Isolation and Characterization of All Eight Bisadducts of Fulleropyrrolidine Derivatives

Konstantinos Kordatos,[†] Susanna Bosi,[†] Tatiana Da Ros,[†] Alfonso Zambon,[‡] Vittorio Lucchini,[‡] and Maurizio Prato*[,†]

[†]*Dipartimento di Scienze Farmaceutiche, Università di Trieste, Piazzale Europa 1, 34127 Trieste, Italy, and* [‡]*Dipartimento di Scienze Ambientali, Università di Venezia, Dorsoduro 2137, 30133 Venezia, Italy*

prato@univ.trieste.it

Received December 5, 2000

We report the isolation and characterization of bisadducts of fulleropyrrolidine derivatives. The compounds were characterized by means of a variety of spectroscopic techniques, including ES-MS, UV−vis, ^{1}H NMR, and ^{13}C NMR. The whole series of bisadducts was separated for the first time in the case of the bispyrrolidines, and the determination of their structure was obtained by NMR spectroscopy with the help of HMQC and HMBC techniques.

Introduction

Many research groups have systematically investigated the chemical reactivity of fullerenes over the past decade, thus providing us with a solid background toward the design and synthesis of novel and sophisticated architectures.[1] Most of the studies have been limited to monoadditions, mainly because of the great difficulty in obtaining pure isolated multiple addition products, which requires time-consuming intensive HPLC separations. This can be understood easily if one takes into account that in the cases of bisaddition, trisaddition, and tetrakisaddition of a symmetrical addend, there are 8, 46, and 262 possible regioisomers, respectively.[2]

However, different approaches have been developed for synthesizing very complex multiple adducts with perfect control of fullerene stereochemistry. Probably, the most effective means for controlling multiple additions is the tether-directed remote multifunctionalization methodology,[3] which is based on a combination of cyclopropanation and Diels−Alder addition reactions.[4] By controlling the length and geometry of the tether, either *equatorial*,[3] or *cis-2*,[4] or even *trans-2*[5] and *trans-1*[6,7] structures could be almost exclusively obtained. Other attempts to tether-control bisadditions have given alternate fortunes.[8−13]

On the other hand, the systematic investigation of stepwise multiple additions of osmium tetraoxide,[14] bromomalonates,[15] and/or nitrenes[16] to C_{60} has shed light on this complicated subject. All *equatorial* multiple adducts, as well as more complicated structures such as chiral trisadducts,[15,17] and T_h-symmetric hexakisadducts,[18] could be synthesized. These studies have shown that, for sterically demanding addends (methano bridge), there is a marked preference for the second attack to occur in *equatorial* or *trans-3* positions, while in the case of sterically less demanding addends (imino bridge), *cis-1* is also favored. This experimental result was confirmed by theoretical computations.[18a] Thus, the use of sterically less demanding addends led for the first time to the successful isolation and characterization of the complete series of nine $C_{61}(COOEt)_2(NCOOEt)$ and eight $C_{60}(NCOOEt)_2$ regioisomeric bisadducts.[16,19]

Smart approaches to obtain specific addition patterns, not otherwise easily accessible, have also been developed, which include (1) the synthesis of *trans-1*,[20] through solid-state topochemically controlled intermolecular anthracene-

[†] Università di Trieste.
[‡] Università di Venezia.

(1) (a) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157−161. (b) Hirsch, A. *The Chemistry of the Fullerenes*; Thieme: Stuttgart, 1994. (c) Hirsch, A. Fullerenes and Related Structures. In *Topics in Current Chemistry*; Springer: Berlin, 1999; Vol. 199. (d) Diederich, F.; Thilgen, C. *Science* **1996**, *271*, 317−323. (e) Prato, M. *J. Mater. Chem.* **1997**, *7*, 1097−1109. (f) Wilson, S. R.; Schuster, D. I.; Nuber, B.; Meier, M. S.; Maggini, M.; Prato, M.; Taylor, R. *Fullerene, Chemistry, Physics and Technology*; John Wiley & Sons Inc., New York, 2000; pp 91−176.
(2) Fowler, P. W. *J. Chem. Soc., Faraday Trans.* **1995**, *91*, 2241−2247.
(3) Isaacs, L.; Haldimann, R. F.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2339−2342.
(4) Diederich, F.; Kessinger, R. *Acc. Chem. Res.* **1999**, *32*, 537−545.
(5) Dietel, E.; Hirsch, A.; Eichhom, E.; Rieker, A.; Hackbarth, S.; Röder, B. *Chem. Commun.* **1998**, 1981−1982.
(6) Bourgeois, J.-P.; Echegoyen, L.; Fibbioli, M.; Pretsch, E.; Diederich, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2118−2121.
(7) Qian, W.; Rubin, Y. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2356−2360.
(8) Da Ros, T.; Prato, M.; Lucchini, V. *J. Org. Chem.* **2000**, *65*, 4289−4297.
(9) Nakamura, E.; Isobe, H.; Tokuyama, H.; Sawamura, M. *Chem. Commun.* **1996**, 1747−1748.
(10) Isobe, H.; Tokuyama, H.; Sawamura, M.; Nakamura, E. *J. Org. Chem.* **1997**, *62*, 5034−5041.
(11) Ishi-i, T.; Nakashima, K.; Shinkai, S. *Chem. Commun.* **1998**, 1047−1048.
(12) (a) Taki, M.; Sugita, S.; Nakamura, Y.; Kasashima, E.; Yashima, E.; Okamoto, Y.; Nishimura, J. *J. Am. Chem. Soc.* **1997**, *119*, 926−932. (b) For a recent contribution of this group on the isolation of bisadducts derived from addition of *o*-quinodimethane to C_{60}, see: Nakamura, Y.; O−Kawa, K.; Matsumoto, M.; Nishimara, J. *Tetrahedron* **2000**, *56*, 5429−5434.
(13) Kanakamma, P. P.; Huang, S.-L.; Juo, C.-G.; Her, G.-R.; Luh, T.-Y. *Chem. Eur. J.* **1998**, *4*, 2037−2042.
(14) Hawkins, J. M.; Meyer, A.; Lewis, T. A.; Bunz, U.; Nunlist, R.; Ball, G. E.; Ebbesen, T. W.; Tanigaki, K. *J. Am. Chem. Soc.* **1992**, *114*, 7954−7955.
(15) Hirsch, A.; Lamparth, I.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 437−438.
(16) Schick, G.; Hirsch, A.; Mauser, H.; Clark, T. *Chem. Eur. J.* **1996**, *2*, 935−943.
(17) (a) Djojo, F.; Hirsch, A. *Chem. Eur. J.* **1998**, *4*, 344−356. (b) Djojo, F.; Hirsch, A.; Grimme, S. *Eur. J. Org. Chem.* **1999**, 3027−3039.
(18) (a) Hirsch, A.; Lamparth, I.; Grösser, T.; Karfunkel, H. R. *J. Am. Chem. Soc.* **1994**, *116*, 9385−9386. (b) Lamparth, I.; Maichle-Mössmer, C.; Hirsch, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1607−1609.
(19) Djojo, F.; Herzog, A.; Lamparth, I.; Hampel, F.; Hirsch, A. *Chem. Eur. J.* **1996**, *2*, 1537−1547.

