Pergamon

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Tetrahedron Letters 44 (2003) 3565–3567

TETRAHEDRON LETTERS

The structure and first ^{1}H NMR spectral assignment of piperazine-C_{60} adducts

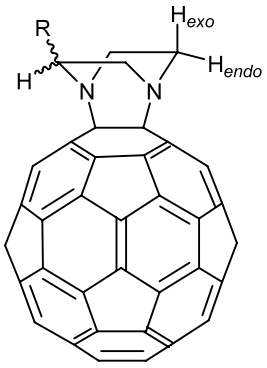
Craig P. Butts,[a,*] Remco W. A. Havenith,[a] Mikael Jazdzyk,[a] Thomas Drewello[b] and Sotirios Kotsiris[b]

[a]*School of Chemistry, University of Exeter, Exeter EX4 4QD, UK*
[b]*Department of Chemistry, University of Warwick, Coventry CV4 7AL, UK*

Received 30 January 2003; revised 14 February 2003; accepted 28 February 2003

Abstract—The ^{1}H NMR spectrum of the piperazine-C_{60} monoadduct has been assigned for the first time almost 10 years after it was synthesised. The preparation and characterisation of the first (C2-substituted piperazine)-C_{60} monoadduct are also described, revealing the C2-substituent as occupying an *exo* position on the addend.

The oxidative dehydrogenation reactions of C_{60} with amines[1] and diamines[2] were established early in the story of fullerene chemistry. These are not particularly facile or selective, indeed the only yield above 25% for a diamine-C_{60} monoadduct reported to date is 50%[3] for the preparation of monoadduct **1** from the reaction of 8 equiv. of piperazine with C_{60} for 3 days at 80°C. The structure of the adduct **1** has been confirmed by X-ray crystallography[4] as the 1,2-dihydrofullerene with the piperazine adopting a 'boat' configuration.



1 R=H
2 R=CH_3

A rapid photochemical procedure ($KMnO_4$ filter, 505 nm cutoff) for the preparation of **1** was subsequently reported by Sun et al.[5] which required only 70 minutes at room temperature, but gave a relatively low yield of monoadduct **1** (<25%) and still employed a large excess (7 equiv.) of the diamine reagent. Again acyclic diamines gave much lower yields than piperazine **1**. Recently, reactions employing both of these thermal and photochemical conditions were reported again, by Wang,[6] with essentially identical results.

In all of these studies, the very simple ^{1}H NMR spectrum of adduct **1** (Fig. 1) has been reported, but not assigned. Indeed the only comment on it comes from

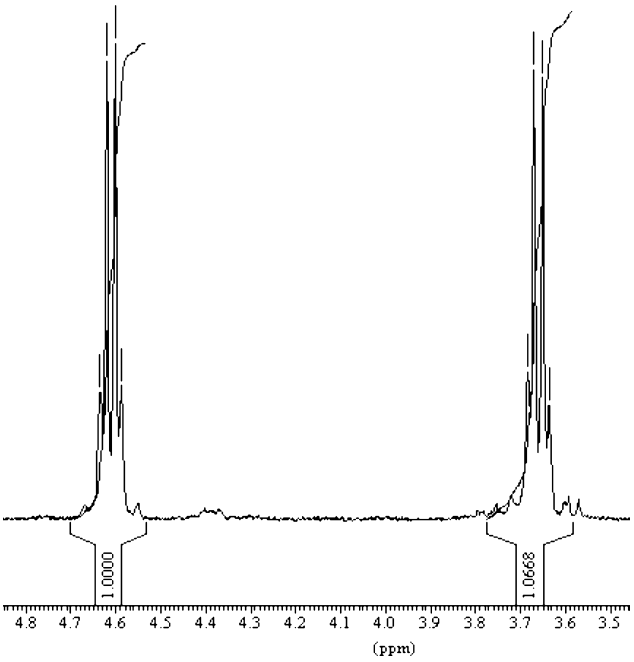


Figure 1. ^{1}H NMR spectrum of adduct **1** in $CDCl_3/CS_2$.

* Corresponding author.

