CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200700591

# $^1$H NMR Spectroscopic Studies of the Conformational Isomers of Pyrrolidinofullerenes

**Olena Lukoyanova, Alex Kitaygorodskiy, Claudia M. Cardona, and Luis Echegoyen*[a]**

**Abstract:** Mixed bis-adduct derivatives of $C_{60}$ containing a pyrrolidine and a malonate methano group were synthesized. Three regioisomers, the *e'*, the *trans*-2, and the *trans*-3, were isolated and characterized. In-depth NMR studies of these methano-pyrrolidinofullerenes showed that the nitrogen inversion on the pyrrolidine moiety is not a fast event in the $^1$H NMR time scale as previously regarded. Solvent effects, variable temperature experiments, and protonation of the pyrrolidine nitrogen are addressed.

**Keywords:** conformation analysis · fullerenes · NMR spectroscopy · pyrrolidinofullerenes

## Introduction

Since the discovery of Buckminsterfullerene, its functionalization has been extensively explored and has resulted in a large number of derivatives.[1–3] Functionalization of $C_{60}$ has facilitated the preparation of compounds with potential applications in the fields of material science, photovoltaics, and medicinal chemistry.[4–6] Among the numerous fullerene derivatives, a particular class, the pyrrolidonofullerenes, has been extensively synthesized. These are prepared via 1,3-dipolar cycloadditions to $C_{60}$ at double bond junctions between two six-membered rings, [6,6]-sites.[7,8] The popularity of this reaction arises from its simplicity and from the wide selection of commercially available starting materials that can be utilized. The reaction usually proceeds with efficient yields and results in a pyrrolidine ring attached to the fullerene sphere. Even though these compounds were recently shown to be unstable under thermal and electrochemically oxidative conditions,[9,10] this reaction is still of great value from a synthetic point of view since it can be employed as an intermediate pathway in protection/deprotection strategies.

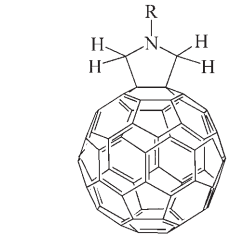
Functionalized fullerenes, like many other organic compounds, are characterized by common methods such as TLC, HPLC, MS, and NMR. Since commonly used fullerenes are composed of just carbon atoms, characterization of their derivatives is often done by focusing on the structure of the addends. Frequently, NMR experiments are the methods of choice. In particular, $^1$H NMR spectroscopy is often employed because protons are very sensitive to environmental electronic effects and their NMR spectra can provide unambiguous structural assignments.

Pyrrolidinofullerenes can have substituents attached either to the nitrogen or to the methylene carbons on the pyrrolidine ring. If a substituent is attached at the nitrogen (R), the methylene protons are inherently not equivalent due to the presence of the lone pair of electrons on the nitrogen, and their positions are either *cis* or *trans* with respect to the R group (see below; *N*-methyl pyrrolidinofullerene, R = $CH_3$ (**1**), *N*-methyl pyrrolidine (**2**) and 1-methyl-3-pyrroline (**3**)). However, nitrogen inversion of the pyrrolidinofullerenes has always been regarded as a fast event on the $^1$H NMR time scale, and therefore, this inequality has not been observed. For example, the methylene hydrogens of the pyrrolidine ring in compounds such as **1** appear as a single resonance in $^1$H NMR spectra in carbon disulfide/[D]chloroform ($CS_2$/$CDCl_3$), and therefore, they are considered magnetically equivalent.[7]

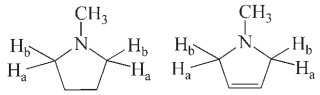
This observation is consistent with earlier reports describing the nitrogen inversion of alkylamines[11] and cyclic alkylamines.[12] Generally, the conformers are not resolved on the $^1$H NMR time scale because of the energetically low nitrogen inversion barrier. However, the $^1$H NMR spectra of these conformational isomers can be differentiated at low temperatures. For instance, the *N*-methyl pyrrolidine **2** was shown to have magnetically equivalent α-protons ($H_a$ and

[a] O. Lukoyanova, Dr. A. Kitaygorodskiy, Dr. C. M. Cardona, Prof. L. Echegoyen
Department of Chemistry, Clemson University
219 Hunter Laboratories, Clemson SC 29630-0973 (USA)
Fax: (+1) 864-656-6613
E-mail: luis@clemson.edu

Supporting information for this article is available on the WWW under http://www.chemeurj.org/ or from the author.



1



2 3

$H_b$), giving rise to a sharp singlet when the resonance frequencies of the β-protons were irradiated.[13] Upon lowering the temperature the singlet reversibly broadened and ultimately separated into two signals corresponding to the protons *cis* and *trans* to the methyl group.

Many other factors have been found to affect the inversion frequency. For example, the rate of nitrogen inversion in compound **3** was found to be much faster than the inversion rate in **2** due to the homoconjugation of the nitrogen lone pair with the π system.[12] In addition, the nitrogen inversion was slowed down in compounds with electronegative substituents on the nitrogen and compounds with higher C-N-C angle strain.[13] The frequency of inversion was also found to be dependent on the solvent employed,[12] as well as on the protonation of the nitrogen, which slows down the inversion process.[14]

Recently it was established that [60]fullerene has a small electron-withdrawing effect on a directly fused pyrrolidine ring.[15] Remarkably, the pyrrolidine nitrogen of *N*-methyl 2-[2-(2-methoxyethoxy)ethoxymethyl] pyrrolidinofullerene was found to be six orders of magnitude less basic than the nitrogen on a similar pyrrolidine without the fullerene unit.[15] The lower basicity of the pyrrolidinofullerenes suggests a through-space interaction of the nitrogen lone pair and the fullerene π system, which makes the lone pair less available for protonation. Pyrrolidinofullerenes also have larger C-N-C angles than pyrrolidines lacking the fullerene adduct. Larger C-N-C angles minimize constrains to the nitrogen inversion. Based on the lower basicity, π conjugation of the nitrogen lone pair with the fullerene, and the near coplanar C-C-N and C-N-C angles in the pyrrolidine ring, it is reasonable to expect that the nitrogen inversion of the pyrrolidinofullerenes should be faster than that of their nonfullerene counterparts.

