Controlled regio- and chemoselective addition of isothiocyanate to the dione moiety of a cage-opened fullerene-mixed peroxide derivative†

Xiaobing Yang,[ac] Liangbing Gan*[ab] and Zheming Wang*[a]

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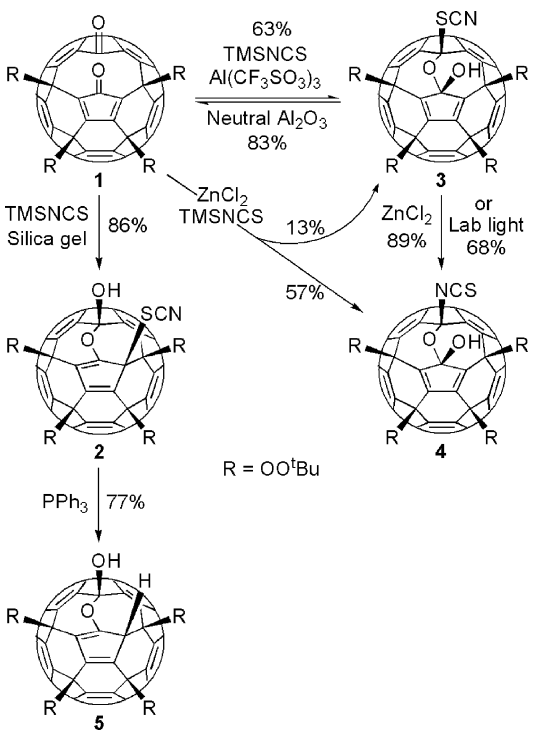
Addition of the ambident SCN group to a fullerendione derivative follows two different pathways in the presence and absence of Lewis acid.

Fullerene chemistry has been extensively studied over the past two decades. While most of the known fullerene reactions follow the well-established principles of organic chemistry, many novel reactions have also been reported for fullerenes due to their unique spherical structure.[1] For example, the Bingel[2] and Prato reactions[3] are two named reactions developed from fullerene chemistry. In spite of the rich chemistry already known, unexpected and unexplained novel reactions are still being reported for fullerenes.[4] We have reported the synthesis of fullerene-mixed peroxides.[5] Further study indicates that these oxygen-rich compounds are good precursors for cage-opened fullerene derivatives with carbonyl groups on the rim of the orifice.[6] Here we report the reaction of the fullerendione **1** with trimethylsilylisothiocyanate (TMSNCS). An unexpected reaction pattern was observed. Optimization of the reaction conditions gave high regio- and chemo-selectivity.

The cage-opened fullerene derivative **1** was readily prepared from the oxidation of a diol precursor according to the procedure we reported previously.[6a] In an effort to prepare sulfur-containing fullerene derivatives, we treated compound **1** with TMSNCS (Scheme 1).‡ The reaction was very slow when **1** was stirred with TMSNCS alone. It was found that addition of some silica gel could accelerate the reaction. Thus, compound **2** was obtained in 86% yield after stirring the reaction solution for 2 days at 0 °C. Compound **3** was obtained as a minor product (4%).

To further accelerate the reaction, we added $Al(CF_3SO_3)_3$ instead of silica gel. As expected the reaction was much faster. The dione derivative **1** was consumed in about 4 h. However, the C_s symmetric product **3** was obtained as the major product instead of **2**. When the Lewis acid was changed to $ZnCl_2$, the isothiocyano isomer **4** was obtained as the major product and the thiocyano derivative **3** as the minor product. Other Lewis acids such as $BF_3{\cdot}Et_2O$ could also be used to give **3** but with lower yields (53%). Water should be avoided for good selectivity because it could compete with the addition of the thiocyano group to form the C_s symmetric bis-hemiketal adduct $C_{60}(O)(OH)_2(OO^tBu)_4$, which was reported before.[6a]

To test the reactivity of the thiocyano group, compound **2** was treated with triphenylphosphine. Similar to the reactions of halofullerene derivatives,[6b,7] the pseudohalo derivative **2** was converted to the hydro derivative **5**. The same reaction did not occur with compound **3**. Stirring a dichloromethane solution of **3** under lab light led to its isomer **4**. The conversion of **3** to **4** occurred in 89% yield with $ZnCl_2$, together with a minor amount of **1**. Addition of neutral alumina into a solution of **3** in dichloromethane regenerated the dione **1** in 83% yield. Under similar conditions the isothiocyano derivative **4** decomposed into unknown mixtures, which contained **1** in very low yield.



