J. Chem. Research (S), 1999, 680–681†

1,3-Dipolar Cycloaddition of 3-Azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and C_{60}†

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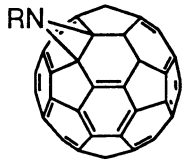
The thermal cycloaddition of azido sugar **3** with C_{60} gives the chiral azafulleroid **4** in 2.55% yield (8% based in recovered C_{60}).

Since the first report from Vasella's laboratory[1] on the synthesis of deprotected, spiro linked *C*-glycosides of C_{60}, the synthesis and reactivity of new *glycofullerenes* have been almost neglected. This is really surprising regarding the potential, large mass of new molecular architectures possible from the reactivity between sugars and C_{60}. In fact, the simple and easy manipulation (owing to the increased solubility in common solvents) and the interesting biological properties that have been claimed in some of the new polyfunctionalized fullerene derivatives[2] have been an important motive to search for diversely substituted C_{60} molecular frameworks.

Two recent publications on the cycloaddition of per-*O*-acetyl glycosyl azides[3a] and methyl 2-azido-2-deoxy-3,4-*O*-isopropylideneerythronate[3b] to C_{60}, and the current interest of some of us in the reaction of azides with C_{60},[4] prompt us to report here the 1,3-dipolar cycloaddition of the azido sugar **3**[5] (3-azido-3-deoxy-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose) and C_{60}.

1

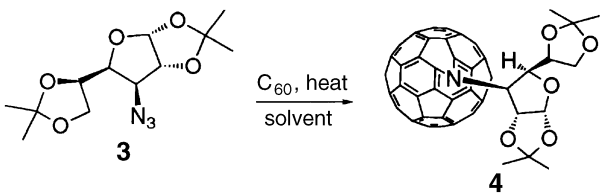


2

The reaction of azides with C_{60} has been extensively analyzed and documented in the literature.[6,7] Two types of monoadducts **1**[6a] and **2**[7] are obtained depending on reaction conditions. For example, under thermal conditions, alkyl azides preferentially add at the ring junction between five- and six-membered rings ([5,6]-junction) to give **1**, whereas *N*-alkoxycarbonyl azides predominantly afford compounds **2**. The iminofullerenes (azafulleroids) **2** are of special interest because to date they are the only fullerene derivatives which provide chemospecific cycloaddition reactions,[8] a key step for the formation of heterofullerenes.[9] The first step of the reaction is a [3 + 2]-cycloaddition to a [6,6]-double bond with the formation of a triazoline which on thermolysis gives the azafulleroid **1**.[10] In the case of unstable azafulleroids (those containing *N*-phenyl or *N*-alkoxycarbonyl substituents) the thermolysis leads to the thermodynamically stable [6,6]-bridged isomers.[11]

3-Azido-3-deoxy-1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose **3**[5] was reacted with fullerene in chlorobenzene, at 130 °C for 30 h to give a new product **4** (Scheme 1) in 2.55% yield (8% based in recovered C_{60}). The reaction conditions are not optimised. This low yield probably would indicate that a large amount of bis-adducts should be formed,[12] but we could not detect or isolate them. Note that no reaction took place at 60 °C, and at reflux, the reaction was very slow at short reaction times (*ca.* 10 h). When using 1-chloronaphthalene as solvent no reaction was observed. The structure of product **4** was established by analytical and spectroscopic data. A correct microanalysis for $C_{72}H_{19}NO_5$ established the product has to be a monoadduct. The UV–VIS spectrum was very similar to that of C_{60}. FAB MS showed the typical M^+ cluster with loss of the sugar moiety to give $[C_{60}N]^+$ and C_{60}^+. The ^{1}H NMR spectrum of the sugar part of the molecule is very similar to that of the sugar azide **3** with a small downfield shift due to the influence of the carbon sphere[6a] [observe that H-1 and H-2 appear at 5.86 (6.12, $\Delta + 0.26$ ppm) and 4.62 (5.06, $\Delta + 0.44$ ppm), respectively, on going from product **3** to **4**]. The ^{13}C NMR spectrum of **4** exhibits the signals for the sugar residue at δ 112.08 and 109.57 $\{2 \times [\text{–}OC(CH_3)_2O\text{–}]\}$, 104.84 (C-1), 83.90, 82.67, 72.30, 68.95, 67.12 (C-2, C-3, C-4, C-5, C-6), 26.81, 26.66, 26.42, 25.67 $\{2 \times [\text{–}OC(CH_3)_2O\text{–}]\}$, as well as 32 peaks in the aromatic region in the range δ 148–133. Because all the fullerene carbons were in the sp^2 region of the spectrum (no C_{60} sp^3 signals at δ *ca.* 80 and no C_{2v} symmetry is present, compound **4** is a [5,6]π monoadduct, ruling out the aziridine structure. Note also that product **4** was soluble in common organic solvents as $CDCl_3$, for instance, confirming that the sugar moiety around the fullerene residue has modified considerably its solubility properties.

