Unusual Regioselectivity in the Singlet Oxygen Ene Reaction of Cyclohexenobuckminsterfullerenes

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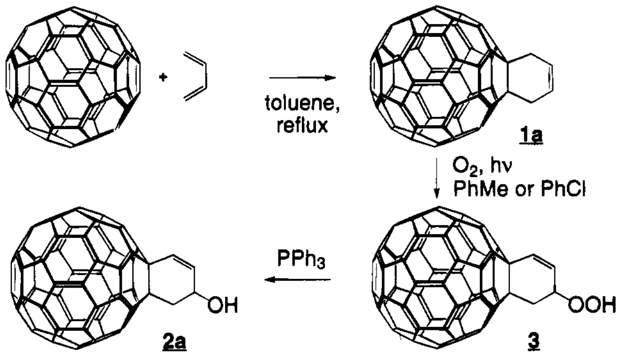
One of the many interesting and potentially useful properties of fullerenes is their efficient photoexcitation to a triplet excited state and subsequent energy transfer to form singlet oxygen ($^1O_2$) in high yield.[1,2] This property has been exploited in the $^1O_2$ ene reaction with simple olefins, matching results previously obtained with conventional dyes.[3,4] Recently, our studies on the Diels–Alder functionalization of C_{60} have provided us with a variety of C_{60}-fused cyclohexenes.[5] These 1,2-dihydrofullerenes retain the photochemical properties of the parent compounds[6] which can be used with advantage in systems of biological interest.[7,8] We have found that the photosensitized generation of $^1O_2$ by adducts **1a–k** can concomitantly effect the chemical modification of the cyclohexene framework to give a rich variety of interesting oxygenated systems (**2a–k′**). Unexpected regioselectivity which goes contrary to the observations made in the $^1O_2$ ene reaction with cyclohexenes is explained in conformational and electrostatic terms.

The cycloaddition product **1a**, resulting from Diels–Alder reaction of 1,3-butadiene and C_{60}, was noted in a previous report for its instability toward air and light, affording hydroperoxide **3** (Scheme 1).[5d] Deliberate reaction of **1a** with $^1O_2$ afforded the allylic alcohol **2a** in 83% yield after reduction with PPh_3. Interestingly, the dihydrofullerene moiety in **1a** plays the role of $^1O_2$-sensitizer, and the cyclohexene moiety that of an unavoidable reaction center.[9–11]

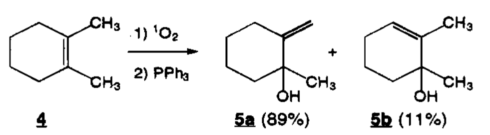
We have carried out this general reaction on several cyclohexene derivatives of C_{60} (**1b–k**) as an efficient means of further functionalization (Table 1). The cyclohexenes **1b–k** were obtained by Diels–Alder reaction of the corresponding 1,3-dienes with C_{60} (toluene, reflux). $^1O_2$ ene reaction of **1b–k** afforded a variety of oxygenated products (**2b–k′**) after reduction of the corresponding hydroperoxides with PPh_3. Interestingly, the solvent in which the ene reaction is carried out plays an important role on the yields of products. A dramatic increase in the yield of alcohol **2e** from 6 to 91% was observed when adduct **1e** was reacted with $^1O_2$ in toluene and chlorobenzene, respectively. A small amount of benzylic radicals generated from toluene must be sufficient to effect the polymerization of the C_{60}-containing material.[12]

Scheme 1



Rates in the $^1O_2$ ene reaction are determined by both electronic and steric effects.[11] In Table 1, the reaction rates of substrates **1b–k** (except **1e**) are ordered by increasing time to completion, which qualitatively relates electronic effects on reaction rates. Interestingly, the electron-rich system **1b** should undergo competing [2 + 2] cycloaddition with $^1O_2$, but the diacetate expected from the cleavage of the intermediate dioxetane was not observed.[11b,13]

The "*cis*-effect" observed in the $^1O_2$ ene reaction of cycloalkenes, but not of most cyclohexenes, can be attributed to rotational barrier[14] and nonbonding interaction effects[15] favoring H-abstraction of those hydrogens perpendicular to the alkene plane.[16] Cyclohexenes are the exception because they exist in half-chair conformations unfavorable to placing both H's in axial position. Accordingly, reaction of $^1O_2$ with alkyl-substituted cyclohexenes affords a majority of products with an exocyclic double bond.[11a,16] For example, 1,2-dimethylcyclohexene (**4**) affords a 9 to 1 mixture of alcohols **5a** and **5b**.[11a] The C_{60}-cyclohexenes in the present study show *strong* preference for the formation of allylic alcohols with endocyclic double bonds, whenever a choice is possible. Remarkably, the fullerene analog of **4**, alkene **1f**, gave products **2f** and **2f′** with a reverse selectivity (85:15). Ene reaction of methylcyclohexene system **1g** gave only products **2g** and **2g′** in 1:1 ratio.