10.1021/jo001708z CCC: $20.00
Published on Web 03/21/2001

transfer reaction; (2) all *equatorial* tetrakisadducts, via selective tether removal;[21] and (3) all *equatorial* hexakisadducts by means of reversible template addition.[18b]

Recently, the utilization of a stepwise "mer 3 + 3" cyclopropanation to C_{60} has led to the successful synthesis of a complete series of C_{60} hexakisadducts,[7,22] all having three pairs of addends (2 + 2 + 2 patterns) with topologies similar to those of the octahedral transition metal complexes.

Most of the work on multiple additions, however, has been performed on cyclopropanation reactions. No such extensive work has been carried out for larger ring size adducts, even though the 1,3-dipolar cycloaddition of azomethine ylide to C_{60} is one of the most widely used functionalization of fullerenes.[23,24] Reports on the characterization of the *N*-methyl bispyrrolidine series have appeared: Wilson and Schuster, in fact, were the first to undertake such a difficult task.[25] However, since then, our knowledge on the chemistry of fullerenes has strongly increased. Some of the structural characterization reported in ref 25 have necessitated reassignment.[26] Since fulleropyrrolidines are increasingly used and have different electronic properties from cyclopropano- and aziridino-fused systems, we deemed important to provide a complete and unequivocal characterization of the bispyrrolidine series.

Here, we report for the first time the isolation and full characterization of the whole series of the pyrrolidine bisadducts (*trans-1*, *trans-2*, *trans-3*, *trans-4*, *equatorial*, *cis-3*, *cis-2*, and *cis-1*, in order of distance between addends, following Hirsch nomenclature,[15] see Figure 1). Five of these patterns have been at least partly characterized in the past.[25−27] We confirm here the structure of these five isomers, and in addition we report for the first time the successful isolation of the *cis-3*, *cis-2*, and *cis-1* isomers, never observed before.

Results and Discussion

mTEG amino acid, **1**, was synthesized according to previous work (mTEG = triethylene glycol mono methyl ether, $CH_2CH_2OCH_2CH_2OCH_2CH_2OCH_3$, Scheme 1).[28] The mTEG group was chosen and introduced in order to increase the solubility of the resulting fulleropyrrolidine derivatives. This led to higher solubility of the obtained materials, when compared with that of the *N*-methyl derivatives, in common organic solvents and therefore it made easier to use them as the basis for the preparation of Langmuir−Blodgett monolayer films.[29] Their increased solubility was also essential for biological studies.[28]

The mTEG fulleropyrrolidine bisadducts were synthesized by reaction of 2 equiv of mTEG amino acid, 1 equiv of C_{60}, and 10 equiv of paraformaldehyde in refluxing toluene (Scheme 1), while the reaction was followed by HPLC equipped with a diode array detector, which allows UV−visible spectra comparisons. It was noticed that, if the reaction is carried out for a long period of time, then a large amount of trisadducts was formed (checked by

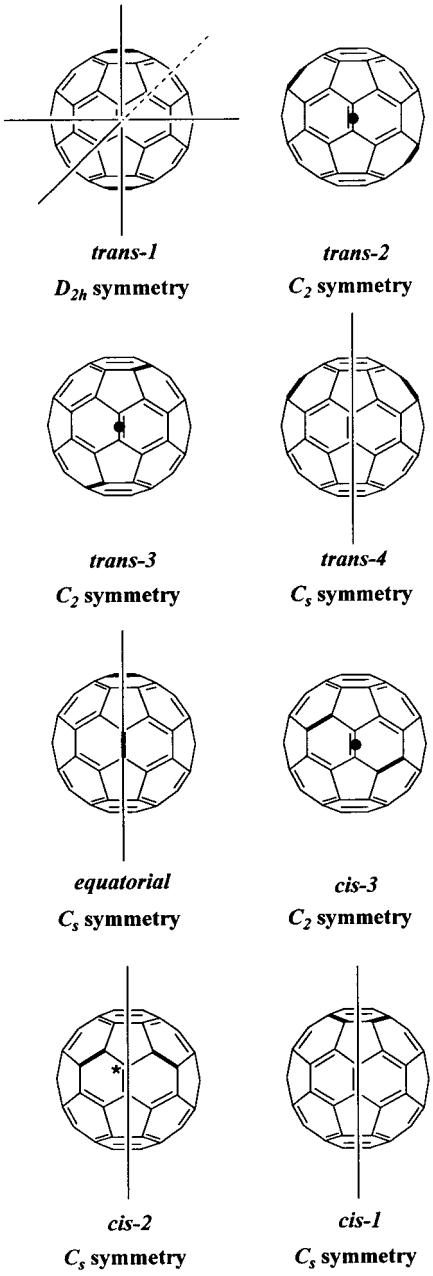


Figure 1. Addition patterns and symmetries of the eight possible bisadducts for a symmetrical addend. The starred carbon in *cis-2* corresponds to the only sp^2 carbon vicinal to the pyrrolidine rings with intensity 1 (see text).

(20) Kräutler, B.; Müller, T.; Maynollo, J.; Gruber, K.; Kratky, C.; Ochsenbein, P.; Schwartzenbach, D.; Bürgi, H.-B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1204−1206.

(21) Cardullo, F.; Isaacs, L.; Diederich, F.; Gisselbrecht, J.-P.; Boudon, C.; Gross, M. *Chem. Commun.* **1996**, 797−799.

(22) (a) Qian, W.; Rubin, Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 3133−3137. (b) Qian, W.; Rubin, Y. *J. Am. Chem. Soc.* **2000**, *122*, 9564−9565.

