The First Hetero-Diels–Alder Reaction of C60 with 1-Azadienes. Synthesis of Tetrahydropyrido[2′,3′:1,2][60]fullerene Derivatives

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Heterocycle-fused [60]fullerene derivatives have been mainly prepared by 1,3-dipolar cycloaddition reactions leading to carbon–heteroatom bond formation on the C_{60} cage. Thus, a wide variety of organofullerenes bearing fused heterocycles such as pyrrolidines, pyrazolines, triazolines, isoxazolines, oxazolidines, furans, pyrroles, and thiazoles have been reported.[1]

Much less is known, however, about [4+2] cycloadditions of heterodienes to C_{60} yielding organofullerenes bearing a six-member heterocycle fused to the C_{60} cage as a consequence of the instability of these highly reactive intermediates and the synthetic difficulties of the preparation of their precursors. This fact is in sharp contrast with the Diels–Alder reaction of homodienes to [60]-fullerene, which is among the best studied procedures for the derivatization of [60]fullerene.[2]

Eguchi and co-workers have reported the only two examples of hetero-Diels–Alder reactions to C_{60} yielding dihydropyran-[3] and dihydrothiopyran-fused[4] [60]fullerene derivatives through C–O and C–S bond formation, respectively, on the [60]fullerene surface. Recently, a Diels–Alder reaction of 1,3-disubstituted 2-aza-1,3-dienes with C_{60} to form the respective cycloadduct, which was stabilized by a further chemical transformation, has been reported as the first example involving a nitrogen-containing heterodiene.[5]

In this note we present our preliminary results on the first example of nitrogen-bonded [60]fullerene derivatives prepared by hetero-Diels–Alder reaction. *o*-Quinone methide imines are highly reactive intermediates which have been successfully used in the synthesis of different nitrogen-containing heterocycles.[6] These unstable intermediates have been generated in situ by different procedures involving flash vacuum pyrolysis, flash vacuum thermolysis, and pyrolytic, photolytic, or thermal reaction from the respective precursors.[7]

We have generated in situ *o*-quinone methide imines **4a**–**c** (Scheme 1) by thermolysis of the corresponding *o*-aminobenzyl alcohols **3a**–**c** in refluxing *o*-dichloroben-

Scheme 1

Reagents: a) (*i*-Pr)2EtN, CH2Cl2; b) C60, *o*-DCB, reflux.
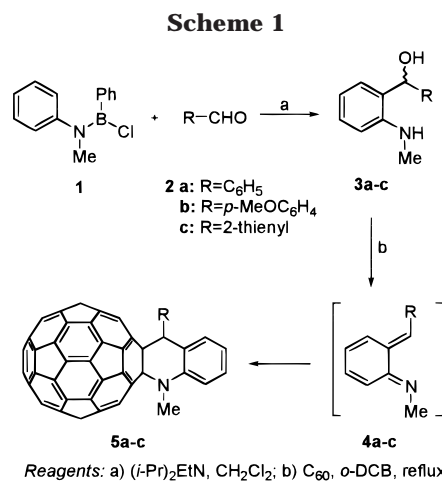
zene, following the procedure recently reported by Lau.[8] *o*-Aminobenzyl alcohols **3a**–**c** were prepared by reaction of an aldehyde **2a**–**c** with *N*-methylanilinochlorophenyl-borane (**1**), obtained from *N*-methylaniline and dichloro-phenylborane, in the presence of diisopropylethylamine.

These highly reactive intermediates **4a**–**c** are efficiently trapped by [60]fullerene, acting as a dienophile, to form the novel cycloadducts **5a**–**c** in moderate yields. Theoretical calculations (PM3) predict that this cycloaddition is controlled by the HOMO of the *o*-quinone methide imines. The calculated LUMO(C_{60})–HOMO-(diene) energy differences (5.2 eV) are clearly in the range of energetically favored cycloadditions. Organofullerenes **5a**–**c** are thermodynamically stable compounds due to the aromatic character of the resulting cycloadduct, thus avoiding the undesired cycloreversion process observed in other C_{60}-based Diels–Alder reactions.[9] In this regard, *o*-quinodimethanes[10] and the heterocyclic analogues[11] have been successfully used to afford stable carbo- and heterocyclic organofullerenes.[1,2]

