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# Addition of diprotic nucleophiles to a $C_{60}$–tetrazine monoadduct: structural reassignment and correction of a novel rearrangement†

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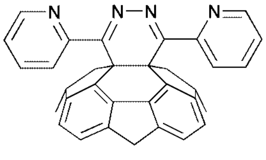
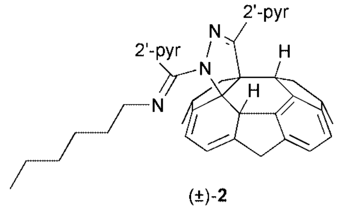
**$C_{60}$–tetrazine Diels–Alder adducts bearing electron deficient dihydropyridazine groups undergo chemoselective amination and hydration reactions upon addition of primary aliphatic amines and water, respectively, to form new adducts with 4,5-dihydropyrazole groups nested atop the [60]fullerene skeleton.**

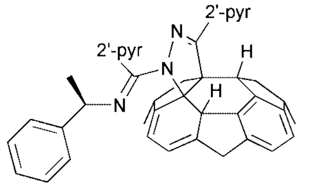
Recently, we reported[1] Diels–Alder reactivity between $C_{60}$ and electron deficient 3,6-disubstituted-1,2,4,5-tetrazines. With 3,6-di-2′-pyridyl-1,2,4,5-tetrazine, the corresponding monoadduct **1** bears a 4,5-dihydro-3,6-di-2′-pyridylpyridazine group fused to the [60]fullerene skeleton. Compound **1** behaves as an isolable but reactive intermediate capable of considerable further chemistry. Previously a facile, regioselective 1,4-hydrogenation of **1** was reported.[1] Continued work on this and related compounds shows that the structure reported for the hydrogenated monoadduct was incorrect. Compound **1** does hydrogenate in a 1,4 fashion, but only in concert with a novel rearrangement which effectively converts the fused 4,5-dihydropyridazine function into a 4,5-dihydropyrazole group. The reaction is a net hydration. With the aid of an X-ray crystal structure, we are now able to redefine the chemistry of **1** as it pertains to the addition of diprotic nucleophiles. A variety of nucleophiles including water, alcohols, thiols, and primary and secondary aliphatic amines add smoothly to **1**. Chemoselective additions of the diprotic nucleophiles, primary aliphatic amines and water, are followed in each case by a novel rearrangement reaction on the [60]fullerene surface leading to new compounds bearing fused 4,5-dihydropyrazole groups.[2]



**1**



**(±)-2**



**3**
1 of 2 diastereomers

Monoadduct **1** was formed as previously described[1] and reacted with several diprotic nucleophiles including hexylamine and (*R*)-(+)-α-methylbenzylamine. The reactions yield new compounds, (±)-**2** and **3** (as a mixture of 2 diastereomers), respectively. Compounds (±)-**2** and **3** bear 1,3-disubstituted-4,5-dihydropyrazole groups nested atop the corresponding [60]fullerene skeletons.

The structure of **3** was obtained by single crystal X-ray diffraction. Black crystals of **3** ($C_{84}H_{19}N_5$·$2CS_2$) form in the chiral space group $P2_12_12_1$ through vapor diffusion of hexane into a carbon disulfide solution of the compound.‡ The structure is disordered with both diastereomers present, but in unequal amounts. Fig. 1 shows a view of the entire molecule for the major diastereomer, which has a refined population of 0.529(3). (The minor diastereomer has an analogous structure, but the location of the [60]fullerene moiety is switched such that the positions of the 5- and 6-membered rings adjacent to C2 and C3 are reversed relative to those shown in Fig. 1. The ability of these two diastereomers to co-crystallize at a common crystallographic site is related to the orientational disorder seen in many fullerene crystals.[3,4]) Structurally the adduct can be viewed as involving addition to two adjacent 6:6 ring junctions of the fullerene, analogous to a *cis*-1 bisadduct.[5] The C2–C3–N3–N2–C61 ring spans a 6:5 ring junction, protrudes radially from the [60]fullerene skeleton, and is very nearly planar. The hydrogen atoms attached to C1 and C4 were located in a difference Fourier map for both the major and minor diastereomers. As is usual with additions to fullerenes,[6] geometric changes in the carbon cage are localized at the sites of attachment. Thus, the C1–C2 and C3–C4 bond lengths (1.670(8) and 1.712(10) Å in the major diastereomer, 1.720(8) and 1.731(11) Å in the minor diastereomer) are longer than the 1.38 Å distance found for 6:6 ring junction of C60. The C2–C3 bond, 1.622(5) Å, is also long.