In summary, we have described the synthesis and characterization of a chiral azafulleroid from the cycloaddition of a C-3 azido sugar in a furanose template and C_{60}. It belongs to a new family of glycofullerenes. Work is now in progress in order to apply this protocol to new sugar derivatives, study the reactivity and analyze the biological profile of these molecules.



3 **4**

Scheme 1

* To receive any correspondence.

† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

Experimental

Reactions were monitored by TLC using precoated silica gel alumina plates containing a fluorescent indicator (Merck, 5539). Detection was done by UV (254 nm) followed by charring with sulfuric–acetic acid spray, 1% aqueous potassium permanganate solution of 0.5% phosphomolybdic acid in 95% EtOH. Anhydrous $MgSO_4$ was used to dry organic solutions during workups. Flash column chromatography was performed using Kieselgel 60 (230–400 mesh, Merck). The melting point of **4** was determined in a Kofler apparatus and is uncorrected. Optical rotation was determined with a Perkin-Elmer 257 instrument. The ^{1}H NMR spectrum was recorded with a Varian VXR-300S spectrometer.

1,6-[N-(3-*Deoxy*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranos*-3-*yl)*]*aza*[60]*fulleroid* **4**.—C_{60} (404 mg, 0.561 mmol) was dissolved in chlorobenzene (35 mL) using a sonicator. Then the azide **3**[5] (160 mg, 0.561 mmol) was added to the fullerene solution. The reaction mixture was stirred at 130–135 °C for 30 h. The solvent was evaporated under vacuum and the residue was chromatographed on silica gel eluting with toluene and toluene–methanol (95 : 5) mixtures, to give unreacted C_{60} (275 mg) and compound **4** as a black solid. Yield: 14 mg (2.55% yield; 8% based in recovered C_{60}); IR (KBr) ν/cm^{-1} 1426, 1032; $[\alpha]_D^{25} - 60$ (*c* 0.025, $CHCl_3$); UV–VIS ($CHCl_3$) λ_{max} 262, 330 nm; δ_H ($CDCl_3$) 6.13 (d, $J_{1,2} = 3.81$ Hz, 1 H, H-1), 5.07 (d, d, $J_{1,2}$ =3.81, $J_{3,4} = 3.00$ Hz, 2 H, H-2, H-3), 4.59 (td, $J_{5,6} = J_{5,6'} = 6.41$, $J_{4,5} = 9.00$ Hz, 1 H, H-5), 4.38 (dd,1 H, H-4), 4.27 (dd, $J_{6,6'} = 8.49$ Hz, 1 H, H-6), 3.96 (dd,1 H, H-6′), 1.59, 1.41, 1.39, 1.24 (s, s, s, s, 12 H); δ_C ($CDCl_3$) 147.44, 144.68, 144.39, 144.04, 143.88, 143.60, 143.60, 143.36, 143.06, 142.83, 142.75, 142.48, 142.38, 141.80, 141.70, 141.34, 141.28, 140.47, 140.03, 139.90, 139.84, 139.09, 138.92, 138.80, 138.75, 137.70, 137.59, 137.36, 135.74, 135.05, 134.99, 134.60, 112.08, 109.57, 104.84, 83.90, 82.67, 72.30, 68.95, 67.12, 26.81, 26.66, 26.42, 25.67; FAB MS (NBA) *m/z* 978 ($M + 1^+$, 28%), 734 ($C_{60}N^+$, 13%), 720 (C_{60}^+, 100%).

J. M.-C thanks CAM for financial support and to Dr. Angeles Martínez-Grau (Lilly, S.A.) for suggestions and reading the manuscript.

Received, 12th July 1999; Accepted, 10th August 1999
Paper E/9/05639D

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