Monoadducts **5a**–**c** were isolated as adducts on 6/6 junctions in agreement with that observed for other related cycloadducts prepared from *o*-quinodimethanes,[12] *o*-quinone methide,[3] and *o*-thioquinone methide.[4] The structure of **5a**–**c** was unambiguously determined from ^{1}H and ^{13}C NMR spectra in addition to the FAB-MS, UV–vis, and FT-IR data. The UV–vis spectra show the weak absorption band of dihydrofullerenes at 430 nm, confirming the presence of the [6,6]isomer.[13] The positive liquid secondary ion mass spectra (LSIMS) in NBA matrix showed the molecular ions for **5a**–**c** at *m/z* 915, 945, and 921, respectively (**5b:** accurate mass, 945.1155; calculated

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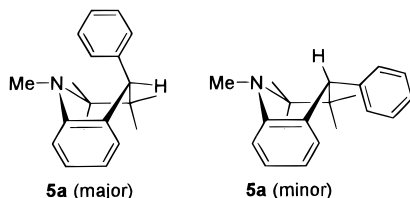
Figure 1. Boat conformations for compound **5a**.

for $C_{75}H_{15}NO$, 945.1154), with the base peak at m/z 720. The ^{13}C NMR spectra of compound **5a** show signals due to two sp^3 junction carbons at 84.26 and 75.60 ppm. The ^1H NMR spectra of compounds **5a**−**c** show the presence of two sets of signals, in a ratio of about 6:1, which coalesce at 75 °C for **5a** and should be attributed to a slow boat-to-boat interconversion at room temperature of the tetrahydropyridine ring, as it has already been reported for related carbocyclic organofullerenes.[14] In addition to the aromatic protons, the required ^1H NMR signals of cycloadducts **5a**−**c** appeared around 6.0 ppm (CH) and 3.9 ppm (N-CH$_3$). The coalescence temperature allows the calculation of $\Delta G^{\ddagger}$ for the boat−boat inversion, which for compound **5a** was estimated at 20.0 ± 0.1 kcal/mol. This inversion barrier is higher than those reported for related structures[4,14a−c] but quite similar to those reported by Foote[14b] for related carbocyclic analogues bearing substituents on the methylene bridge (17.6−19.3 kcal/mol).

The major conformer was assigned to the boat conformation of the tetrahydropyridine ring with the hydrogen atom in a pseudoequatorial position and a flagpole phenyl group (Figure 1), in agreement with that determined by NOE experiments for related carbocyclic analogues.[14b]

To ascertain the proposed major conformation, we have carried out theoretical calculations of **5a** at the semiempirical PM3 level. Figure 2 presents the optimized geometry for **5a** showing the boat conformation of the tetrahydropyridine and the phenyl group in a pseudoaxial position. The energy difference calculated for both conformers **5a** and **5b** is 1.54 kcal/mol. The calculated bond length for C(1)−C(2) at the [6,6] junction is 1.598 Å, which is only slightly shorter than 1.62 Å, determined by X-ray analysis for 63,66-dimethyl-64,65-diphenyl-1,9-(methano[1,2]benzenomethano)[60]fullerene by Rubin.[14a]