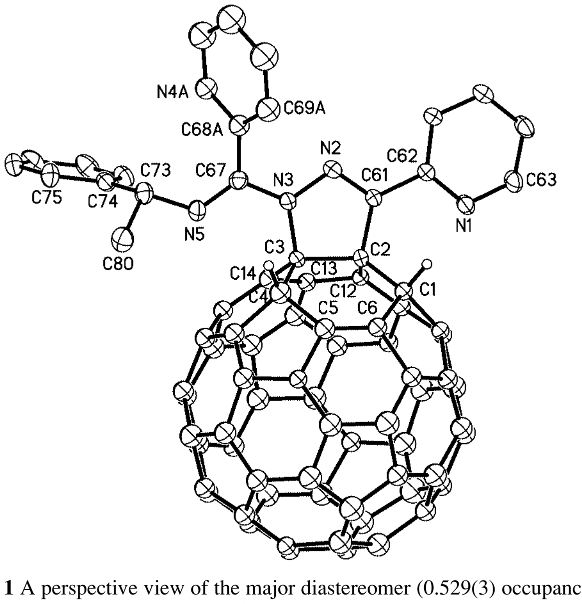


**Fig. 1** A perspective view of the major diastereomer (0.529(3) occupancy) of the adduct **3**, $C_{84}H_{19}N_5$, with 50% thermal contours for all non-hydrogen atoms. Only the hydrogen atoms on C1 and C4 are shown.

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† Electronic supplementary information (ESI) available: select spectroscopic data for (±)-**2**, **3** and (±)-**4**. See http://www.rsc.org/suppdata/cc/b1/b104151g/

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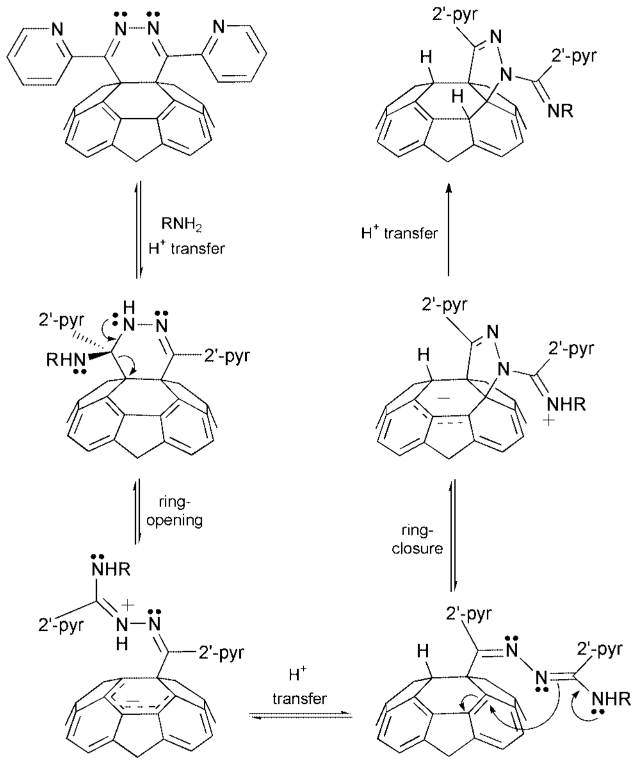


**Scheme 1** Possible mechanism for amination of $C_{60}$–tetrazine monoadduct.

Strong spectroscopic similarities ($^1H$ and $^{13}C$ NMR†) between (±)-**2** and **3** suggest an analogous structure for (±)-**2**.

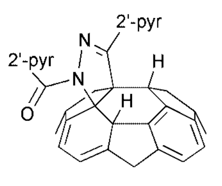
The structures for (±)-**2** and **3** are consistent with amination across a single imine C=N bond of **1** followed by a rearrangement of the amination adducts (Scheme 1). Chemoselective amination across an imine C=N bond of **1** is somewhat surprising considering that $C_{60}$ itself is readily aminated by primary and secondary aliphatic amines.[7] EPR and UV–VIS–NIR evidence[7a,b] suggests that the amination of $C_{60}$ involves initial electron transfer from the amine to $C_{60}$. In our laboratory, the amination of $C_{60}$ usually requires ambient light when relatively nonpolar organic solvents are employed (*e.g.* toluene, chloroform). This observation is consistent with a mechanism involving electron transfer from amine to photoexcited fullerene (for similar observations involving tertiary amine addition, see refs. 7*f* and 7*g*). However, compounds (±)-**2** and **3** are formed equally well in ambient light or darkness, consistent with but by no means specific to a mechanism involving simple nucleophilic additions (Scheme 1).

Other diprotic nucleophiles show similar reactivity. Water adds to **1** to give the analogous hydration product (±)-**4**. The reaction is catalyzed by weak acid catalysts such as silica gel and requires ambient light.

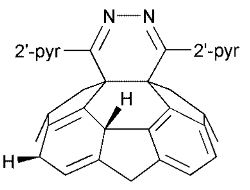
Compounds (±)-**2** and **3** are formally imine derivatives of (±)-**4**, but do not originate from (±)-**4**. Thus, addition of the appropriate amine to (±)-**4** does not produce (±)-**2** or **3** under otherwise identical reaction conditions employed for the synthesis of (±)-**2** or **3** from **1**. Consequently, (±)-**4** is not an intermediate in the amination reactions leading to (±)-**2** and **3**. Compounds (±)-**2** and **3**, however, are converted to (±)-**4** under harsh hydrolysis conditions (conc. HCl, $CH_3CN$, 80 °C), thereby confirming the structure of (±)-**4**.