(23) (a) Maggini, M.; Scorrano, G.; Prato, M. *J. Am. Chem. Soc.* **1993**, *115*, 9798−9799. (b) Prato, M.; Maggini, M. *Acc. Chem. Res.* **1998**, *31*, 519−526.

(24) Hexakisadducts of fulleropyrrolidines with two different addition patterns and unique photophysical properties have been prepared: (a) Schick, G. L., M.; Kvetko, L.; Johnson, B. A.; Lamparth, I.; Lunkwitz, R.; Ma, B.; Khan, S. I.; Garcia-Garibay, M. A.; Rubin, Y. *J. Am. Chem. Soc.* **1999**, *121*, 3246−3247. (b) Hutchison, K.; Gao, J.; Rubin, Y.; Wudl, F. *J. Am. Chem. Soc.* **1999**, *121*, 5611−5612.

(25) Lu, Q.; Schuster, D. I.; Wilson, S. R. *J. Org. Chem.* **1996**, *61*, 4764−4768.

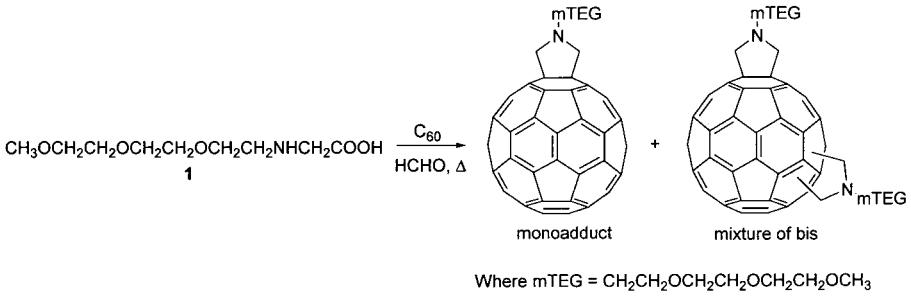
(26) Pasimeni, L.; Hirsch, A.; Lamparth, I.; Herzog, A.; Maggini, M.; Prato, M.; Corvaja, C.; Scorrano, G. *J. Am. Chem. Soc.* **1997**, *119*, 12896−12901.

(27) For the isolation and characterization of five bisadducts of tetramethyl fulleropyrrolidines, see ref 24a.

(28) Da Ros, T.; Prato, M.; Novello, F.; Maggini, M.; Banfi, E. *J. Org. Chem.* **1996**, *61*, 9070−9072.

(29) Wang, P.; Chen, B.; Metzger, R. M.; Da Ros, T.; Prato, M. *J. Mater. Chem.* **1997**, *7*, 2397−2400.

Scheme 1



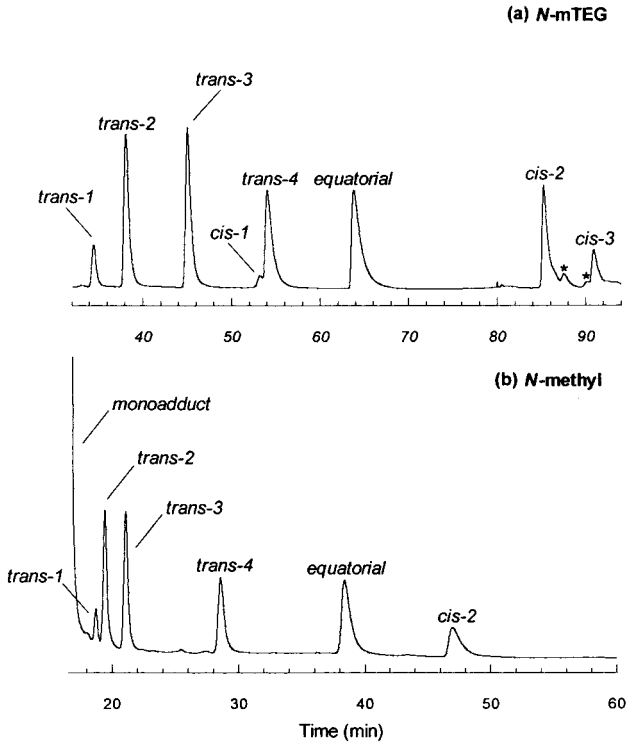


Figure 2. HPLC chromatograms of the reaction mixtures of the bisaddition of (a) *N*-mTEG fulleropyrrolidine and (b) *N*-methyl fulleropyrrolidine. The asterisks in (a) correspond to trisadducts (detected by ES-MS).

ES-MS). Therefore, to be able to isolate reasonable amounts of bisadducts without interference from trisadducts, the reaction was stopped after 30 min, when the ratio of C_{60}/monoadduct was about 0.75 as estimated by the integration of their HPLC traces. The bisadducts were purified by medium-pressure column chromatography and further purified by semipreparative HPLC. Figure 2a shows a representative chromatogram of the reaction mixture. In analogy to other bisadducts,[15] their order of elution time depends on their polarity, and thus in the case of *N*-mTEG, the less polar *trans-1* (**1a**) is eluted first and followed by *trans-2* (**1b**), *trans-3* (**1c**), *trans-4* (**1d**), and *equatorial* (**1e**). There is a deviation in this behavior for the *cis-1* (**1f**), *cis-2* (**1g**), and *cis-3* (**1h**) bisadducts, where it is observed that the more polar *cis-1* is eluted before *trans-4*, and the *cis-2* isomer is eluted before *cis-3*. However, similar observations have been also reported by Hirsch and co-workers,[19] for other series. The reaction was also followed for the case of *N*-methyl derivatives (**2a**−**f**), and the corresponding chromatogram is reported in Figure 2b. The structure of the bisadducts of this series was clearly deduced from comparisons of the corresponding visible spectra. Thus, in the case of *N*-methyl bisadducts, *cis-2* was observed for the first time in analogy with *N*-mTEG, whereas *cis-3* and *cis-1* were not observed. The chromatogram was scanned with the help of the diode array detector, but the patterns observed for *cis-3* and *cis-1* in the *N*-mTEG case could not be seen. The reason for this unexpected result is not clear. If the reaction is let go longer, then too many trisadducts start to appear, making the mixture very complex and the HPLC analysis difficult.