Since C_{60} exhibits interesting electron-acceptor properties,[15] we have determined the redox properties of the novel organofullerenes **5a**−**c** by cyclic voltammetry measurements at room temperature (Table 1). Compounds **5a**−**c** show a quasi-reversible electrochemical behavior with four one-electron reduction waves corresponding to the reduction of the fullerene moiety which are cathodically shifted in comparison with the parent C_{60} (−0.60, −1.00, −1.52, −2.04 V). Thus, organofullerenes **5a**−**c** show a slightly poorer acceptor ability (**5a**, E^1_{red} = −0.69 V; **5b**, E^1_{red} = −0.67 V; **5c**, E^1_{red} = −0.66 V) than the parent [60]fullerene (Figure 3). This fact indicates that the presence of the nitrogen atom covalently attached to
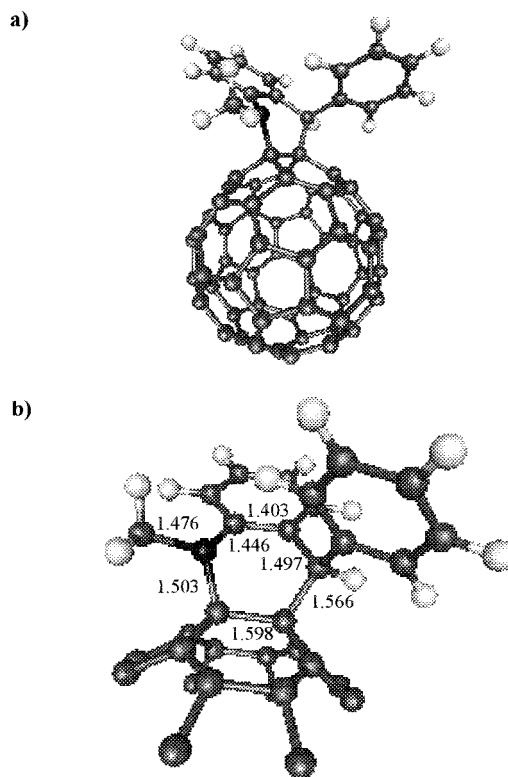

Figure 2. (a) Minimum energy conformation for **5a**. (b) Detail of the PM3-optimized geometry of the organic addend for **5a**, showing some significant bond lengths (Å).

Table 1. Redox Potentials of Compounds 5a−c^a

compound	E^1_{red}	E^2_{red}	E^3_{red}	E^4_{red}
5a	−0.69	−1.11	−1.65	−2.14
5b	−0.67	−1.09	−1.64	−2.12
5c	−0.66	−1.08	−1.63	−2.15

^{a} Experimental conditions: V vs SCE; GCE as working electrode; Bu$_4$N$^+$ClO$_4^-$ (0.1 M) as supporting electrolyte; scan rate 200 mV/s; CH$_2$Cl$_2$ as solvent.
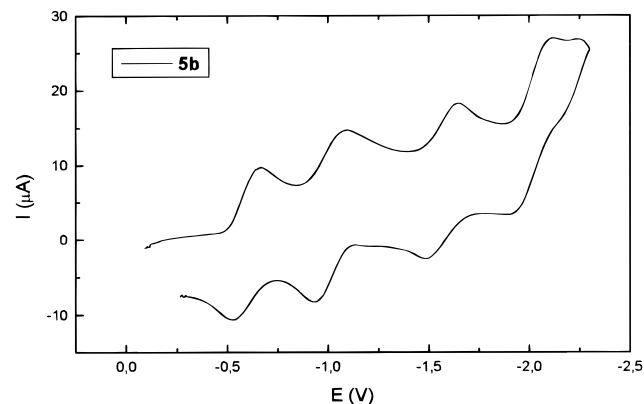
Figure 3. Cyclic voltammetry of compound **5b** at 200 mV/s.

the C_{60} cage does not significantly modify the redox behavior of most dihydrofullerenes as a result of the saturation of a double bond in the C_{60} framework.[16]

In summary, hetero-Diels−Alder reaction of 1-azadienes to [60]fullerene affords a novel type of heterocycle

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fused to the C_{60} surface in which a C−N bond is constructed on the C_{60} framework. The *o*-quinone methide imine precursors are generated in situ from readily available *o*-aminobenzyl alcohols. This procedure expands the available methods for the functionalization of [60]fullerene, since different aldehydes can, in principle, be covalently attached to the formed cycloadduct, which can be seen as a versatile approach to modified fullerenes.

Experimental Section

General Procedure for the Synthesis of Compounds 5a−c. To a solution of [60]fullerene (0.3 g, 0.42 mmol, 1.0 equiv) in 1,2-dichlorobenzene (12 mL) was added the corresponding *N*-methyl-2-hydroxyalkylaniline (**3a−c**) (0.63 mmol, 1.5 equiv). The reaction mixture was refluxed for 5 h. The crude mixture was submitted to flash chromatography (cyclohexane:toluene, 19:1), obtaining compounds **5a−c** as brown solids that finally were washed with methanol.

