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Organic Chemistry with Heterofullerenes: Photosensitized Oxygenation of Alkenes

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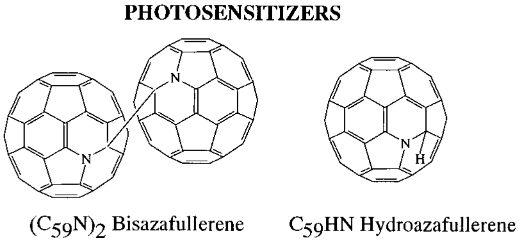
ABSTRACT



Heterofullerenes $C_{59}HN$ and $(C_{59}N)_2$ sensitize the reaction of olefins with molecular oxygen under photolytic conditions. 2-Methyl-2-butene and α-terpinene undergo ene and Diels–Alder photooxygenation reactions, respectively, even in the presence of minute amounts of azafullerenes to produce the corresponding peroxides.

Modification of C_{60} by rational organic synthesis led to the successful incorporation of a heteroatom—nitrogen—into the fullerene framework. As a result of the different valencies of carbon and nitrogen, however, the resulting species is a radical. As such, it has been found to either rapidly dimerize, yielding bisazafullerene $(C_{59}N)_2$,[1] or abstract a hydrogen atom to form the parent hydroazafullerene $C_{59}HN$.[2] Although the introduction of such a heteroatom in the fullerene cage fundamentally affects its structural and electronic properties,[3−6] only a few studies have been carried out to investigate its chemical reactivity and possible applications. Moreover, all the work that has been carried out to date deals with bisazafullerene $(C_{59}N)_2$.[7−11]

The special molecular geometry of these materials and the presence of the electronegative nitrogen atom may be responsible for some unique photochemical and photophysical properties. As a part of our continuing interest in azafullerenes,[12−14] we have posed the question of whether

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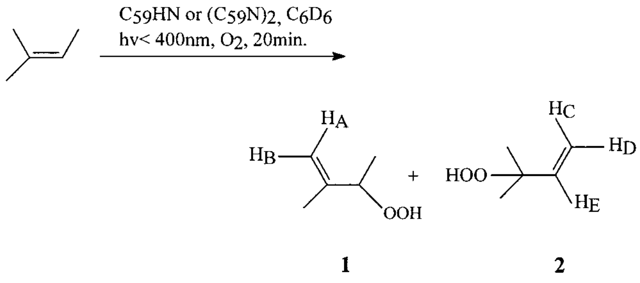
they could act as photosensitizers to promote the conversion of $^3O_2$ to $^1O_2$ upon UV irradiation.[15,16] The interesting mechanistic and synthetic aspects of singlet oxygen have attracted much attention during the past years,[17] and singlet oxygen is closely related to the major environmental and biomedical significance among the numerous applications involved.[18−20] For example, it has been postulated to be responsible for phototoxicity in biological systems and it has also been applied to photodynamic therapy of cancer.[21−23]

Ene and Diels−Alder reactions are among the most widely used reactions of singlet oxygen with olefins. It is already known that normal fullerenes have the ability to convert molecular oxygen to singlet oxygen on a preparative scale.[24−29] Hence, 2-methyl-2-butene and α-terpinene have been subjected to heterofullerene-sensitized photooxygenations.

For the reaction of 2-methyl-2-butene, a catalytic amount of the corresponding azafullerene ($<10^{-3}$ % mol) dissolved in a benzene-d_6 solution was added to the alkene in an NMR tube. A stream of pure oxygen was passed through and the mixture was subsequently irradiated with a UV lamp equipped with a Kapton filter (cutoff wavelength <400 nm) for 20 min. When hydroazafullerene $C_{59}HN$ was used as a sensitizer, the photooxygenation went to completion and afforded a 1:1 mixture of two allylic hydroperoxides **1** and **2** (Scheme 1).[30] The two olefinic protons H_A and H_B of isomer **1** appear as an AB system (2H, $d_A = 4.88$, $d_B = 4.79$, $J_{AB} = 1.0$ Hz) while the three olefinic protons H_C, H_D, and H_E give rise to doublets of doublets and resonate at 4.92 (1H, dd, $J_1 = 0.9$ Hz, $J_2 = 10.7$ Hz), 5.03(1H, dd, $J_1 = 0.9$ Hz, $J_2 = 17.6$ Hz), and 5.81(1H, dd, $J_1 = 10.7$ Hz, $J_2 = 17.6$ Hz), respectively. Similar results were obtained when bisazafullerene $(C_{59}N)_2$ was used as a photosensitizer; an ene reaction between 2-methyl-2-butene and the so-produced singlet oxygen afforded once again an equimolar mixture of hydroperoxides **1** and **2** (Scheme 1). Interestingly, after irradiation the green color of the reaction mixture faded out and some insoluble materials appeared at the bottom of the tube. After filtration and a careful HPLC analysis of the clear reaction mixture on a 5PYE column (toluene eluent, 10 mL/min flow rate), we found that the corresponding peak of the bisazafullerene had disappeared. Instead, two new pronounced peaks appeared which were identified as a monomeric hydroazafullerene species (minor amounts) and its oxidation adduct.[31] Upon irradiation, the weak interdimer bond of the bisazafullrene was disrupted and, in the presence of oxygen, finally oxidized. This was not surprising because we already knew that the C−C interdimer bond of $(C_{59}N)_2$ could easily be either photochemically or thermally cleaved.[32,33] Also, very recently we found that hydroazafullerene is susceptible to oxygenation under ultraviolet irradiation.[31]