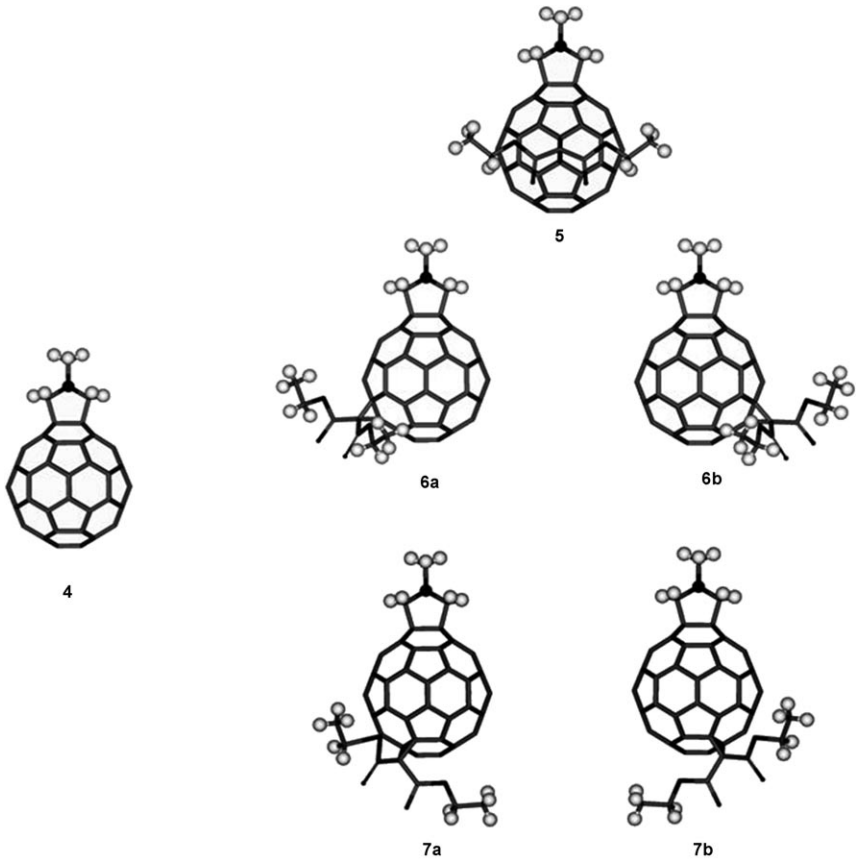
In the course of our studies on the electrochemical stability of fullerenes with mixed bis-adducts, bearing a pyrrolidino and a methano addend,[9] we noticed a significant broadening of the resonances of the pyrrolidine ring in $CDCl_3$, while the resonances of the other groups in the same molecule remained sharp. In some cases the broadening was so significant that the signal could not be detected. This behavior suggests that the nitrogen inversion of the pyrrolidinofullerenes in chloroform solutions is significantly slower than commonly believed. A brief reference to the broadening of the pyrrolidine protons of *N*-methyl pyrrolidino $Sc_3N@C_{80}$ has been previously mentioned;[16] however, this phenomenon has not been properly addressed in the fullerene literature, especially for pyrrolidine addends on $C_{60}$. This article investigates this issue in detail.

## Results and Discussion

Our first step was to synthesize and isolate the fullerene mixed bis-adducts containing both a bis(ethylcarboxy)methano and a pyrrolidino addend (Scheme 1). The reactions to produce bis-adducts of $C_{60}$ usually result in a distribution of isomeric products of which up to eight isomers are possible when the addends are equivalent and symmetrical. Bis-addition reactions with this type of addends have been extensively studied.[17] For example, Hirsch and co-workers have investigated cyclopropanation reactions in depth, including highly selective cycloadditions where bromomalonates were added to $C_{60}$ to form symmetrical bis-adducts.[17,18] Among the seven isomers of bis(ethoxycarbonyl)-methano-$C_{60}$ products that were isolated, the addition to equatorial (*e*) and *trans*-3 positions were favored. On the other hand, the 1,3-dipolar azomethine ylide cycloaddition reactions are much less selective.[19] The distribution of the bis-pyrrolidino adducts depends on the substituents, but often *trans*-2, *trans*-3, *trans*-4 and *cis*-3 adducts are found in larger quantities.[19,20] Furthermore, when a cycloaddition reaction forms a bis-adduct with identical and symmetrical addends, some of the bis-adducts are chiral and racemic mixtures are often obtained.[21–24] In particular, *trans*-2, *trans*-3 and *cis*-3 adducts are mixtures of enantiomers due to their inherently chiral addition pattern. Although there have been studies of fullerene bis-adducts with two different substituents, only a few reports describe mixed bis-adducts bearing a cyclopropane and a pyrrolidine addend.[25,26] If the addends are different, but symmetrical, all of the regioisomers except for *trans*-1, *e′* and *e″* will be produced as racemic mixtures.