Scheme 1 Preparation of thiocyano- and isothiocyano-fullerene derivatives.

[a] *Beijing National Laboratory for Molecular Sciences, Key Laboratory of Bioorganic Chemistry and Molecular Engineering of the Ministry of Education, College of Chemistry and Molecular Engineering, Peking University, Beijing 100871, China. E-mail: gan@pku.edu.cn. E-mail: zmw@pku.edu.cn*
[b] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*
[c] *Beijing Institute of Pharmaceutical Chemistry, P.O. Box 925 (West Building), 100083, China*

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Spectroscopic data support the structures depicted in Scheme 1. The ^{13}C NMR chemical shifts of the thiocyano groups in **2** and **3** appear at 109.8 and 109.3 ppm, respectively. The same carbon in the isothiocyano group appeared in the fullerene carbon region above 135 ppm. An intense signal is observed in the IR spectrum of **4** at 1979 cm^{-1}, which is characteristic of an NCS stretching band. These features agree with those in classical organic thiocyano and isothiocyano compounds.[8] The ^1H NMR spectra of **3** and **4** are virtually the same. Their OH shifts are 5.09 and 4.99 ppm respectively, indicating the same location in the molecule. The C_1 symmetric compounds **2** and **5** showed similar NMR patterns. Their hemiketal fullerene carbons appeared at 107.3 and 106.8 ppm respectively, which are very close to those of compounds **3** (107.8 ppm) and **4** (106.6 ppm).

Structural assignments of compounds **2** and **4** are further confirmed by single crystal X-ray analysis (Fig. 1). The SCN group is slightly bent in both compounds. The SCN angle is 174° for **2** and 171° for **4**. The single S–C bond in the thiocyano group SCN of compound **2** is 1.696 (5) Å. The double S=C bond in the isothiocyano –N=C=S group of compound **4** is 1.604(14) Å. The SCN moiety lies above the central pentagon in compound **2**. It is on the mirror plane of the molecule in compound **4**. Such arrangements have the minimum steric hindrance as can be seen from their space-filling models. The hydroxyl group of **4** forms a H-bond with an adjacent peroxo oxygen atom which is bound to the *tert*-butyl group. The O–H···O bond distance is 2.909 Å.

The regio- and chemoselectivity observed in the present work is reminiscent of those in classical organic reactions. The proposed electron flow path leading to compound **2** (top figure in Scheme 2) is analogous to the conjugate addition of unsaturated carbonyl compounds. Both steric and electronic factors favor the addition pattern observed for **2**. TMSNCS is

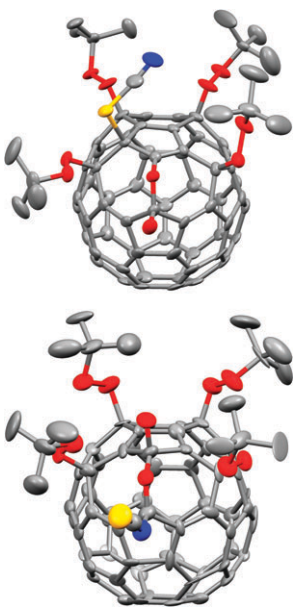
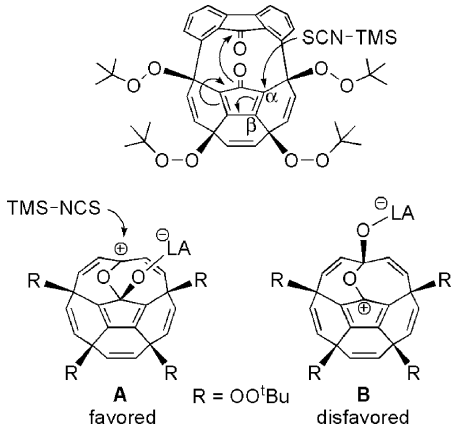


Fig. 1 X-Ray structures of compounds **2** (above) and **4** (below). Ellipsoids were drawn at the 50% level. For clarity hydrogen atoms are not shown. Colour scheme: grey = carbon, red = oxygen, blue = nitrogen, yellow = sulfur.



