Synthesis and complexation of polytopic adamantane-based probes

[F004]

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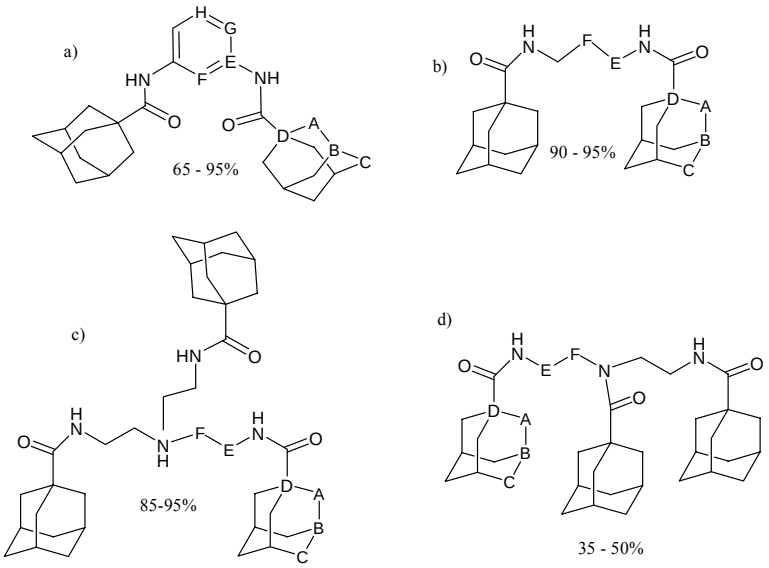
The complexation of adamantane derivatives with cyclodextrins has been the subject of numerous studies during the last twenty years.[1-18] This is due to several reasons. First, adamantane derivatives form strong complexes with β-cyclodextrin and the equlibrium constants are the strongest which can be found for the formation of this kind of inclusion complexes. This is because of the adamantyl residue perfectly fits inside the β-cyclodextrin cavity since the radios of this residue is slightly larger thant the radius inside the cavity available for guest in this cyclodextrin. Second, unimers simultaneously having guest (adamantyl residue) and host (β-cyclodextrin residue) moieties in their structure have been obtained and by self-association formed linear supramolecular structure.[19,20] Third, adamantyl dimers have been synthesized and complexed with β-cyclodextrin dimers to form the so called "chelate complexes".[6] Fourth, adamantyl dimers have used to obtain linear and dentritic-like supramolecular polymers when they are complexed with polytopic hosts derived from β-cyclodextrin.[21-23] Finally, polytopic hosts and polytopic guests can be used to form other macromolecular assemblies.[24,25] In such cases, high viscosity enhancements have been observed, which are maximum for a composition in which the stoichiometry is one host (*β*CD residue):one guest (adamantyl residue).[26]

Thus the synthesis of both polytopic hosts and guests have a growing importance in designing new supramolecular entities mainly supramolecular polymers. The aim of this paper is the synthesis of adamantyl oligomers (dimers and trimers) which can later be used as polytopic guests. The synthesis of another adamantyl dimer has been published elsewhere.[23]

Results and Discussion

Figure 1 shows the structures of four new polytopic guests, two dimers ("a" and "b"). They were characterized by NMR (see an example in Figure 2), IR Table 1), Electronic Impact, Fab and elemental analysis. In all cases, IR spectra shows the typical amide and hydrocarbon absorption bands. All NMR signals were assigned confirming the expected structure for the compounds.

Figure 1.- Amide-type oligomers of adamantane synthesized here.