Due to the higher selectivity and efficiency of the Bingel–Hirsch reaction, we prepared hybrid pyrrolidino-bis(ethylcarboxy)methano-fullerene bis-adducts starting with *N*-methyl pyrrolidinofullerene (**4**). Compound **4** was treated with bromomalonate under the Bingel–Hirsch conditions and the products were purified by column chromatography (silica gel). With this purification, three major fractions were obtained: fraction I (**7a** and **7b**), II (**6a** and **6b**), and III (**5**). All three fractions were characterized with techniques such as MALDI-TOF and NMR. The most notable feature of the $^1H$ NMR spectra of the three fractions was the sharp resonances in the regions $\delta$ 4.75–4.30 ppm (quartet) and 1.65 −1.25 ppm (triplet) in $CDCl_3$ at room temperature. These signals are characteristic of the ethyl moieties of the bis(ethylcarboxy)methano group attached to the $C_{60}$ sphere.[27] The *N*-methyl group and the methylene protons




Scheme 1. *N*-Methyl pyrrolidino[60]fullerene (**4**); mixed bis-adducts with *N*-methyl pyrrolidine and bis(ethoxycarbonyl)methano attached to $C_{60}$ sphere: *e′* isomer (**5**), *trans*-3 composed of two enantiomers **6a** and **6b**; *trans*-2 composed of two enantiomers **7a** and **7b**.

of the pyrrolidine ring are expected to give rise to two sharp resonances between $\delta$ 2.80 and 4.3 ppm in $CDCl_3/CS_2$.[7,19] However, only very broad and hardly discernible peaks were observed in this spectral region (Figure 1).

On the other hand, when the $^1$H NMR of **5** (fraction III), for example, was taken in $[D_6]$acetone/$CS_2$ instead, the protons of the *N*-methyl and the pyrrolidine ring were clearly

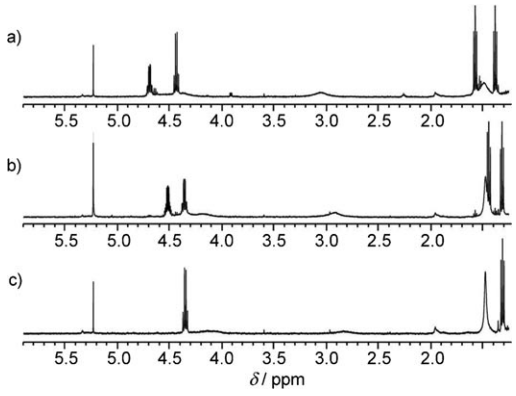



Figure 1. $^1$H NMR (500 MHz) spectra in $CDCl_3$ of a) fraction I, later assigned to compounds **7a** and **7b**; b) fraction II, later assigned to **6a** and **6b**; c) fraction III (compound **5**).

observed in the expected spectral regions (Figure 2). We attribute the extreme broadness of the pyrrolidino signals in $CDCl_3$ to intermediate exchange rates for ring inversion, which has no effect on the signals of the ethyl groups of the bis(ethylcarboxy)methano moiety.

The solvent employed has proven to be a major factor in the nitrogen inversion rates. It has been reported that the inversion barrier of the nitrogen in alkylamines, including pyrrolidines, is larger in $CDCl_3$ than in other less polar organic solvents.[12] To confirm this effect we recorded the $^1$H NMR of a simple pyrrolidinofullerene, **4**. Its spectrum in $CDCl_3$ showed very broad proton resonances, which sharpened significantly when $[D_8]$toluene was used instead (Figure 3). Therefore, the inversion of the pyrrolidine nitrogen seemed to be slower in $CDCl_3$ than previously reported.[7,19]

The structure of fraction III was determined based on

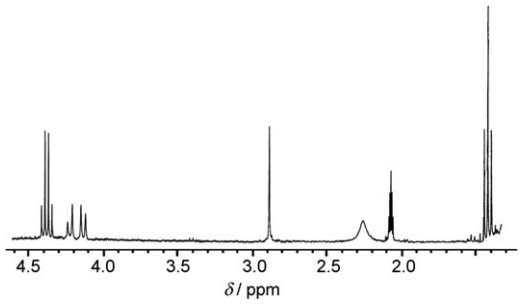



Figure 2. $^1$H NMR (500 MHz) spectra in $[D_6]$acetone/$CS_2$ of fraction III (compound **5**).

$^1$H NMR analysis conducted in $[D_6]$acetone/$CS_2$ (Figure 2) and unambiguously assigned to the *e′* isomer **5** after symmetry considerations were taking into account. The methylene protons on the pyrrolidine ring of **5** were not equivalent because of the presence of the bis(ethylcarboxy)methano group on one side of the fullerene sphere, and therefore, these geminal protons exhibited an AB quartet splitting pattern. On the other hand, the ethyl protons of the methano addend were magnetically equivalent and they resonated as a quartet and a triplet. The quartet and triplet of the meth-

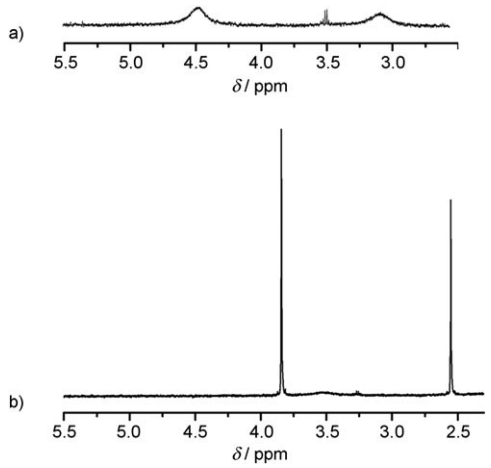



Figure 3. $^1$H NMR (500 MHz) spectra of **4** in a) $CDCl_3$ and b) [$D_8$]toluene (both referenced to TMS).

ano addend in the *e′* isomer are also clearly present in the spectra recorded in $CDCl_3$ (Figure 1c).