All the *N*-mTEG fulleropyrrolidine bisadducts, **1a**−**h**, were isolated and fully characterized by ES-MS, UV−vis, ^{1}H and ^{13}C NMR. The ES-MS corroborated that all eight molecules are *N*-mTEG fulleropyrrolidine bisadducts ($MH^+ = 1099$). The compounds showed distinct absorption patterns in the visible region of the UV−vis spectrum (Figure 3). The ^{1}H and ^{13}C NMR spectra of **1a**−**h** were analyzed based on symmetry considerations. The various NMR techniques, which were employed in the present work, such as ^{1}H and ^{13}C NMR, and HMQC and HMBC heteronuclear correlation spectroscopies, could be used to assign safely the structure of five out of the eight isolated bisadducts.

The number and intensity of the ^{13}C signals of the residual sp^2 fullerene carbons in the eight potential bisadduct isomers are reported in Table 1. Four groups of symmetry are defined, each of which gives rise to a well-defined number of resonances in the ^{1}H and ^{13}C NMR spectra. On these bases, eluate **1a**, which displays in its ^{13}C NMR spectrum eight signals between $\delta = 136-154$ ppm, with six of them integrating for eight sp^2 carbon atoms and the remaining two integrating for four, could be assigned the *trans-1* structure. Its ^{1}H NMR spectrum shows one singlet at $\delta = 4.76$ ppm for the eight methylene protons of the two pyrrolidine rings and one singlet at $\delta = 3.38$ ppm for the six methoxy protons, consistent with the D_{2h} symmetry of the *trans-1* isomer. This corresponds to isomer **2a** in ref 25, also attributed to *trans-1*. The ^{13}C NMR spectrum of **1e** is consistent with the C_s symmetry of an *equatorial* structure and shows 29 signals between $\delta = 135-160$ ppm, 27 of which integrate for two carbon atoms and two integrate for one carbon. This isomer is also characterized by the nonequivalence of the two pyrrolidine moieties, as clearly seen by the anisochronicity of the ^{1}H NMR signals of the mTEG moiety. Its ^{1}H NMR spectrum shows two singlets at $\delta = 4.14$ and 3.98 ppm for the two methylene groups of the pyrrolidine rings and an AB quartet for the remaining two CH_2 groups of the pyrrolidine rings along with two singlets at $\delta = 3.39$ and 3.55 ppm for the two methoxy groups, respectively. The visible spectrum of this isomer (Figure 3) is reminiscent of that of **2f** in ref 25 erroneously attributed to a *cis-3* structure.

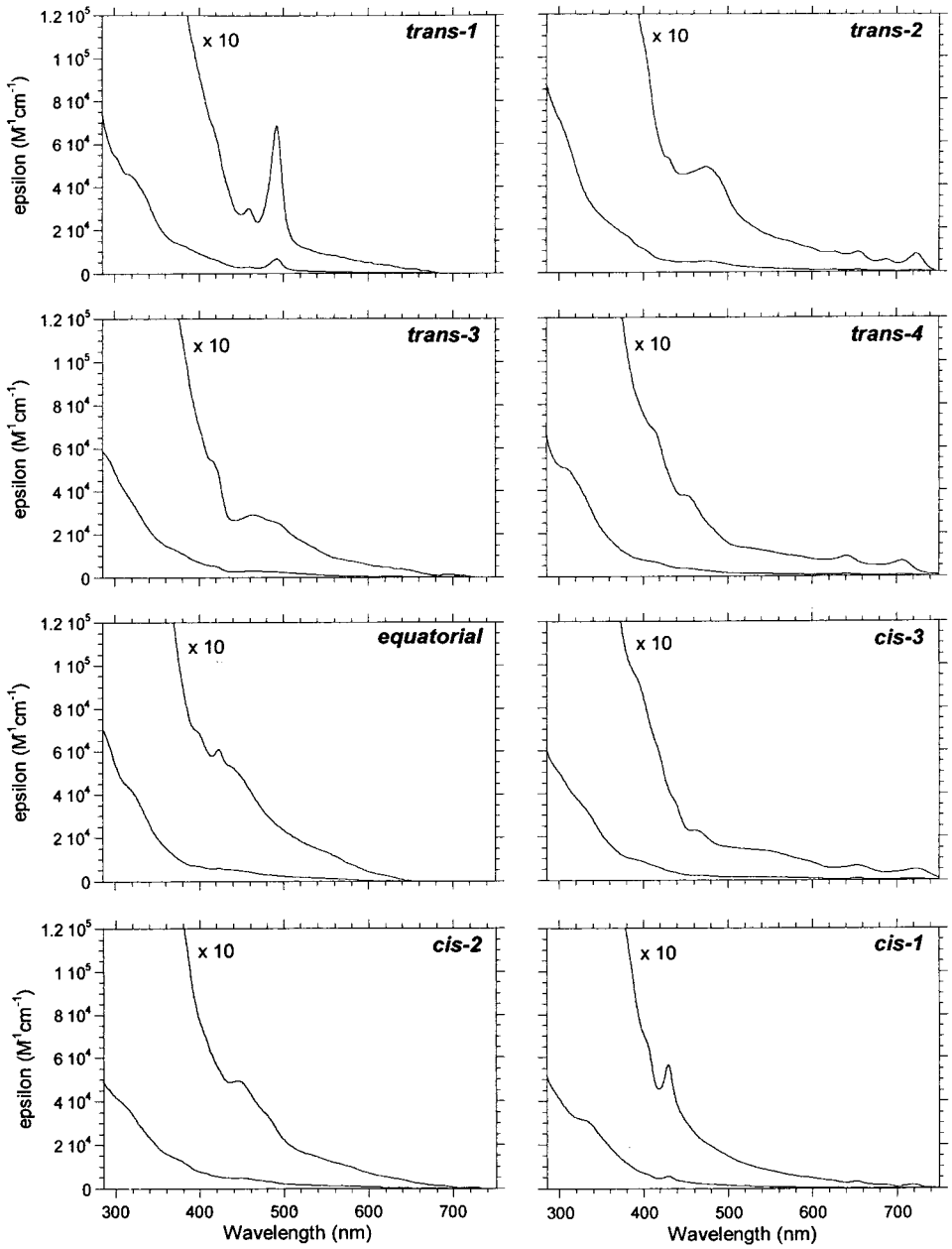


Figure 3. UV−vis spectra of the eight isomers of bis-*N*-mTEG fulleropyrrolidine in toluene (2×10^{-5} M).