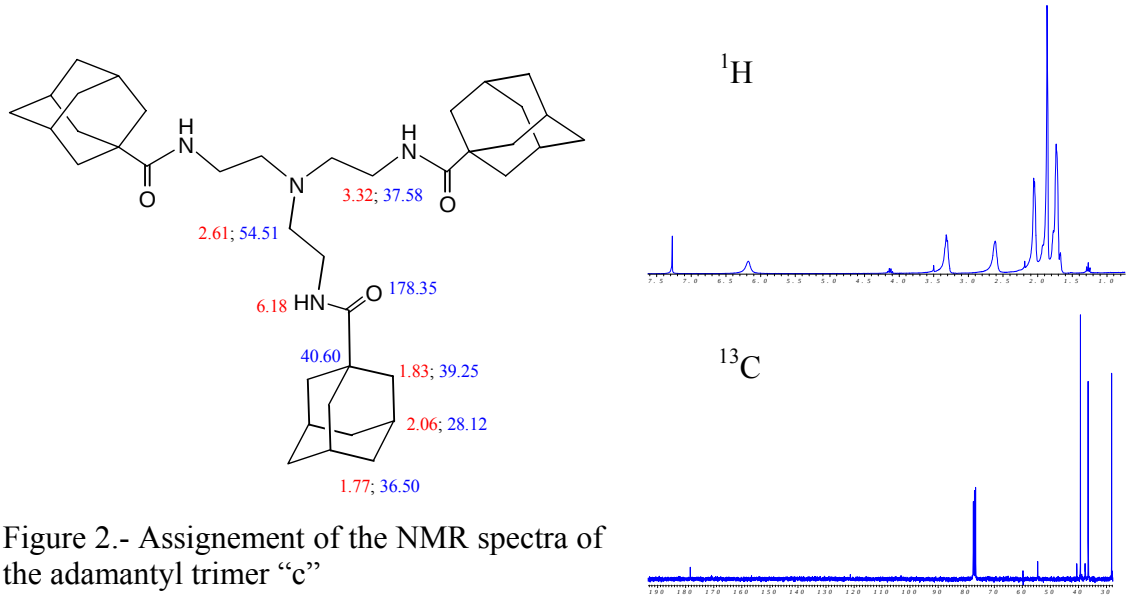


Figure 2.- Assignement of the NMR spectra of the adamantyl trimer "c"

Table 1: IR absorption data of the synthesized guest oligomers.

ν/ (cm^{-1})	Assigment
3200 – 3300	N—H
2840 – 2910	(CH_2); (CH)
1620 – 1640	C=O (Amide I)
1510 – 1550	N-C=O (Amide II)

The four adamantyl guests were complexed with β-CD. Since all of these oligomers are rather insoluble in water, there are difficulties in their characterization. ROESY spectra of all complexes indicate that the adamantyl moiety enters into the β-cyclodextrin cavity by its secondary side, in agreement with Rüdiger *et al*[17] Notice in Figure 3 the cross-peaks between the adamantyl protons and inner cyclodextrin protons, H3, located close to the secondary side of the cavity.

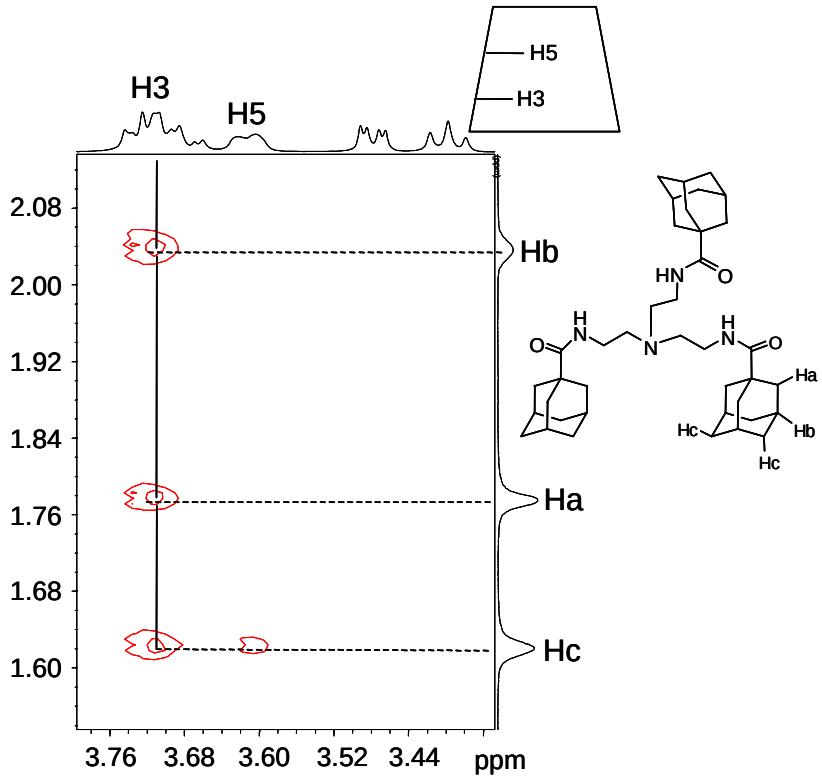


Figure 3.- ROESY spectra for the trimer "c"/β-CD complex in aqueous solution.

Experimental

NMR spectra (^1H, ^{13}C) for the complete characterization of derivatives were obtained in a Brücker model AC300 (300 MHz: ^1H; 75 MHz: ^{13}C: 75 MHz), ROESY

experiments were performed in a 500 MHz Brücker AMX500, all the samples were 10mM in β-CD with one equivalent of the desired oligomer.

