268 nm, which is highly specific to $^1\text{O}_2$, in solutions of fullerene derivatives under argon laser excitation at 514.5 nm.³⁸ This amount of $^1\text{O}_2$ generated can then be compared among the tested samples. The efficiency of singlet oxygen production can be calculated by dividing the emission intensity at 1268 nm by the absorption coefficient at 514.5 nm (I/ε). This I/ε term includes the efficiency of the transition from $S_0 \rightarrow S_1$, as well as the total efficiency of $^1\text{O}_2$ production from the process of $S_1 \rightarrow T_1 \rightarrow (\text{energy transfer}) \rightarrow \text{O}_2 \rightarrow ^1\text{O}_2$.

The fullerene-heterocycle adducts proposed may have several applications in technology, in electronic and optical devices, as well as in medicine, in the form of photosensitizers.

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