Table 1. Symmetry Groups with Number and Intensities (in parentheses) of the ^{13}C Fullerene sp^2 Signals of the 8 Possible Bisadducts

group	names	symmetry	number (intensity)
1	*trans-1*	D_{2h}	6(8) + 2(4)
2	*trans-2*		
	trans-3	C_2	28(2)
	cis-3		
3	*trans-4*		
	cis-1	C_s	26(2) + 4(1)
	cis-2		
4	*equatorial*	C_s	27(2) + 2(1)

Further assignments are possible from the detection of the $^3J_{CH}$ couplings between the pyrrolidine methylene ring protons and the vicinal sp^2 or sp^3 fullerene carbons.

In the set of the three structures in group 3 (Table 1), all with C_s symmetry, the pyrrolidine protons are coupled as follows: first of all in the structure of *trans-4*, the pyrrolidine protons should couple with four sp^2 carbon atoms with intensity 2; in *cis-1*, the protons of the pyrrolidine ring should couple with three sp^2 and one sp^3 carbon atom, all having intensity 2. However, it is difficult to unambiguously detect the coupling with the vicinal sp^3 carbon, as the cross signal may be also attributed to a coupling with the isochronous geminal sp^3 carbon; finally, in the *cis-2* structure, we should observe the coupling of the pyrrolidine protons with three sp^2 carbon atoms with intensity 2 and one sp^2 carbon atom with intensity 1 (see in Figure 1 the starred fullerene carbon with intensity 1).

The **1d**, **1f**, and **1g** eluates are the only bisadducts that exhibit 26(2) + 4(1) sp^2 ^{13}C signals in their ^{13}C NMR spectra and therefore correspond to group 3 (Table 1). In the HMBC spectrum of eluate **1d** one can detect the $^3J_{CH}$ coupling of the high field AB system of one pyrrolidine methylene with the ^{13}C resonances at δ 151.55 and 154.85, with intensity 2, and of the low field AB system of the other methylene with the resonances at δ 150.90 and 152.79, again with intensity 2. The former resonance

is very close to a resonance at δ 150.85, with intensity 1; only a very high resolution along the ^{13}C direction allows the correct assignment of the corresponding cross-peaks. It is therefore safe to attribute to this eluate the structure *trans-4*. The visible spectrum of this isomer (Figure 3) does not seem to correspond to that of **2e** in ref 25, attributed also to *trans-4*.

In the HMBC spectrum of eluate **1f** only three vicinal correlations are detected between the pyrrolidine protons and the sp^2 fullerene carbons: that of an AB system of one pyrrolidine methylene with the ^{13}C resonances at δ 151.26 and 152.21, both with intensity 2, and that of the other methylene AB system with only one sp^2 resonance at δ 150.58, with intensity 2. The forth-vicinal correlation is with a sp^3 resonance at δ 65.97, with intensity 2, which as already stated, can also be attributed to a geminal coupling. However, the lack of a detectable forth correlation with a sp^2 fullerene carbon unambiguously leads to the *cis-1* structure, never seen before in this series.

The HMBC spectrum of the eluate **1g** shows the correlation of one of the pyrrolidine methylene protons with the ^{13}C resonances at δ 156.51 and 158.67, both with intensity 2, while the other methylene protons couple with a ^{13}C resonance at δ 147.84, with intensity 2, and with a resonance at δ 147.66, with an unmistakable intensity 1. The structure of eluate **1f** is therefore *cis-2*, also never observed before for this series of bisadducts.

The attribution of the structures of the remaining eluates, **1b**, **1c**, and **1h**, all with 28(2) ^{13}C sp^2 resonances, to the structures of group 2 (Table 1) cannot be deduced from similar considerations, as in all cases the correlations of the pyrrolidine methylene protons with the vicinal sp^2 carbons correspond to ^{13}C resonances with intensity 2. This fact has been indeed verified on the corresponding HMQC spectra. The identified sp^2 ^{13}C resonances are given in the Experimental Section.

The assignment of *trans-2* and *trans-3* structures to the compounds **1b** and **1c**, respectively, rely then on their elution time (different polarity) in the HPLC chromatography. In addition, evidence for *trans-2* and *trans-3* structures were also previously obtained from transient EPR spectroscopy studies.[26] These two isomers correspond to **2b** and **2c** in ref 25, already assigned correctly to *trans-2* and *trans-3*, respectively.

As for the last eluate **1h**, besides symmetry considerations and NMR data, its structure could be corroborated by visible spectrum comparison with the *cis-3* structures reported by Taki et al.[12a] and Da Ros et al.[8] for two different intramolecular bisadducts, which exhibited very short tether lengths, something that precludes any possibility for either a *trans-2* or *trans-3* structure. From this comparison we can easily assign the *cis-3* structure to the compound **1h** due to its identical visible pattern. In addition to that, *cis-1* and *cis-2* bisadducts **1f** and **1g** (Figure 3) have visible spectra identical to those observed for *cis-1* and *cis-2* addition patterns by Hirsch et al.,[16,19] Da Ros et al.,[8] and Taki et al.[12a]

Finally, for obtaining a reasonable estimate of the relative yield of all bisadducts, we have measured the experimental absorption coefficients in toluene. Figure 4 shows the histogram of the relative yields of the *N*-mTEG and *N*-methyl bisadditions obtained by the integration of their HPLC traces and using the corresponding absorption coefficients of **1a**−**h** and **2a**−**f** at 320 nm. From the histogram it is clear that the bisaddition of azomethine ylides to C_{60} is much less selective compared to bisadditions of bromomalonates, as already noticed by Wilson and Schuster,[25] giving rise to five isomers with similar yields. This is probably due to the extremely high reactivity and addition inversibility of azomethine ylides as compared to malonate nucleophiles.

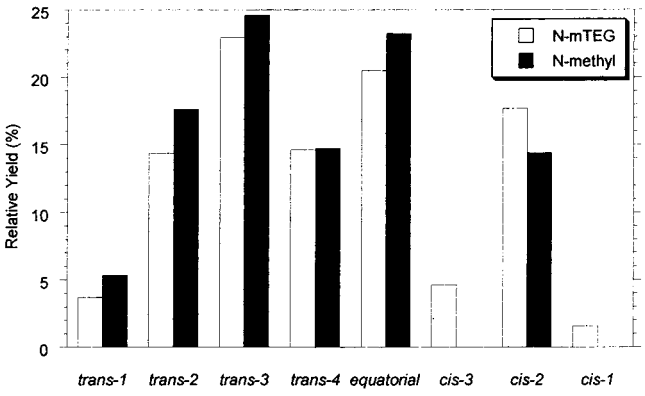


Figure 4. Relative yields of bisadducts in *N*-mTEG and *N*-methyl bisadditions obtained by integration of their HPLC traces and using the corresponding absorption coefficients of **1a**−**h** at 320 nm. The absorption coefficients used are as follows ($M^{-1}cm^{-1}$): *trans-1*: 45,980; *trans-2*: 50,400; *trans-3*: 35,930; *trans-4*: 45,420; *equatorial*: 42,270; *cis-3*: 38,850; *cis-2*: 34,390; *cis-1*: 32,590.