Scheme 1. Ene Photooxygenation of 2-Methyl-2-butene in the Presence of Azafullerenes $C_{59}HN$ or $(C_{59}N)_2$ as Sensitizers Produces an Equimolar Mixture of Two Allylic Hydroperoxides **1** and **2**



Furthermore, when we performed the photooxygenations in the presence of a catalytic amount of 1,4-diazabicyclo-[2.2.2]octane (DABCO), we could barely observe the progress of the reaction and only after prolonged UV irradiation was the formation of the corresponding hydroperoxides identified in very low yields. This gives strong evidence that singlet oxygen is responsible for the photooxygenation reaction rather than some kind of azafullerene−$^1(O_2)$ complex.[34]

To explore potential applications of the azafullerenes as useful photosensitizers, we decided to investigate whether a Diels−Alder reaction of α-terpinene with singlet oxygen could occur. Following experimental procedures similar to those described previously, we observed the formation of endoperoxide **3** in two separate experiments by using either

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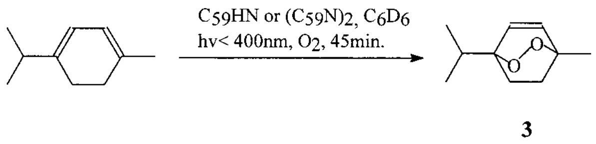
the monomeric hydroazafullerene $C_{59}HN$ or the dimer bisazafullerene $(C_{59}N)_2$ as sensitizer for the photooxygenations. However, reaction between α-terpinene and oxygen did not proceed as smoothly as the ene reaction of 2-methyl-2-butene.[35]

The progress of the reaction and the identification of the product were monitored and achieved by ^1H NMR analysis of the reaction mixture.[36] The olefinic protons of the produced endoperoxide **3** (Scheme 2) were found to resonate at 6.08 ppm and 6.17 ppm as doublets with coupling constants of 8.5 Hz and are in full accordance with literature spectroscopic data.[37] The fact that both catalytic amounts of azafullerenes were needed and especially the presence of the fast completion of photooxygenation of 2-methyl-2-butene gives strong evidence that generation of singlet oxygen is high and is similar to the amounts produced by the standard photooxygenation techniques especially with tetraphenylporphyrin and rosebengal.[28] The turnover of the sensitizers is calculated to be more than 1000 for 2-methyl-2-butene and more than 100 for α-terpinene.[35] Another important aspect that should be noted is that azafullerenes are relatively reactive to the photooxygenation conditions. As mentioned earlier, they tend to be oxidized and thus any photodynamic damage to biological systems is prevented. Further studies are currently underway in order to further investigate photophysical and photochemical properties of both $C_{59}HN$ and $(C_{59}N)_2$.