IR spectra were obtained in a ABB Bomem model MB series, Electronic Impact in a Hewlett Packard, model HP 5988[a] and elemental analysis in a Sisons model EA 1108.

Amines and solvents were purified as usually.[27] Adamantane-1-carbonyl chloride was prepared by refluxing 30-90 minutes the acid with $SOCl_2$.[28]. Thionyl chloride excess was eliminated in vacuo and the resulting solid were used without further purification.

Synthesis of compounds "a"-"d".[10,11]

In a dry 100 mL flask 7 mL (5g; 0.05 mol) of triethyl amine, 1 equivalent of the amine were mixed in 50 mL of dry $CHCl_3$. After cooling 15 minutes with an ice-water bath, adamantane-1-carbonyl chloride was added dropwise in 20 mL of dry $CHCl_3$. The cooling bath was keeped during 1 hour and, after removal, the reaction mixture was stirred at rt for 20 hours and then concentrated in vacuo. The product was purified by column chromatography.

Compound "a":Rf: 0.3 (Hexane: ethyl acetate; 7:3). ^{1}H-NMR 300 MHz, $CDCl_3$, $\delta_{ppm:}$ 8.00 (*m*, H_f), 7.36 (*bs*, H-N-C=O); 7.26 (*m,* H_H); 2.11 (*bs,* H_B); 1.76 (*bs,* H_A); 1.45 (*bs,* H_C); ^{13}C-NMR, 125 MHz, $CDCl_3$, δ_{ppm}:176.3.38 (C=O, amide), 138.7 (C_E) 129.5 (C_H), 115.2 (C_G), 111.0 (C_F), 41.5 (C_D), 39.2 (C_A), 36.3 (C_C), 28.0 (C_B). *m/z*; (Electronic Impact) 433.1. Elemental analysis: %N: 6.41; %C: 76.21; %H: 8.37 %O: 9.01.

Compound "b":Rf: 0.5 (ethyl acetate: methanol; 8:2). ^{1}H-NMR 300 MHz, $CDCl_3$, $\delta_{ppm:}$ 6.52 (*bs*, H-N-C=O); 3.26 (*m,* H_E); 1.53 (*bs,* H_F); 2.04 (*bs,* H_B); 1.88 (*bs,* H_A); 1.72 (*bs,* H_C) ^{13}C-NMR, 125 MHz, $CDCl_3$, δ_{ppm}:178.8.38 (C=O, amide), 40.7 (C_D) 39.3 (C_A) 36.5 (C_C) 35.1 (C_E), 30.0 (C_F), 28.0 (C_B). *m/z*; (Electronic Impact) 399.1. Elemental analysis: %N: 6.94; %C: 74.49; %H: 9.71 %O: 8.86.

Compound "c":Rf: 0.24 (ethyl acetate: methanol; 8:2). ^{1}H-NMR 300 MHz, $CDCl_3$, $\delta_{ppm:}$ 6.18 (*bs*, H-N-C=O); 3.32 (*m,* H_F); 2.61 (*bs,* H_E); 2.06 (*bs,* H_B); 1.83 (*bs,* H_A); 1.77 (*bs,* H_C) ^{13}C-NMR, 125 MHz, $CDCl_3$, δ_{ppm}:178.8.35 (C=O, amide), 54.5 (C_F), 40.6 (C_D) 39.3 (C_A), 37.6 (C_E), 36.5 (C_C), 28.1 (C_B). *m/z*; (Electronic Impact) 633.3. Elemental analysis: %N: 8.81; %C: 73.77; %H: 9.74 %O: 7.67.

Compound "d":Rf: 0.3 (ethyl acetate). ^{1}H-NMR 300 MHz, $CDCl_3$, $\delta_{ppm:}$ 6.52 (*bs*, H-N-C=O); 3.57 (*m,* H_F); 3.40 (*bs,* H_E); 2.01 (*bs,* H_B); 1.82 (*bs,* H_A); 1.68 (*bs,* H_C) ^{13}C-NMR,

125 MHz, $CDCl_3$, δ_{ppm}:178.9 (C=O, amide), 47.4 (C_F), 40.5 (C_D), 39.2 (C_A), 38.9 (C_E), 36.5 (C_C), 28.1 (C_B). *m/z*; (Electronic Impact) 590.3. Elemental analysis: %N: 7.10; %C: 75.05; %H: 9.64 %O: 8.22.

Acknowledgements

The authors thank the Ministerio de Ciencia y Tecnología (Project MAT2001-2911) and Xunta de Galicia (PGIDIT02PXIC26202PN) for financial support. V. H. Soto thanks AECI (Beca Mutis)/University of Costa Rica for a research scholarship.

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