4 **5a** (89%) **5b** (11%)

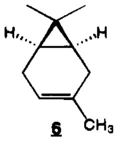


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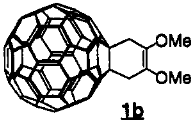
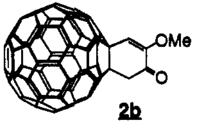
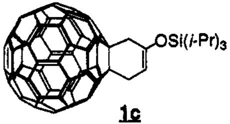
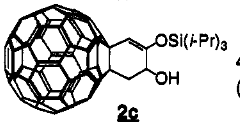
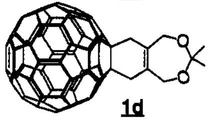
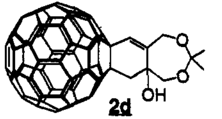
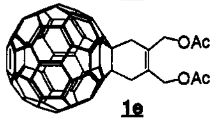
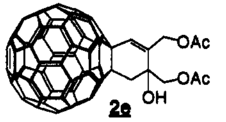
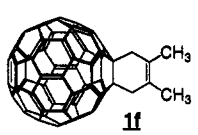
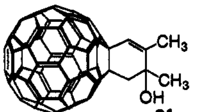
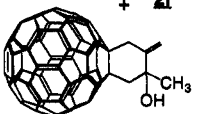
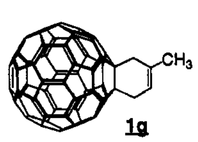
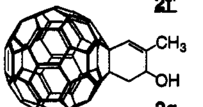
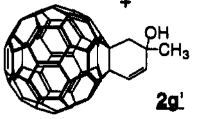
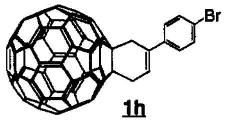
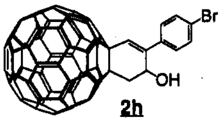
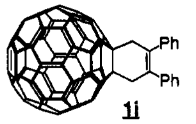
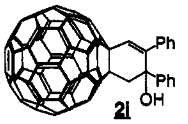
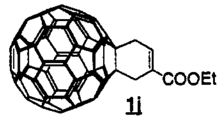
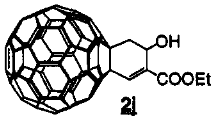
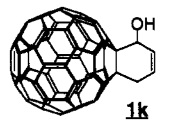
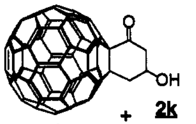
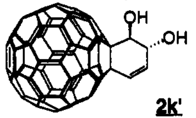
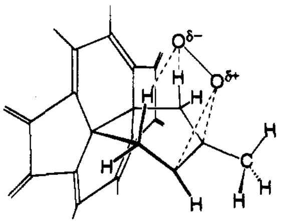
Table 1. Structures and Yields of Diels–Alder Adducts and $^1O_2$ Ene Reaction Products Obtained from C_{60}

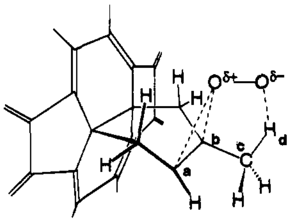
Cyclohexene	Yield	Product	Yield (Time)
 **1b**	- a -	 **2b**	32%[b,c] (<1h)
 **1c**	- a -	 **2c**	45%[c] (1h)
 **1d**	59%	 **2d**	76%[c] (1.5h)
 **1e**	52%	 **2e**	91%[d] (7h)
 **1f**	- a - (ref. 9)	 + **2f**  **2f'**	19%[d] (1.5h) (85:15) 3.1%[d]
 **1g**	- a -	 + **2g**  **2g'**	20%[c] (2h) (1:1) 19%[c]
 **1h**	59%[b]	 **2h**	38%[c] (2h)
 **1i**	49%	 **2i**	76%[c] (3.5h)
 **1j**	30%	 **2j**	47%[c] (23h)
 **1k**	56%	 + **2k**  **2k'**	6.8%[d] (22h) 6.8%[d]

[a] Adduct unstable (**1b**) or not isolated. [b] Yield based on recovered C_{60}. [c] Reaction in $PhCH_3$. [d] Reaction in PhCl.

Another peculiar observation is the lack of silyl migration in the reaction of **1c**.[17] This and the above observations can be attributed to the following: The boat conformation of the C_{60}-fused cyclohexenes confers a rigid framework to the six-membered ring in which two of the 3,6-hydrogens are pseudoaxial.[5a,c] Because of favorable interactions between the incoming $^1O_2$ and these axial hydrogens, the *endo*-perepoxide resulting from transition state **7a** is formed, rather than the *exo*-isomer derived from **7b**. As a result, silyl migration cannot happen with the *endo*-perepoxide formed from enol ether **1c**.[17c]



7a



7b

The *strong* preference for the formation of an *endo*-perepoxide transition state, e.g. **7a**, may be due to additional factors. Comparison of product distributions between **1g** and 3-carene (**6**),[16] which has a rigid, but somewhat flattened, boat conformation provided by its fusion to a cyclopropane ring (MM3), shows that a significant amount of exocyclic hydrogen abstraction (22%) results with **6**, while **1g** affords only the endocyclic products **2g** and **2g'**. Consideration of the MM3 energy difference[14] between conformations of **1g** with a dihedral angle a–b–c–d of 0° and 90° (Me group rotation; 0.60 kcal mol^{-1}) and the corresponding conformations of 3-carene (0.58 kcal mol^{-1}) does not provide a simple explanation for this discrepancy. It is therefore likely that additional favorable electrostatic or electronic interactions exist between the negative oxygen of the developing *endo*-perepoxide (**7a**) and C_{60}, which is strongly electron deficient.

Interestingly, allylic alcohol **1k** underwent significant conversion to β-hydroxy ketone **2k** and the unexpected *trans*-diol **2k'**. The allylic hydroxy-directing effect[18] is apparently inefficient here as shown by the slow rate of reaction of **1k** with $^1O_2$ and the absence of the *cis*-diol. The hydroxy group in **1k** must assume an equatorial position, unfavorable to a productive O—H···O=O interaction in a transition state of type **7a**.

Further experimental and theoretical studies are being pursued to fully understand the origins of this reversed regioselectivity.

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Supporting Information Available: Experimental section and ^1H and ^{13}C NMR spectroscopic data for compounds **1d**, **1e**, **1h–k**, and **2b–k'** (51 pages).

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