Conclusions

A complete series of isomeric bisadducts has been isolated and fully characterized for the bisaddition of azomethine ylides to C_{60}. For the first time, we were able to fully characterize the three missing bisadducts of this family, *cis-1*, *cis-2*, and *cis-3*, in addition to the five previously observed isomers (*trans-1*, *trans-2*, *trans-3*, *trans-4*, and *equatorial*). The addition patterns of the bisadducts have been assigned based on symmetry considerations and corroborated by analysis of their NMR spectra. The use of HMBC heteronuclear correlation spectroscopy was essential for the structural determination of the new isomers **1f** and **1g** as *cis-1* and *cis-2* by taking advantage of the correlation of the $^3J_{CH}$ couplings between the pyrrolidine ring protons and the vicinal sp^2 fullerene carbons. In addition to that, the work of Taki et al.,[12a] on the intramolecular *cis-3* bisadduct was very helpful for the determination of the structure of **1h** as *cis-3*. Since the UV−vis spectra of *cis-2*, *cis-3*, and *equatorial* isomers are identical to those obtained by the Japanese group on the *cis-2*, *cis-3*, and *equatorial* cyclohexano-bisadducts; and the UV−vis spectrum of a *trans-4* cyclohexano-bisadduct reported by Shinkai and co-workers,[11] exhibits λ_{max} similar to our *trans-4* **1d** isomer, we would suggest that the UV−vis spectra of the bispyrrolidine series reported in Figure 3 can be used as references for future assignments on five- and six-membered ring bisadditions.

Experimental Section

NMR. The spectra have been obtained using a Varian Unity 400 NMR spectrometer at 400 and 100 MHz for ^1H and ^{13}C NMR, respectively, in $CDCl_3$ solutions. The heterocorrelated reverse-mode HMQC[30,31] and HMBC[31,32] (multiple bonds HMQC) spectra have been acquired from a total of 256 (HMQC) or 1024 (HMBC) t_1 measurements in the phase sensitive acquisition mode, with 16 (HMQC) or 32 (HMBC) scans for t_1 value. The delay for the BIRD filter is matched to the average $^1J_{CH}$ =

140 Hz. The fixed delay for the detection of multiple bond correlations is tuned to $^nJ_{CH} = 5$ Hz. The elevated number of t_1 measurements in the HMBC experiments was mandatory in order to achieve the necessary resolution along the ^{13}C dimension. The resolution was further enhanced by zero filling (to 4096) and digitally filtered by shifted Gaussian functions.

Materials and Methods. C_{60} was purchased from Bucky USA (99.5%). All other compounds were used as purchased from Fluka and Aldrich. All solvents were distilled prior to use. Electrospray mass spectra were taken in THF/MeOH 1:1 solutions. UV−vis spectra were obtained in toluene.

Synthesis of Bis-*N*-methylfulleropyrrolidine Derivatives. The synthesis of the bisadducts has been already reported.[26]

Synthesis of Bis-*N*-mTEGfulleropyrrolidine Derivatives 1a−g. A solution of 1 g of C_{60} (1.38 mmol), 613 mg (2.77 mmol) of *N*-(3,6,9-trioxadecyl)glycine,[28] and 470 mg (13.87 mmol) of paraformaldehyde in 700 mL of toluene was heated to reflux for 30 min. The solution was concentrated under reduced pressure, and *N*-mTEGfulleropyrrolidine bisadducts were purified from unreacted C_{60} and *N*-mTEGfulleropyrrolidine monoadduct (396 mg, yield 31.37%) and higher adducts by medium pressure column chromatography on silica gel, eluting initially with toluene (separation of C_{60}) and then with a mixture of toluene−ethyl acetate, starting with 90:10 (separation of monoadduct and **1a**) followed by 80:20 (separation of **1b** and **1c**) and then 75:25 (separation of **1f**, **1d**, and **1e**) and finally 68:30 and 2% of 2-propanol (separation of **1g** and **1h**). All the bisadducts were further purified using a semipreparative HPLC Phenomenex silica column with eluent solvent, toluene−2-propanol 90:10.

The ^{13}C resonances are given with the relative intensities (under parentheses). The sp^2 (also sp^3 in the case of *cis-1*) fullerene carbons vicinal to the pyrrolidine protons are starred.

1a (*trans-1*): ^1H NMR δ (ppm): 4.76 (s, 8H, pyrrolidine), 4.15 and 3.49 (2 t, 8 H, $J = 5.4$ Hz, OCH_2CH_2N), 3.91 and 3.83 (2 m, 8 H, OCH_2CH_2O), 3.76 and 3.59 (2 m, 8 H, OCH_2CH_2O), 3.38 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 153.74 (*, 8 C), 147.68 (4 C), 146.21 (8 C), 145.43 (8 C), 144.25 (8 C), 142.31 (4 C), 140.72 (8 C), 136.47 (8 C), 72.06 (2 C), 70.82 (2 C), 70.74 (2 C), 70.71 (2 C), 70.67 (2 C), 68.72 (4 C), 68.64 (4 C), 59.13 (2 C), 54.31 (2 C). UV−vis: λ_{max} (nm) 316, 460, 492. ES-MS: *m*/*z* 1099 (MH^+).