The structures of the compounds present in fractions I and II were also assigned based on their NMR spectra. Since the polarity of the mixed bis-adducts was expected to increase with a decreasing distance between the addends, due to the formation of a molecular dipole moment (*e′* > *trans*-4 > *trans*-3 > *trans*-2 > *trans*-1), the elution order suggested that the isomers in fractions I and II, the more non-polar adducts, were *trans*-2, *trans*-3 or *trans*-4. Careful examination of the $^1$H NMR spectra of these fractions indicated that the compound in fraction I had the *trans*-2 isomeric structure and fraction II was assigned the *trans*-3, which had been reported earlier.[25] Due to the chirality of the addition site, the *trans*-**2** isomer is a racemic mixture composed of **7a** and **7b**, and so is *trans*-3 (**6a** and **6b**) as depicted in Scheme 1. One of the criteria employed to resolve the structures of those compounds present in the less polar fractions was the chemical shifts of their resonances. The proton resonances of bis-adducts composed of bis(ethylcarboxy)methano and *N*-methyl pyrrolidine had been shown to be more shielded as the distance between the addends decreases from *trans*-**1** to *cis*-**3**.[19]

2D NMR experiments, such as COSY, were also employed in the structural assignment. An interesting aspect of the $^1$H NMR spectra of the *trans*-2 and *trans*-3 regioisomers was the complexity of the bis(ethylcarboxy)methano resonances. Because of the position of the pyrrolidine addend on the $C_{60}$ sphere relative to the methano addend, the two ethyl groups are not equivalent, resulting in two different $CH_2$ groups and two different $CH_3$ groups. Furthermore, the addition patterns of **6a**, **6b** and **7a**, **7b** are inherently chiral. Therefore, the methylene groups of the ethyl moieties in the bis(ethylcarboxy)methano addend are diastereotopic, and their prochiral nature was clearly observed in the $^1$H NMR spectrum which was easily simulated (see Supporting Information) as depicted in Figure 4.

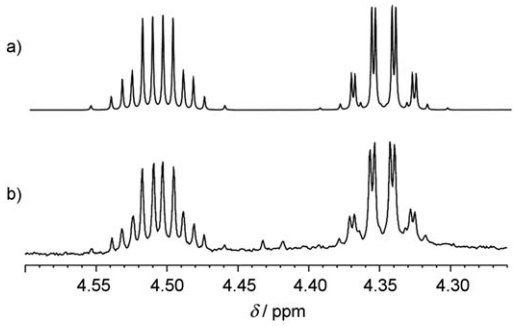



Figure 4. a) Simulated and b) experimental $^1$H NMR spectra (500 MHz) of the racemic mixture composed of **6a** and **6b**.

After synthesizing the mixed bis-adducts, we decided to slow down the nitrogen inversion as much as possible to determine its effect on the $^1$H NMR spectra. One factor that affects the rate of inversion of the nitrogen in alkylamines is protonation of the nitrogen which gives rise to an ammonium salt. In order to understand the changes, if any, we first assessed the effect of protonation on a mono-adduct. The formation of the *N*-methyl pyrrolidino[60]fulleronium was accomplished by the addition of a drop of [D]trifluoroacetic acid directly to an NMR tube containing a solution of compound **4** in $CDCl_3$. As a result, the $^1$H NMR spectrum of **4** exhibited a dramatic change. The broad resonances observed for both the methyl and the methylenes of the pyrrolidine group (Figure 5b), were transformed into a sharp singlet and an AX quartet, respectively, as shown in Figure 5c. The broad *N*-methyl signal resolved into a very sharp singlet and it was also significantly shifted downfield from $\delta$ 3.10 to 3.80 ppm. At the same time, the geminal protons of the pyr-

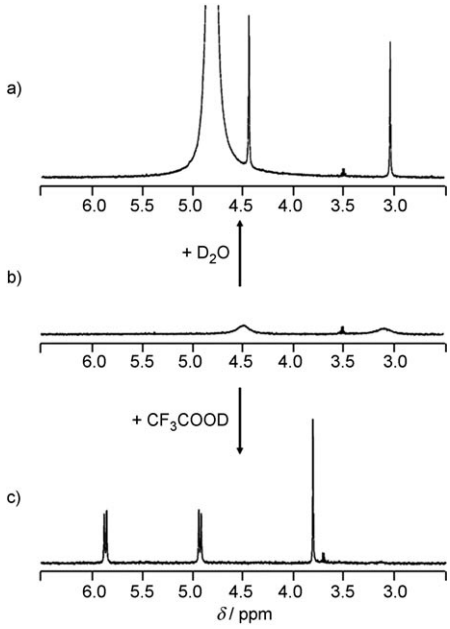
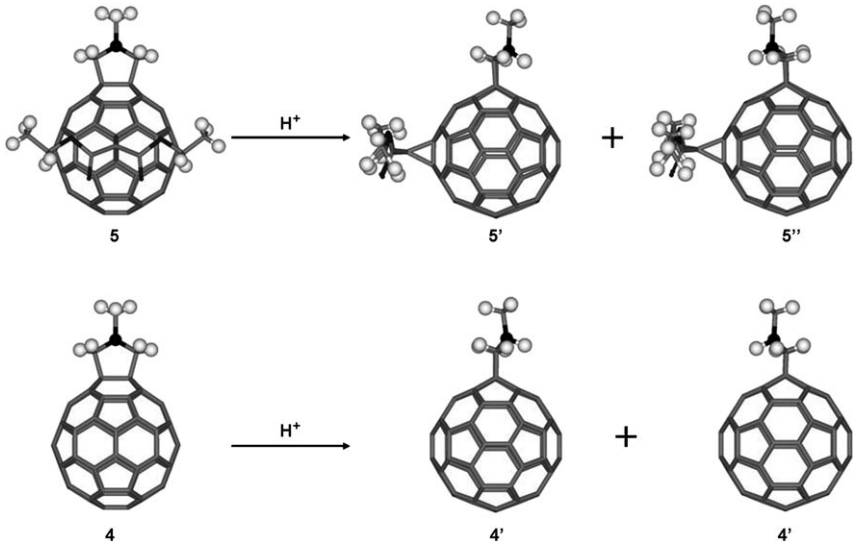