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00624-5

Wang who described the observed coupling pattern as an AA′A″A‴BB′B″B‴ system. The two observed resonances at ca. δ 3.65 and δ 4.60 (relative to TMS) obviously arise from the different environments of the *exo* and *endo* protons on the boat-configured piperazine addend of **1**. However, it is not immediately obvious which resonance arises from which nucleus, as the effect of the fullerene substituent on the nuclear shieldings of each proton are not clear. The high symmetry of adduct **1** makes decoupling, NOE or correlation methods unhelpful in this assignment.

The following is a report of the assignment of this apparently simple ^{1}H NMR spectrum by a combination of computational, spectroscopic and synthetic experiments.

Ab initio calculations[7] of the ^{1}H nucleus chemical shifts of **1** (δ 3.16 and δ 4.08, relative to the calculated value for TMS) gave a good match with the experiment (δ 3.65 and δ 4.60). In particular the calculated chemical shift separation of 0.92 ppm almost perfectly matches the experimental observation of 0.95 ppm. The calculation suggests assignment of the observed resonances to the *exo* (δ 3.65) and *endo* (δ 4.60) protons respectively.

In order to conduct more complex NMR spectroscopic experiments to confirm the assignment, the synthesis of an unsymmetrical piperazine-C_{60} adduct was undertaken. The photochemical reaction[7] of C_{60} (80 mg, 0.11 mmol) with an excess of commercially available (racemic) 2-methylpiperazine (33 mg, ca. 0.33 mmol) in toluene for 64 hours gave the corresponding monoadduct **2** in 41% yield after chromatographic separation. It should be noted that fewer equivalents of the diamine were employed for this preparation than in previous reports. Indeed in our hands, monoadduct **1** could be prepared in 75% yield by photochemical reaction of C_{60} with 1 equiv. of piperazine in toluene for 18 hours. The corresponding stoichiometric reaction using 2-methylpiperazine was found to be too slow for synthetic application.

Adduct **2** was identified by ^{1}H and ^{13}C NMR spectroscopy and the parent ion was observed at 818 mass units by MALDI mass spectrometry in the negative ion mode.[8] No bisaddition products were observed in the mass spectrum of the isolated material. All other mass spectrometric methods (EI/CI/FAB/ES) gave little or no signal at the expected mass. The ^{13}C NMR spectrum of **2** shows 38 independent resonances in total.[9] The seven most upfield resonances correspond to the piperazine adduct carbons (δ 19.48–55.11) and the sp^3 hybridised fullerene carbons (δ 77.54 and 80.53). The remaining 31 observed resonances (δ 137–154) correspond to the sp^2 hybridised fullerene carbons, of which a number are coincidental. A simple numeric analysis based on the peak height of the observed resonances suggests that all expected 58 carbon resonances are present in the spectrum.

The ^{1}H NMR spectrum of **2** displays eight resonances (Table 1). The resonances for **2** appear significantly further downfield than that of 2-methylpiperazine, as is expected for an addend on electron deficient C_{60}. The conformation of the piperazine ring in adduct **2** is assumed to be similar to that of **1** with two possible arrangements for the methyl group, either *exo* or *endo*, as shown schematically in Figure 2. In all preparations of **2**, only a single monoadduct was isolated, but it is not immediately clear which arrangement is adopted in this isolated material.

Table 1. ^{1}H NMR spectroscopic data for adducts **1** and **2** (in $CDCl_3/CS_2$)

	1	**2**
exo protons [calculated]	δ 3.65 [3.16]	δ 3.19 (H3), 3.57 (H5), 3.91 (H6)
endo protons [calculated]	δ 4.60 [4.08]	δ 4.50 (H6), 4.55 (H5), 4.72 (H3), 4.94 (H2)
C2-Me	–	δ 1.78

Semi-empirical calculations (AM1) on both configurations of **2** and the corresponding C2-ethyl analogue, suggest that there is little energy difference between the two possible configurations. Analysis of the COSY spectrum of **2** reveals the two expected coupling systems corresponding to the C2/C3/Me protons and the C5/C6 protons. All the data from NOE experiments are consistent with the COSY data, except for an additional, small (ca. 2%), enhancement of the C2-methyl doublet (δ 1.78) on irradiation of the proton resonance at δ 3.91. The resonance at δ 3.91 is part of the C5/C6 coupling system according to the COSY spectrum, so the observed NOE is almost certainly caused by a 1,3-'diaxial' relationship between this proton and the methyl group. Hence the resonance at δ 3.91 is assigned to the C6-*exo* proton ($H6_{exo}$) and the C2-methyl group must also occupy an *exo* position in the isolated adduct **2**. The assignment of $H6_{exo}$ is also supported by the calculated chemical shifts for piperazine adduct **1**, in which the more upfield resonance arises from the *exo* protons.