Scheme 2 Mechanism consideration for the formation of compounds **2** (above) and **3** (below). Only part of the fullerene cage is drawn.

a bulky nucleophile, making it difficult for it to approach the β-position in the central pentagon. Simple modeling indicates that the two carbonyl groups are pushed out of the spherical surface because they are close to each other. Thus, the conjugation between the alkene and the carbonyl on the cyclopentadienone moiety in the center is limited because they are not planar. So the classical 1,4-addition pattern of unsaturated carbonyl derivatives is not observed for the present case. Double bonds adjacent to the other carbonyl group on the outside are less reactive towards TMSNCS because they are part of a partially aromatic six-membered ring.

In the absence of Lewis acid, the carbonyl carbons of **1** are apparently not reactive towards TMSNCS and 1,2-addition does not occur. But in the presence of a Lewis acid, the carbonyl group on the central pentagon is activated by the Lewis acid. Addition of the oxygen atom of the adjacent carbonyl group to this activated carbonyl carbon then forms cation **A** (Scheme 2). TMSNCS adds to cation **A** to form **3**. Interaction of the Lewis acid with the other carbonyl on the outside is unfavorable since it would form intermediate **B** with an anti-aromatic ring in the center. In the formation of both **2** and **3**, the TMS group probably adds to the hydroxyl oxygen to form TMSO, which is then hydrolyzed on silica gel.

The hard–soft acid–base (HSAB) theory can explain the driving force for conversion of the sulfur-bound **3** to the nitrogen-bound **4**. Under similar conditions the thiocyano group in **2** did not isomerize. This is in agreement with the fact that the α-carbon atom of **2** with only C–C bonds is softer than the hemiacetal carbon atom of **3** with a C–O bond and two C–C bonds. The isomerization of the thiocyano **3** to isothiocyano **4** probably involves heterolysis and homolysis of the fullerene–sulfur bond in the $ZnCl_2$ and light induced conversions, respectively. Similar isomerizations of thiocyano to isothiocyano derivatives have been reported in classical organic chemistry.[8]

Sulfur-containing fullerene derivatives have attracted much attention due to their interesting photophysical properties. A number of methods have been reported for their synthesis.[9] In most of the known sulfur-containing fullerene derivatives, the sulfur atom is not bound to the fullerene cage carbon atoms.[10] Compounds with fullerene carbon–sulfur bonds are relatively rare.[11] The additions of thiocyano or isothiocyano groups to

fullerenes have not been reported before in the literature.[12] Under similar conditions pristine C_{60} did not react with TMSNCS. The presence of the peroxo and carbonyl groups in particular facilitates the addition of SCN to compound **1**.

In summary, regio- and chemoselectivity of the reaction between the fullerendione derivative **1** and TMSNCS can be effectively controlled by Lewis acid. Steric and electronic factors, aromaticity and HSAB rules all affect the unique addition pattern observed here. Detailed investigation of the chemistry of fullerene-mixed peroxides is in progress to explore their possible applications in fullerene skeleton modification such as the synthesis of cage-opened fullerenes and heterofullerenes.