Figure 5. $^1$H NMR (500 MHz) of **4**: a) $CDCl_3/H_2O$; b) $CDCl_3$; c) $CDCl_3$/[D]TFA.

rolidine group, $H_a$ and $H_b$, split into two sharp doublets that are shifted downfield by one ppm. These results indicate that protonation of the pyrrolidine nitrogen of **4** gave rise to two identical structures, **4′** (Scheme 2, bottom). In the slow exchange regime, structures **4′** were conformationally locked and the geminal protons of the pyrrolidinium ring were positioned in different environments, which caused the AX splitting pattern.

The effect of the solvent on the nitrogen inversion was also clearly observed in another revealing experiment. As discussed above, the NMR resonances of the pyrrolidine protons of a simple mono *N*-methyl pyrrolidinofullerene **4** were unusually broad in $CDCl_3$. Addition of [D]TFA led to a dramatic change where an AX quartet appeared and all resonances were shifted downfield due to the deshielding effects of the positive charge on the nitrogen. On the other hand, when traces of water were added to a solution of **4** in $CDCl_3$ the inversion rate seemed to increase: the two broad resonances were transformed into two sharp singlets (Figure 5a), similar to those observed in [$D_8$]toluene at room temperature (Figure 3). Therefore, NMR experiments of pyrrolidinofullerenes conducted in deuterated solvents containing traces of water exhibit fast inversion rates. We believe that this is probably the situation for most pyrrolidinofullerenes reported to date, since extremely broad resonances for the pyrrolidino addend (Figure 1) are otherwise observed in very dry media.




Scheme 2. Protonation of compounds **4** (bottom) and **5** (top).

In the case of mixed bis-adducts, protonation of the pyrrolidine nitrogen would lead to the formation of multiple diastereomers (Schemes 2 and 3). Consequently, we observed a more complicated splitting pattern in these cases. The *e′*-bis-adduct **5** was protonated in the same manner as **4**, and upon the addition of the [D]TFA (Figure 6c), its spectrum confirmed the formation of two diastereomeric salts **5′** and **5″** (Scheme 2). The α-$CH_2$ protons of compound **5′** appeared as two **AX** doublets while the other diastereomer **5″** gave rise to two other pairs of doublets. Clearly, the **AX** doublet of doublets at $\delta \approx 5.4$ ppm appeared as a triplet because of accidental overlap of resonances, which was subsequently confirmed by two-dimensional correlation spectra (COSY) experiments. The other two AB doublets resonate at $\delta \approx 4.6$ ppm. The presence of two diastereomers was further corroborated by the presence of two *N*-methyl resonances at 3.55 and 3.56 ppm.

Protonation of the *trans*-3 racemic mixture of bis-adducts **6a** and **6b** led to the formation of four species (compare Figure 1b and 6b). Enantiomer **6a** was converted to two diastereomeric salts, **6a′** and **6a″**, and **6b** was converted to **6b′** and **6b″** (Scheme 3).

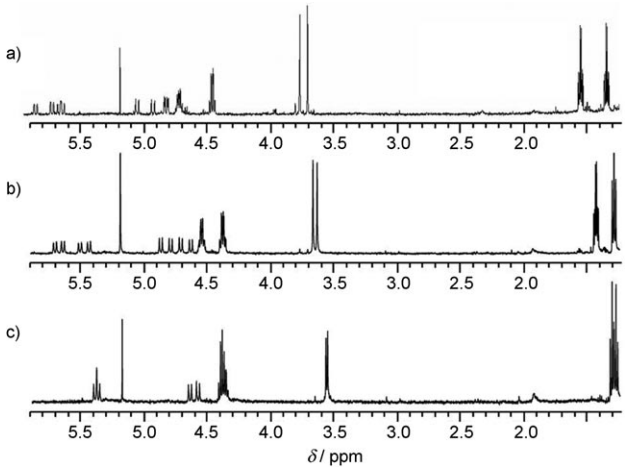
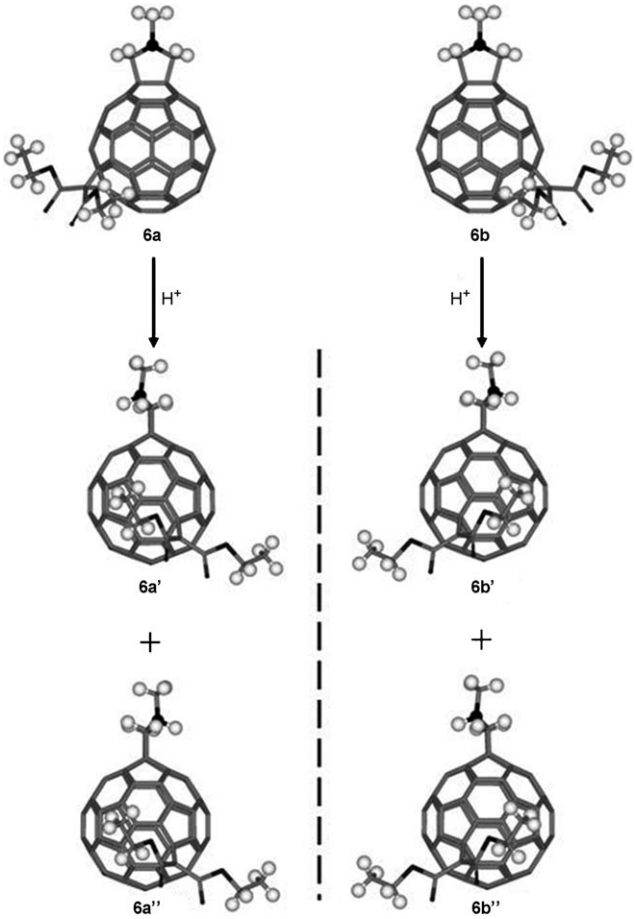