Assignment of the resonance at δ 4.94 to the $H2_{endo}$ proton can be made from an observed correlation with the C2-Me group in the COSY spectrum (confirmed by HMQC and DEPT spectra). An NOE experiment, irradiating $H2_{endo}$ assigned the $H3_{endo}$ proton and hence $H3_{exo}$ to the resonances at δ 3.19 and δ 4.72 respectively. Again, these assignments all fit the suggested upfield/downfield groupings for *endo* and *exo* protons respectively, based on the calculated values for adduct **1**.

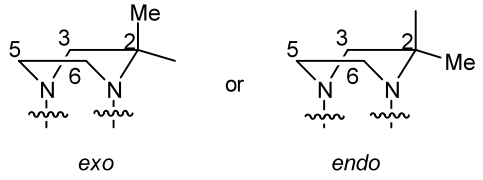


Figure 2. Schematic diagrams of possible addend configurations in adduct **2**.

With the resonance at δ 3.91 assigned to $H6_{exo}$, then the resonance at δ 4.50 is assigned to $H6_{endo}$ on the basis of HMQC data. However, there are no observed NOEs between the C5 and C6 protons, so definite assignment of the resonances at δ 3.57 and δ 4.55 to $H5_{exo}$ or $H5_{endo}$ is not possible. However, given that all of the other assigned resonances fit with the pattern of the calculated data (i.e. the assigned *endo* resonances are all downfield of the assigned *exo* resonances), the δ 3.57 and δ 4.55 resonances are assigned as the $H5_{exo}$ and $H5_{endo}$ protons respectively.

With the assignment of the ^{1}H NMR spectrum of **2** confirming the pattern of the calculated chemical shifts for C_{60}-piperazine adduct **1** (except for $H5_{exo}$ and $H5_{endo}$), we feel that the observed ^{1}H NMR spectrum of **1** can be assigned in line with the calculated values, with reasonable confidence. Hence the more upfield resonance (δ 3.65) is assigned to the *exo* protons of the addend ring of adduct **1** while the more downfield resonance (δ 4.60) is assigned to the *endo* protons.

This assignment is consistent with homologous piperazine-based systems, assigned in other manners. For example, Ciccarese et al. reported[10] a platinum complex of *N*,*N*′-dimethylpiperazine (in a boat configuration) with ^{1}H NMR resonances at δ 2.76 and δ 3.76 arising from the axial (*exo*) and equatorial (*endo*) protons respectively. These assignments were made on the basis of Pt–^{1}H coupling constants in this case.

Surprisingly, this implies that there is essentially no differential shielding of the *endo* nuclei of **1** or **2** by the surrounding fullerene π-system. To probe this further, Nucleus-Independent Chemical Shift (NICS) values[11] were calculated for 1,2-dihydrofullerene, fixed in a geometry to match that of **1**, at the positions of the axial and equatorial protons of **1**. The NICS values of 0.91 ppm (*exo* position) and 0.97 ppm (*endo* position) suggest a small deshielding influence of the fullerene core, which is only slightly larger at the *endo* position (0.06 ppm).

In summary, the assignment of the ^{1}H NMR spectrum of the C_{60}-piperazine monoadduct **1** has been made, almost 10 years after the first report by Kampe et al. Surprisingly it appears that the fullerene π-system has little differentiating effect on the nuclear shielding of the protons on the piperazine addend. Synthesis of the desymmetrised C_{60}-(2-methylpiperazine) monoadduct **2** was accomplished by photochemical methods in yields comparable to those achieved by Kampe et al. and significantly higher than those of previous photochemical methods for preparations of the parent system **1**. We are currently investigating other piperazine-derivatives as addends in these systems.

Acknowledgements

We thank the TMR networks USEFULL and BIO-FULL (CT 960126 and 980192) for financial support for M.J. and R.W.A.H.

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