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Notes and references

‡ **Preparation of 2**. Compound **1** (132 mg, 0.12 mmol) was dissolved in 26 ml freshly distilled CH_2Cl_2 and stirred in an ice-bath in the dark. Then TMSNCS (160 μL, 1.2 mmol) and silica gel (160 mg) were added. Progress of the reaction was monitored by TLC. When **1** was nearly completely consumed (2 days), the solvent was evaporated and the residue was chromatographed on a silica gel column. Eluting with CH_2Cl_2 gave compound **3** (6 mg, yield: 4%) as the first band; the second band was the main product **2** (120 mg, yield: 86%). Characterization data for **2**: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 5.29 (1H, OH), 1.48 (s, 9H), 1.41 (s, 18H), 1.36 (s, 9H). ^{13}C-NMR ($CDCl_3$, 100 MHz) all signals represent 1C except those noted. δ: 159.11, 150.03, 149.98, 149.38, 149.26, 149.12, 149.01, 148.74, 148.54 (2C), 148.25 (2C), 148.14 (2C), 148.09, 148.01, 147.91, 147.86, 147.82 (2C), 147.66, 147.53, 147.04, 146.45, 146.39, 145.59 (2C), 147.47, 145.32, 145.25, 144.78, 144.29, 144.21, 144.16, 143.96, 143.84, 143.14, 143.11, 143.08, 142.77, 142.59, 142.36, 142.30, 142.28, 141.95, 141.17, 140.31, 139.69, 139.63, 139.60, 139.22, 138.21, 137.18, 129.41, 109.82, 107.33, 88.71 (*C*-OO^{t}Bu), 84.26 (*C*-OO^{t}Bu), 83.20 (1*C*-$(CH_3)_3$), 82.34 (*C*-$(CH_3)_3$), 81.87 (*C*-$(CH_3)_3$), 81.77 (*C*-$(CH_3)_3$), 81.20 (*C*-OO^{t}Bu), 78.55 (*C*-OO^{t}Bu), 66.71 (*C*-SCN), 26.67 ($3CH_3$), 26.65 ($6CH_3$), 26.62 ($3CH_3$). FT-IR (microscope): 3349, 2980, 2931, 2870, 2155, 1615, 1473, 1455, 1427, 1388, 1364, 1328, 1307, 1261, 1244, 1191, 1152, 1113, 1045, 1023, 1006, 907, 868, 756, 733. (+) ESI-MS (VGPlatform II): *m*/*z* (rel. intens.) 1185 (100) [M + NH_4^+], (−) ESI-MS (VGPlatform II): *m*/*z* (rel. intens.) 1109 (100) [M − SCN], 1198 (50) [M + MeO^-], calculated for $C_{77}H_{37}NO_{10}S$ M_w = 1167. Crystal data: monoclinic, space group $P2_1/n$, unit cell dimensions: a = 15.331(3) Å, b = 14.898(3) Å, c = 25.152(5) Å, β = 104.84(3)°, V = 5552.9(19) Å^3. Reflections collected/unique 30 622/9737 [R(int) = 0.0567]. Final R indices [$I > 2\sigma(I)$] R_1 = 0.0673, wR_2 = 0.1627. CCDC 652053.

Preparation of 3. Compound **1** (36 mg, 0.033 mmol) was dissolved in 6 ml freshly distilled CH_2Cl_2 and stirred at room temperature. Then TMSNCS (91 μL, 0.66 mmol) and $Al(CF_3SO_3)_3$ (154 mg, 0.33 mmol) were added. Progress of the reaction was monitored by TLC. When **1** was nearly completely consumed (4 h), the solution was poured onto a silica gel column and chromatographed. Eluting with CH_2Cl_2 gave a trace amount of **4** as the first band, the second band was the main product **3** (24 mg, yield: 63%). Characterization data for **3**: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 5.09 (1H, OH), 1.48 (s, 18H), 1.46 (s, 18H). ^{13}C-NMR ($CDCl_3$, 100 MHz) all signals represent 2C except those noted. δ: 161.84, 149.74, 149.14, 148.89, 148.80 (1C), 148.62, 148.52, 148.27 (1C), 148.25, 148.04, 147.31, 147.09, 146.75, 146.56, 145.81, 145.50, 145.17, 144.81, 144.62, 144.13 (4C), 143.48, 143.17, 142.71, 141.90, 141.52, 139.92, 133.33, 109.32, 107.81, 98.02 (*C*-NCS), 88.08 (*C*-OO^{t}Bu), 82.62 (2*C*-$(CH_3)_3$), 81.99 (2*C*-$(CH_3)_3$), 78.95 (*C*-OO^{t}Bu), 26.78 ($6CH_3$), 26.74 ($6CH_3$). FT-IR (microscope): 3533, 2979, 2931, 2870, 2157, 1473, 1455, 1421, 1388, 1364, 1324, 1305, 1244, 1230, 1192, 1154, 1104, 1088, 1067, 1043, 1020, 1006, 971, 908, 869, 783, 732, 690, 670. (+) ESI-MS (VGPlatform II): *m*/*z* (rel. intens.) 1185 (100) [M + NH_4^+], (−) ESI-MS (VGPlatform II): *m*/*z* (rel. intens.) 1166 (48) [M − H^+], calculated for $C_{77}H_{37}NO_{10}S$ M_w = 1167.
Crystal data for compound **4**: orthorhombic, space group $Pca2_1$, unit cell dimensions: a = 19.9448(2) Å, b = 14.8201(2) Å, c = 37.3546(6) Å, V = 11041.4(3) Å^3. The Flack parameter = 0.32(18). Reflections collected/unique 92 750/17 246 [R(int) = 0.1536]. Final R indices [$I > 2\sigma(I)$] R_1 = 0.0788, wR_2 = 0.1598. CCDC 669268.

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