Figure 6. $^1$H NMR (500 MHz) of compounds a) **7a**/**7b**, b) **6a**/**6b**, c) **5** after addition of [D]TFA.

However, we could only detect two members of this diastereomeric mixture in the NMR spectrum since **6a′** and **6b′** are enantiomers and similarly so are **6a″** and **6b′**. Figures 6b,c and 7 clearly showed the four AX quartets of the four methylene protons of the pyrrolidine ring in compounds **5** and **6a**/**b**. A careful examination established that the ratio of the chemical shift to the coupling constant, $\Delta\nu/J$, was greater than 10.[14] Similar results were obtained for *trans*-2 isomers **7a** and **7b** (compare Figure 1a and 6a). Close inspection of the NMR spectra of the bis-adducts revealed a deshielding effect in both the non-protonated (Figure 1) and protonated (Figure 6) bis-mixed adducts which was directly related to the distance between the addends. The closer the addends were, the less the deshielding effect. Thus, the resonances were more deshielded for **7a**




Scheme 3. Expected isomers upon protonation of compounds **6a**/**6b**.

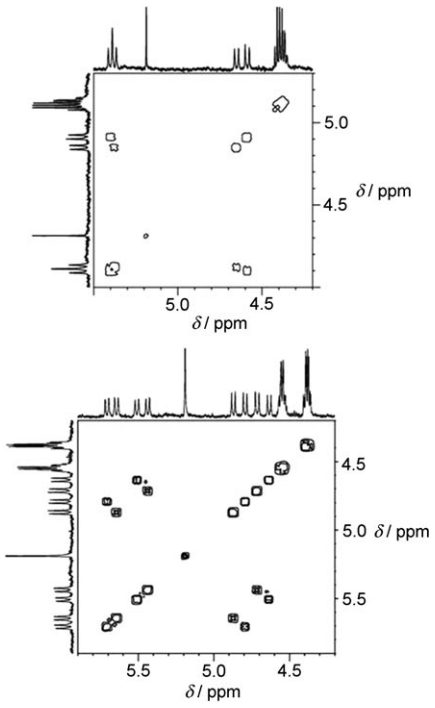



Figure 7. COSY NMR of **5** (top) and **6a**/**6b** (bottom) after addition of [D]TFA.

and **7b** than for **6a** and **6b**, which in turn were more deshielded than for **5**. On the other hand, the chemical shifts of the malonate groups were only slightly altered since they are farther away from the protonation site (compare Figure 1 and 6).

Two-dimensional NMR experiments were crucial in the characterization of the bis-adduct derivatives. The COSY of **5**, and of the **6a**/**6b** mixture, allowed us to determine the identity of the diastereomers since the geminal protons of the pyrrolidine rings ($H_a$ and $H_b$) are correlated only to each other (Figure 7).

Substitution of the *N*-methyl group for an *N*-ethyl did not alter the outcome. The $^1$H NMR spectra in $CDCl_3$ (see Supporting Information) of the two fractions isolated (Figure SII and SIII, Supporting Information), after the mixed bis-adduct were formed from *N*-ethyl pyrrolidino[60]fullerene instead of the *N*-methyl derivative, were very similar to those of fractions II and III (Figure 1b and c). In addition, the proton resonances of the methano addend were identical to those of the *N*-methyl substituted bis-adducts, and the pyrrolidine proton resonances were very broad as well.

As an alternative to "freezing" the conformers via protonation of the nitrogen, we conducted NMR experiments at very low temperatures to slow down the nitrogen inversion. With this aim, $^1$H NMR spectra of **4** were taken at various temperatures in [$D_8$]toluene. As shown in Figure 8, upon

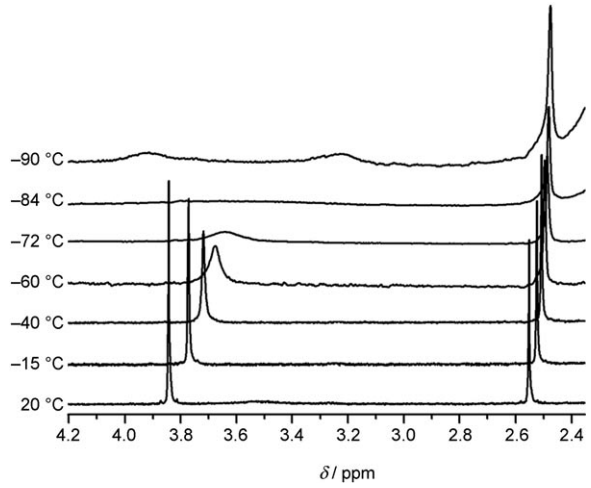



Figure 8. $^1$H NMR spectrum of **4** at various temperatures in [$D_8$]toluene.