1b (*trans-2*): ^1H NMR δ (ppm): 4.73 and 4.43 (2 d, 4 H, $J = 9.4$ Hz, pyrrolidine), 4.55 and 4.40 (2 d, 4 H, $J = 9.4$ Hz, pyrrolidine), 4.09 and 3.39 (2 t, 8 H, $J = 5.6$ Hz, OCH_2CH_2N), 3.87 and 3.81 (2 m, 8 H, OCH_2CH_2O), 3.74 and 3.59 (2 m, 8 H, OCH_2CH_2O), 3.38 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 159.16 (*, 2 C), 153.46 (*, 2 C), 153.28 (*, 2 C), 152.68 (*, 2 C), 148.49 (2 C), 147.75 (2 C), 147.18 (2 C), 147.02 (2 C), 146.42 (2 C), 146.27 (2 C), 146.03 (2 C), 145.73 (2 C), 145.63 (2 C), 145.35 (2 C), 145.14 (2 C), 144.22 (2 C), 143.79 (2 C), 143.71 (2 C), 142.64 (2 C), 142.57 (2 C), 142.49 (2 C), 142.40 (2 C), 141.57 (2 C), 141.45 (2 C), 139.58 (2 C), 139.58 (2 C), 134.51 (2 C), 133.74 (2 C), 72.05 (2 C), 70.79 (2 C), 70.70 (2 C), 70.70 (2 C), 70.57 (2 C), 69.50 (2 C), 69.34 (2 C), 68.61 (2 C), 68.45 (2 C), 59.11 (2 C), 54.27 (2 C). UV−vis: λ_{max} (nm) 429, 475, 655, 688, 724. ES-MS: *m*/*z* 1099 (MH^+).

1c (*trans-3*): ^1H NMR δ (ppm): 4.49 and 4.41 (2 d, 4 H, $J = 9.6$ Hz, pyrrolidine), 4.24 and 4.14 (2 d, 4 H, $J = 9.5$ Hz, pyrrolidine), 4.00 and 3.27 (2 t, 8 H, $J = 5.6$ Hz, OCH_2CH_2N), 3.81 and 3.76 (2 m, 8 H, OCH_2CH_2O), 3.71 and 3.57 (2 m, 8 H, OCH_2CH_2O), 3.37 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 158.48 (*, 2 C), 155.84 (*, 2 C), 155.77 (*, 2 C), 155.13 (*, 2 C), 149.11 (2 C), 149.04 (2 C), 148.89 (2 C), 148.87 (2 C), 148.26 (2 C), 148.16 (2 C), 146.65 (2 C), 145.29 (2 C), 145.27 (2 C), 145.24 (2 C), 145.15 (2 C), 145.15 (2 C), 144.94 (2 C), 144.68 (2 C), 143.94 (2 C), 143.61 (2 C), 142.52 (2 C), 141.56 (2 C), 141.49 (2 C), 141.25 (2 C), 141.04 (2 C), 139.79 (2 C), 136.42 (2 C), 135.51 (2 C), 72.02 (2 C), 70.74 (2 C), 70.66 (2 C), 70.63 (2 C), 70.44 (2 C), 70.11 (2 C), 69.85 (2 C), 68.55 (2 C), 67.73 (2 C), 59.11 (2 C), 54.20 (2 C). UV−vis: λ_{max} (nm) 413, 464, 489. ES-MS: *m*/*z* 1099 (MH^+).

1d (*trans-4*): ^1H NMR δ (ppm): 4.40 and 4.24 (2 d, 4 H, $J = 9.6$ Hz, pyrrolidine), 4.20 and 4.14 (2 d, 4 H, $J = 9.8$ Hz, pyrrolidine), 3.96 and 3.22 (2 t, 8 H, $J = 5.5$ Hz, OCH_2CH_2N), 3.78 and 3.74 (2 m, 8 H, OCH_2CH_2O), 3.69 and 3.55 (2 m, 8 H, OCH_2CH_2O), 3.36 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 154.85 (*, 2 C), 152.79 (*, 2 C), 151.55 (*, 2 C), 150.90 (*, 2 C), 150.85 (1 C), 149.52 (1 C), 149.22 (2 C), 148.26 (2 C), 147.97 (2 C), 147.64 (1 C), 147.51 (2 C), 146.22 (2 C), 146.10 (2 C), 146.08 (2 C), 145.50 (2 C), 145.01 (2 C), 144.98 (2 C), 144.66 (2 C), 142.84 (1 C), 142.58 (2 C), 142.13 (2 C), 141.74 (2 C), 141.71 (2 C), 141.38 (2 C), 141.21 (2 C), 139.09 (2 C), 138.60 (2 C), 136.07 (2 C), 135.41 (2 C), 131.18 (2 C), 72.00 (2 C), 70.72 (2 C), 70.64 (2 C), 70.60 (2 C), 70.42 (2 C), 69.60 (2 C), 69.36 (2 C), 68.55 (2 C), 67.91 (2 C), 59.10 (2 C), 54.17 (2 C). UV−vis: λ_{max} (nm) 412, 451, 642, 706. ES-MS: *m*/*z* 1099 (MH^+).

1e (*equatorial*): ^1H NMR δ (ppm): 4.16 and 4.04 (2 d, 4 H, $J = 9.9$ Hz, pyrrolidine), 4.14 (s, 2 H Hz, pyrrolidine), 3.98 (s, 2 H, pyrrolidine), 3.91 and 3.16 (2 t, 4 H, $J = 5.7$ Hz, OCH_2CH_2N), 3.91 and 3.14 (2 t, 4 H, $J = 5.7$ Hz, OCH_2CH_2N), 3.74 (m, 8 H, OCH_2CH_2O), 3.70 and 3.56 (2 m, 4 H, OCH_2CH_2O), 3.67 and 3.53 (2 m, 4 H, OCH_2CH_2O), 3.39 (s, 3 H, OMe), 3.35 (s, 3 H, OMe). ^{13}C NMR δ (ppm): 159.20 (*, 2 C), 153.78 (*, 2 C), 153.23 (*, 2 C), 152.79 (*, 2 C), 149.80 (1 C), 148.85 (2 C), 148.02 (2 C), 147.75 (2 C), 147.75 (1 C), 147.26 (2 C), 147.20 (2 C), 146.75 (2 C), 146.62 (2 C), 145.71 (2 C), 145.13 (2 C), 144.98 (2 C), 144.66 (2 C), 144.60 (2 C), 144.37 (2 C), 143.66 (2 C), 143.20 (2 C), 142.30 (2 C), 141.71 (2 C), 141.56 (2 C), 141.45 (2 C), 140.68 (2 C), 139.16 (2 C), 136.73 (2 C), 135.52 (2 C), 72.01 (1 C), 71.98 (1 C), 70.70 (1 C), 70.70 (1 C), 70.64 (1 C), 70.64 (1 C), 70.60 (1 C), 70.56 (1 C), 70.38 (1 C), 70.34 (1 C), 69.94 (2 C), 69.76 (1 C), 69.68 (1 C), 68.43 (2 C), 68.04 (1 C), 67.44 (1 C), 59.12 (1 C), 59.10 (1 C), 54.23 (1 C), 54.07 (1 C). UV−vis: λ_{max} (nm) 395, 423. ES-MS: *m*/*z* 1099 (MH^+).