The $^1H$ and $^{13}C$ NMR spectra for (±)-**4** match those reported previously for a compound assigned structure (±)-**5**.[1]

With an X-ray crystal structure now available for **3**, it is clear that the previously assigned structure (±)-**5** is incorrect and should be replaced with the structure (±)-**4**. The original assignment of structure (±)-**5** was based upon the observations that the reaction leading to hydrogenated product is photoinduced, the reaction requires water adsorbed on glass, and the NMR data are uniquely consistent with a 1,4-hydrogenation pattern on the fullerene skeleton. Moreover, the completely regioselective nature of the reaction suggested new C–H bond formation in close proximity to the dihydropyridazine group. Indeed, each of these statements holds true for the hydration of **1** leading to (±)-**4**. A key shortcoming of the earlier work was the failure to recognize rearrangement of the dihydropyridazine function, as well as the erroneous incorporation of the tetrazine–dihydrotetrazine redox cycle into the proposed reaction mechanism.



(±)-**4**



(±)-**5**

Because the hydration and amination reactions produce structurally similar compounds, it is tempting to conclude that they proceed *via* similar mechanisms. However, the hydration of **1** leading to (±)-**4** requires ambient light while the amination reactions leading to (±)-**2** and **3** do not. By analogy to known photoinduced processes involving $C_{60}$,[7f,g] at least one of the steps leading to (±)-**4** likely involves an electron transfer to a photoexcited [60]fullerene skeleton.

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## Notes and references

‡ *Crystal data*: black needles of **3**, $C_{84}H_{19}N_5{\cdot}2\,CS_2$, $M$ = 1202.26, form in the orthorhombic space group $P2_12_12_1$ with $a$ = 13.0656(9), $b$ = 14.3786(9), $c$ = 25.8201(17) Å, at 91(2) K with $Z$ = 4. A total of 64323 reflections were collected with graphite monochromated Mo-K$\alpha$ ($\lambda$ = 0.71073 Å) radiation, $\mu$(Mo-K$\alpha$) = 0.262 mm$^{-1}$, and a Brucker SMART 1000 diffractometer. Refinement of 15217 reflections ($R$(int) = 0.04) and 735 parameters yielded $wR2$ = 0.231 for all data and a conventional $R_1$ = 0.087 based on 12123 reflections with $I > 2\sigma(I)$. All non-hydrogen atoms were assigned anisotropic thermal parameters except 58 of the fullerene carbon atoms (C2 and C3 were refined anisotropically) and a disordered pyridine ring, which were refined with isotropic thermal parameters. All hydrogen atoms were located in difference maps and subsequently refined using a riding model. The largest peak and hole in the final difference map are 0.99 e Å$^{-3}$ and −0.81 e Å$^{-3}$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. CCDC 168187. See http://www.rsc.org/suppdata/cc/b1/b104151g/ for crystallographic data in .cif or other format.

1 G. P. Miller and M. C. Tetreau, *Org. Lett.*, 2000, **2**, 3091.

2 This work was recently presented to the Fullerenes Group at the 199th Meeting of the Electrochemical Society: G. P. Miller and M. C. Tetreau, March 28, 2001.

3 H. B. Bürgi, E. Blanc, D. Schwarzenbach, S. Liu, Y. J. Lu, M. M. Kappes and J. A. Ibers, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 640.

4 A. L. Balch, J. W. Lee, B. C. Noll and M. M. Olmstead, *J. Chem. Soc., Chem. Commun.*, 1993, 56.

5 A. Hirsch, *The Chemistry of the Fullerenes*, Thieme, Stuttgart, 1994, p. 69.

6 A. L. Balch, A. S. Ginwalla, M. M. Olmstead and R. Herbst-Irmer, *Tetrahedron*, 1996, **52**, 5021.

7 (*a*) F. Wudl, A. Hirsch, K. C. Khemani, T. Suzuki, P.-M. Allemand, A. Koch, H. Eckert, G. Srdanov and H. Webb, in *Fullerenes: Synthesis, Properties, and Chemistry of Large Carbon Clusters*, ACS Symposium Series 468, American Chemical Society, ed. G. S. Hammond and V. S. Kuck, Washington, D.C., p. 161, 1992; (*b*) A. Skiebe, A. Hirsch, H. Klos and B. Glotschy, *Chem. Phys. Lett.*, 1994, 397; (*c*) A. Hirsch, Q. Li and F. Wudl, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1309; (*d*) G. P. Miller, J. M. Millar, B. Liang, S. Uldrich and J. E. Johnston, *J. Chem. Soc., Chem. Commun.*, 1993, 897; (*e*) A. L. Balch, B. Cullison, W. R. Fawcett, A. S. Ginwalla, M. M. Olmstead and K. Winkler, *J. Chem. Soc., Chem. Commun.*, 1995, 2287; (*f*) K.-F. Liou and C.-H. Cheng, *Chem. Commun.*, 1996, 1423; (*g*) G. E. Lawson, A. Kitaygorodskiy, B. Ma, C. E. Bunker and Y.-P. Sun, *J. Chem. Soc., Chem. Commun.*, 1995, 2225.