lowering the temperature of the toluene solution, the resonance of the methylene protons, which showed a significant upfield shift, broadened and ultimately split into a doublet. These signals corresponded to the protons *cis* and *trans* with respect to the *N*-methyl group which in turn remained relatively sharp even at low temperatures. We employed the $^1$H NMR lineshape analysis of the methylene signals at variable temperatures to calculate the rate constants for the nitrogen inversion. Dynamic NMR simulations were performed with DNMR3 software, which is included in the SpinWorks package, and the rate constants were determined

(Table 1) by comparing experimental and theoretical spectra between −20 and −90 °C. From these data, an Eyring plot was used to calculate the enthalpy of activation, $\Delta H^{\neq} = 35.6 \pm 1.5\ kJ\,mol^{-1}$, and the entropy of activation, $\Delta S^{\neq} = -3.3 \pm 6.7\ J\,mol^{-1}\,K^{-1}$ (Figure 9). The entropy term is close to zero as expected for an intramolecular process like nitrogen inversion.[12] Interestingly, the enthalpy of activation for the nitrogen inversion of **4** is close to the enthalpy of activation of an unconstrained nitrogen inversion, such as in the five-membered cyclic molecule **2**.[12,13] Unlike compound **3**, where the presence of the π system makes the inversion much faster, there appears to be little or no conjugation of the nitrogen lone pair with the π system of the $C_{60}$ core in **4**, contrary to the conclusions derived from basicity arguments.[15]

Table 1. Rates of nitrogen inversion determined by Dynamic NMR simulations.

| $k_{ex}$ [$s^{-1}$] | $T$ [K] |
|---|---|
| 250 | 185 |
| 760 | 195 |
| 1100 | 199 |
| 3200 | 208 |
| 10000 | 220 |
| 11000 | 225 |
| 30500 | 230 |
| 40000 | 235 |
| 56500 | 245 |
| 110000 | 249 |
| 220000 | 253 |

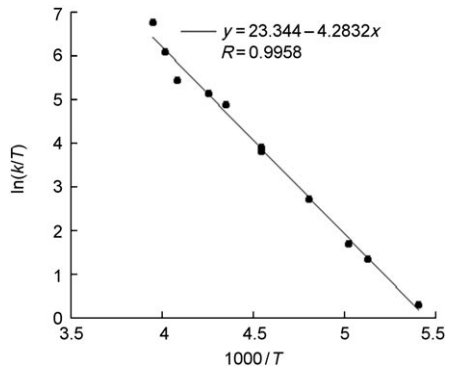



Figure 9. Eyring plot employed to calculate the enthalpy of activation and the entropy of activation for the pyrrolidine nitrogen inversion process.

## Conclusion

Based on the broadening of the $^1$H NMR resonances, we have shown that the pyrrolidine group in pyrrolidinofullerenes can exhibit a much slower inversion of configuration than expected depending on the solvent media. Employing $^1$H NMR as a characterization technique may prove ineffective if the signals are too broad to be noticeable. A drop of [D]TFA can be added to the NMR tube to "freeze" the nitrogen inversion, resulting in sharper peaks with clearly identifiable correlation patterns. TFA can be later easily removed by simple evaporation.

Though a vast amount of pyrrolidinofullerenes have been prepared to date, no detailed investigation of the effect of the media on the NMR characterization had been performed until now. It was assumed that the methylene protons of symmetric pyrrolidine rings in pyrrolidinofullerenes are magnetically equivalent, but we have demonstrated that they are equivalent *only* if their NMR spectra are taken in deuterated solvents with traces of water. We recommend the use of [D]TFA as a standard technique to characterize the structures of pyrrolidinofullerenes in the future.

## Experimental Section

**General:** Commercially available materials were used as received unless otherwise specified. $^1$H spectra were recorded in a Bruker 500 MHz and referenced to TMS or the solvent used, as noted. Compound **4** was synthesized according the literature procedures.[7]

**Compounds 5, 6, 7:** DBU (17 μL, 0.12 mmol) was added to a solution of **4** (50 mg, 0.06 mmol) and diethyl bromomalonate (10 μL, 0.06 mmol) in *o*-dichlorobenzene. After 5 min the reaction mixture was subjected to column chromatography (silica gel, $CH_2Cl_2$).

**Compound 5** was isolated in 9% yield (5.5 mg). The TLC analysis in $CH_2Cl_2$ indicated the retention factor of 0.3. $^1$H NMR (500 MHz, [$D_6$]acetone/$CS_2$): $\delta = 4.38$ (q, $^3J(H,H) = 20$ Hz, 4H), 4.22 (d, $^3J(H,H) = 15$ Hz, 2H), 4.13 (d, $^3J(H,H) = 15$ Hz, 2H), 2.88 (s, 3H), 1.43 ppm (t, $^3J(H,H) = 11$ Hz, 6H); $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 4.45$ (q, $^3J(H,H) = 20$ Hz, 4H), 2.42 (t, $^3J(H,H) = 11$ Hz, 6H); MALDI-TOF MS: $m/z$: 936 [$M^+$].