1f (*cis-1*): ^1H NMR δ (ppm): 4.42 and 3.67 (2 d, 4 H, $J = 9.7$ Hz, pyrrolidine), 4.29 and 4.13 (2 d, 4 H, $J = 8.9$ Hz, pyrrolidine), 4.00 and 3.98 (AB part of an ABXY system, 4 H, $J_{AB} = 10.5$ Hz, $J_{A(B)X(Y)} = 5.6$ Hz, diastereotopic OCH_2CH_2N), 3.82 and 3.76 (2m, 8 H, OCH_2CH_2O), 3.70 and 3.55 (2m, 8 H, OCH_2CH_2O), 3.35 (s, 6 H, OCH_3), 3.18 and 3.16 (XY part of an ABXY system, 4 H, $J_{XY} = 12.5$ Hz, $J_{A(B)X(Y)} = 5.6$ Hz, diastereotopic OCH_2CH_2N). ^{13}C NMR δ (ppm): 152.21 (*, 2 C), 151.26 (*, 2 C), 150.58 (*, 2 C), 149.08 (2 C), 148.20 (2 C), 147.46 (2 C), 147.14 (2 C), 146.47 (2 C), 146.22 (2 C), 146.14 (1 C), 145.59 (2 C), 145.42 (2 C), 145.15 (2 C), 145.14 (2 C), 144.70 (2 C), 144.35 (2 C), 144.15 (2 C), 144.10 (2 C), 143.86 (2 C), 143.06 (2 C), 142.82 (1 C), 142.48 (2 C), 142.48 (1 C), 142.43 (2 C), 142.06 (2 C), 141.78 (2 C), 140.85 (2 C), 137.96 (1 C), 135.30 (2 C), 135.15 (2 C), 71.99 (2 C), 70.76 (2 C), 70.65 (2 C), 70.63 (2 C), 70.60 (2 C), 68.66 (2 C), 68.30 (2 C), 67.10 (2 C), 65.97 (*, 2 C), 59.08 (2 C), 54.48 (2 C). UV−vis: λ_{max} (nm) 430, 653, 683, 720. ES-MS: *m*/*z* 1099 (MH^+).

1g (*cis-2*): ^1H NMR δ (ppm): 4.03 and 3.86 (2 d, 4 H, $J = 9.1$ Hz, pyrrolidine), 4.02 and 3.83 (2 d, 4 H, $J = 9.7$ Hz, pyrrolidine), 3.88 (t, 4 H, $J = 5.7$ Hz, OCH_2CH_2N), 3.13 and 3.10 (AB part of an ABX_2 system, 4 H, $J_{AB} = 12.9$, $J_{AX} = J_{BX} = 5.7$ Hz, diastereotopic OCH_2CH_2N), 3.75 and 3.72 (2 m, 8 H, OCH_2CH_2O), 3.67 and 3.54 (2 m, 8 H, OCH_2CH_2O), 3.36 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 158.67 (*, 2 C), 156.51 (*, 2 C), 149.28 (2 C), 148.86 (1 C), 148.75 (1 C), 147.84 (*, 2 C), 147.73 (2 C), 147.66 (*, 1 C), 147.49 (2 C), 147.10 (2 C), 146.92 (2 C), 146.48 (2 C), 146.11 (2 C), 145.76 (2 C), 145.69 (2 C), 145.52 (2 C), 145.38 (2 C), 145.11 (2 C), 144.86 (2 C), 144.52 (2 C), 144.48 (2 C), 144.21 (2 C), 144.03 (2 C), 142.92 (2 C), 141.63 (2 C), 140.96 (2 C), 138.76 (2 C), 133.86 (2 C), 133.21 (2 C), 129.34 (1 C), 71.98 (2 C), 70.70 (2 C), 70.63 (2 C), 70.57 (2 C), 70.24 (2 C), 69.35 (2 C), 67.28 (2 C), 66.95 (2 C), 66.55 (2 C), 59.09 (2 C), 54.03 (2 C). UV−vis: λ_{max} (nm) 447. ES-MS: *m*/*z* 1099 (MH^+).

(30) (a) Bax, A.; Griffey, R. H.; Hawkins, B. L. *J. Magn. Reson.* **1983**, *55*, 301−315. (b) Bax, A.; Subramanian, S. *J. Magn. Reson.* **1986**, *67*, 565−569.

(31) Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285−4294.

(32) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093−2094.

1h (*cis*-3): ^{1}H NMR δ (ppm): 4.34 and 3.97 (2 d, 4 H, J = 9.6 Hz, pyrrolidine), 4.14 and 3.89 (2 d, 4 H, J = 9.5 Hz, pyrrolidine), 3.94 and 3.17 (2 t, 8 H, J = 5.6 Hz, OCH_2CH_2N), 3.77 and 3.74 (2 m, 8 H, OCH_2CH_2O), 3.69 and 3.54 (2 m, 8 H, OCH_2CH_2O), 3.36 (s, 6 H, OMe). ^{13}C NMR δ (ppm): 152.00 (*, 2 C), 150.18 (*, 2 C), 149.12 (2 C), 148.94 (*, 2 C), 148.75 (2 C), 148.15 (2 C), 147.57 (2 C), 147.14 (2 C), 146.29 (2 C), 146.05 (2 C), 145.89 (2 C), 145.85 (2 C), 145.66 (2 C), 145.54 (2 C), 145.34 (2 C), 145.18 (2 C), 144.76 (2 C), 142.35 (2 C), 142.31 (2 C), 141.86 (2 C), 141.75 (2 C), 141.46 (2 C), 139.80 (2 C), 138.56 (2 C), 136.88 (2 C), 135.18 (2 C), 134.17 (2 C), 130.54 (*, 2 C), 71.99 (2 C), 70.72 (2 C), 70.64 (2 C), 70.56 (2 C), 70.40 (2 C), 69.85 (2 C), 69.51 (2 C), 68.28 (2 C), 65.82 (2 C), 59.10 (2 C), 54.11 (2 C). UV−vis: λ_{max} (nm) 461, 652, 724. ES-MS: m/z 1099 (MH^+).

Acknowledgment. Financial support from MURST (cofin prot. no. 9803194198) and the European Community through contract No. ERB FMRX-CT97-0126 (TMR program USEFULL) is gratefully acknowledged. We also thank Prof. Yves Rubin and Dr. Georg Schick for useful discussions.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of isomers **1a**−**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO001708Z