1′-Methyl-4′-phenyl-1′,2′,3′,4′-tetrahydroquino[2′,3′:1,2]-[60]fullerene (5a). Following the general procedure, compound **5a** was obtained in 25% yield: FT-IR (KBr) 3056, 3032, 2951, 2916, 2848, 1598, 1538, 1485, 1463, 1455, 1435, 1418, 1077, 527 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.71 (m, 2H, aromatics), 7.60 (m, 1H, aromatic), 7.44−7.34 (m, 4H, aromatics), 7.23 (t, 2H, aromatics), 6.02, 5.84 (s, 1H, C*H*−Ph), 3.93, 3.86 (s, 3H, (CH$_3$−N); ^{13}C NMR (75 MHz, CDCl$_3$/CS$_2$) δ 155.3, 152.0, 149.7, 149.3, 148.5, 147.9, 147.8, 147.5, 146.7, 146.5, 146.4, 146.1, 146.0, 145.9, 145.7, 145.6, 145.5, 145.3, 145.25, 145.21, 145.1, 145.0, 144.8, 144.7, 144.6, 144.5, 144.4, 143.0, 142.8, 142.7, 142.6, 142.5, 142.3, 142.2, 142.1, 141.8, 141.7, 141.6, 141.2, 141.1, 138.9, 138.8, 138.3, 137.4, 137.1, 136.3 (Ar), 135.5 (Ar), 134.9, 133.2 (Ar), 130.1, 129.1, 128.2 (Ar), 128.0 (Ar), 126.5 (Ar), 121.6 (Ar), 116.6 (Ar), 84.2, 77.2 (CH), 75.6, 55.4 (N−Me); MS (FAB$^+$) *m/z* 915 (M$^+$, 25), 720 (100).

4′-(*p*-Methoxyphenyl)-1′-methyl-1′,2′,3′,4′-tetrahydroquino-[2′,3′:1,2][60]fullerene (5b). Following the general procedure, compound **5b** was obtained in 31% yield: FT-IR (KBr) 3067, 3034, 2925, 2844, 2803, 1611, 1520, 1485, 1469, 1448, 1421, 1306, 1250, 527 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.60 (m, 3H, aromatics), 7.39 (d, 1H, aromatic), 7.20 (m, 2H, aromatics), 6.93 (d, 2H, aromatics), 5.97, 5.78 (s, 1H, C*H*−Ar), 3.92, 3.84 (s, 3H, N−CH$_3$), 3.81 (s, 3H, O−CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$/CS$_2$) δ 158.9, 155.5, 152.1, 149.6, 149.3, 148.4, 147.9, 147.8, 147.4, 146.7, 146.5, 146.3, 146.1, 146.0, 146.00, 145.8, 145.7, 145.6, 145.5, 145.4, 145.3, 145.2, 145.18, 145.15, 145.09, 145.02, 144.8, 144.7, 144.6, 144.58, 144.50, 144.3, 142.9, 142.7, 142.64, 142.61, 142.5, 142.3, 142.2, 142.1, 142.0, 141.7, 141.69, 141.63, 141.2, 141.1, 139.0, 138.7, 138.2, 137.5, 137.0, 136.3, 136.2, 134.8, 133.6 (Ar), 131.1, 128.9, 128.1 (Ar), 127.3 (Ar), 126.4 (Ar), 121.6 (Ar), 116.6 (Ar), 113.56 (Ar), 113.52 (Ar), 84.1, 77.2 (CH), 75.7, 55.0 (N−Me), 54.6 (O−Me); MS (FAB$^+$) *m/z* accurate mass, 945.1155; calcd for C$_{75}$H$_{15}$NO, 945.1154.

1′-Methyl-4′-(2″-thienyl)-1′,2′,3′,4′-tetrahydroquino[2′,3′:1,2][60]fullerene (5c). Following the general procedure, compound **5c** was obtained in 31% yield: FT-IR (KBr) 2919, 2848, 1623, 1460, 1428, 1285, 1180, 527 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.65−6.99 (m, 7H), 6.39, 6.09 (s, 1H, C*H*-Ar), 3.90, 3.88 (s, 3H, N−CH$_3$); MS (FAB$^+$) *m/z* 921 (M$^+$, 10), 720 (100).