**Compound 6** was isolated in 18% yield (11 mg). The TLC analysis in $CH_2Cl_2$ indicated the retention factor of 0.45. $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 4.53$–$4.48$ (m, 2H), 4.39–4.33 (m, 2H), 1.47 (t, $^3J(H,H) = 6.5$ Hz, 3H), 1.32 (t, $^3J(H,H) = 6.5$ Hz, 3H); MALDI-TOF MS: $m/z$: 936 [$M^+$].

**Compound 7** was isolated in 2.4% yield (1.4 mg). The TLC analysis in $CH_2Cl_2$ indicated the retention factor of 0.49. $^1$H NMR (500 MHz, $CDCl_3$): $\delta = 4.82$–$4.76$ (m, 2H), 4.53 (q, $^3J(H,H) = 7$ Hz, 2H), 1.67 (t, $^3J(H,H) = 7.5$ Hz, 3H), 1.47 (t, $^3J(H,H) = 7.5$ Hz, 3H); MALDI-TOF MS: $m/z$: 936 [$M^+$].

## Acknowledgements

C.C. and L.E. gratefully acknowledge the National Science Foundation for the support (CHE-0509989 while L.E. is working at the Foundation). Any opinion, findings and conclusions or recommendations expressed in this material are those of the authors and do not necessarily reflect the views of the NSF.

[1] A. Hirsch, *The Chemistry of the Fullerenes*, Thieme, Stuttgart, **1994**.
[2] A. Hirsch, *Top. Curr. Chem.* **1999**, *199*, 1.
[3] Y. Nakamura, K. O-kawa, J. Nishimura, *Bull. Chem. Soc. Jpn.* **2003**, *76*, 865.
[4] S. Bosi, T. Da Ros, G. Spalluto, J. Balzarini, M. Prato, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4437.
[5] S. Bosi, T. Da Ros, G. Spalluto, M. Prato, *Eur. J. Med. Chem.* **2003**, *38*, 913.

[6] N. Martin, *Chem. Commun.* **2006**, 2093.
[7] M. Maggini, G. Scorrano, M. Prato, *J. Am. Chem. Soc.* **1993**, *115*, 9798.
[8] M. Prato, M. Maggini, *Acc. Chem. Res.* **1998**, *31*, 519.
[9] O. Lukoyanova, C. M. Cardona, M. Altable, S. Filippone, A. M. Domenech, N. Martín, L. Echegoyen, *Angew. Chem.* **2006**, *118*, 7590; *Angew. Chem. Int. Ed.* **2006**, *45*, 7430.
[10] N. Martín, M. Altable, S. Filippone, A. Martín-Domenech, L. Echegoyen, C. M. Cardona, *Angew. Chem.* **2006**, *118*, 116; *Angew. Chem. Int. Ed.* **2006**, *45*, 110.
[11] C. H. Bushweller, S. H. Fleischman, G. L. Grady, P. McGoff, C. D. Rithner, M. R. Whalon, J. G. Brennan, R. P. Marcantonio, R. P. Domingue, *J. Am. Chem. Soc.* **1982**, *104*, 6224.
[12] J. M. Lehn, J. Wagner, *Tetrahedron* **1970**, *26*, 4227.
[13] J. B. Lambert, W. L. J. Oliver, *J. Am. Chem. Soc.* **1969**, *91*, 7774.
[14] H. Günther, NMR Spectroscopy: Basic Principles, Concepts, and Applications in Chemistry, 2nd ed., Wiley, New York, **1995**.
[15] A. Bagno, S. Claeson, M. Maggini, M. L. Martini, M. Prato, G. Scorrano, *Chem. Eur. J.* **2002**, *8*, 1015.
[16] T. Cai, C. Slebodnick, L. Xu, K. Harich, T. E. Glass, C. Chancellor, J. C. Fettinger, M. M. Olmstead, A. L. Balch, H. W. Gibson, H. C. Dorn, *J. Am. Chem. Soc.* **2006**, *128*, 6486.
[17] F. Djojo, A. Herzog, I. Lamparth, F. Hampel, A. Hirsch, *Chem. Eur. J.* **1996**, *2*, 1537.
[18] A. Hirsch, I. Lamparth, H. R. Karfunkel, *Angew. Chem.* **1994**, *106*, 453; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 437.
[19] Q. Lu, D. I. Schuster, S. R. Wilson, *J. Org. Chem.* **1996**, *61*, 4764.
[20] K. Kordatos, S. Bosi, T. Da Ros, A. Zambon, V. Lucchini, M. Prato, *J. Org. Chem.* **2001**, *66*, 2802.
[21] B. Gross, V. Schurig, I. Lamparth, A. Herzog, F. Djojo, A. Hirsch, *Chem. Commun.* **1997**, 1117.
[22] F. Djojo, A. Hirsch, *Chem. Eur. J.* **1998**, *4*, 344.
[23] Y. Nakamura, K. O-kawa, T. Nishimura, E. Yashima, J. Nishimura, *J. Org. Chem.* **2003**, *68*, 3251.
[24] T. Nishimura, K. Tsuchiya, S. Ohsawa, K. Maeda, E. Yashima, Y. Nakamura, J. Nishimura, *J. Am. Chem. Soc.* **2004**, *126*, 11711.
[25] R. Kessinger, N. S. Fender, L. E. Echegoyen, C. Thilgen, L. Echegoyen, F. Diederich, *Chem. Eur. J.* **2000**, *6*, 2184.
[26] S. Bosi, L. Feruglio, D. Milic, M. Prato, *Eur. J. Org. Chem.* **2003**, 4741.
[27] F. Diederich, R. Kessinger, *Acc. Chem. Res.* **1999**, *32*, 537.

Received: April 16, 2007
Published online: July 20, 2007