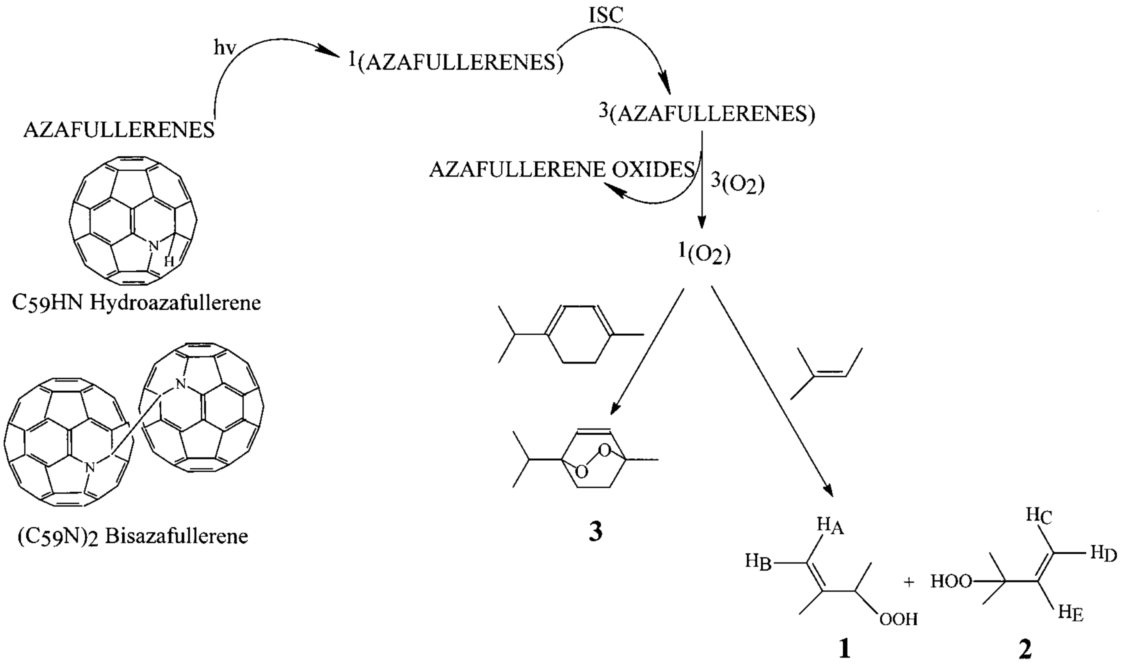
Scheme 2. Diels−Alder Photooxygenation of α-Terpinene in the Presence of Azafullerenes $C_{59}HN$ or $(C_{59}N)_2$ as Sensitizers Produces the Endoperoxide Ascaridole **3**



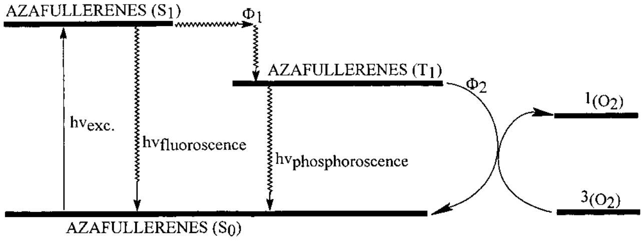
A representative pathway is shown in Figure 3 for the transformation of the examined alkenes to the corresponding peroxides **1** and **2** and endoperoxide **3** by singlet oxygen. The azafullerenes $C_{59}HN$ and $(C_{59}N)_2$ are electronically excited under UV irradiation to the singlet states where they undergo an intersystem crossing to the corresponding triplet states (cf. Scheme 4). The triplet states are then efficiently quenched by molecular oxygen, and the so-produced singlet states give ene and Diels−Alder reactions with the alkenes. Other related photochemical pathways for the electronically excited azafullerenes are presented in an energy level diagram in Scheme 4.

The photosensitization of alkenes with singlet oxygen by hydroazafullerene $C_{59}HN$ is the first example of the use of this unique material in organic chemistry. Along with its derivatives, $(C_{59}N)_2$ can be considered as a useful and powerful sensitizer. The unique spherical structures with the electronegative nitrogen atom incorporated into the conjugated fullerene skeleton differentiate them from conventional sensitizers which usually have flat-shaped conjugated networks. In addition, further functionalization on their skeleton should lead to the production of more soluble materials in a wide variety of solvents—including water—and thus may have important pharmaceutical applications. This would open

Scheme 3. Schematic Pathway for the Generation of Singlet Oxygen $^1(O_2)$ Which Reacts with the Examined Olefins



Scheme 4 Energy Level Diagram for the Azafullerenes and Their Interaction with Oxygen



a new interdisciplinary research in the development and construction of photosensitive material architectures.

In conclusion, we have shown that azafullerenes can indeed photosensitize ene and Diels−Alder reactions of olefins with oxygen.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(35) UV irradiation for 15 min converted only a small fraction of α-terpinene to endoperoxide ascaridole **3**. Further irradiation for 15 min showed an increase of the production of **3** to approximately 50% based on the starting material. However, the maximum yield of conversion of α-terpinene to ascaridole **3** was achieved after a total of 45 min of irradiation and calculated to be 85%. Further exposure to UV light did not increase the formation of **3**. In a separate experiment a higher molecular concentration of azafullerenes was used (ca. 0.01 mol %), and after 20 min irradiation in the presence of oxygen, α-terpinene transformed to the corresponding endoperoxide **3** with the yield of more than 80%. Larger amounts of azafullerenes are needed to sensitize the Diels−Alder reaction of α-terpinene with oxygen.

(36) The photooxygenations were performed in an NMR tube using benzene-d_6 as both reaction solvent and internal lock for the measurement. A Kapton filter was used for the cutoff wavelength (<400 nm).

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