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### STEROIDAL ADAMANTYLAMIDES AND CARBAMATES. POTENTIAL ANTIVIRAL AGENTS

Josef E. Herz<sup>ab</sup>; Tomasa Corro<sup>a</sup>; Maritza Velarde<sup>a</sup>; Julieta A. Herz<sup>c</sup>

<sup>a</sup> Department of Chemistry, CIEA-IPN, Mexico, DF <sup>b</sup> Department of Biotechnology, Institute for Biomedical Research, UNAM, Mexico, DF <sup>c</sup> Colegio de Ciencias y Humanidades, UNAM, Naucalpan, EM, Mexico

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## STEROIDAL ADAMANTYLAMIDES AND CARBAMATES.

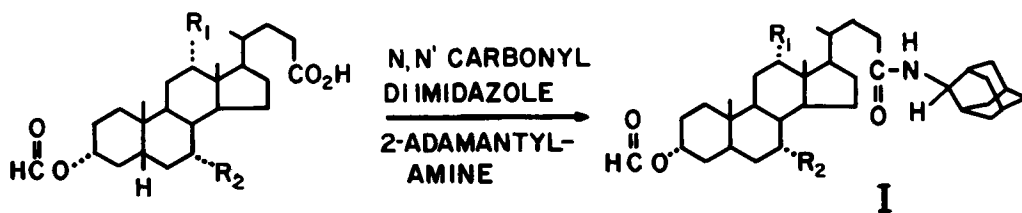
## POTENTIAL ANTIVIRAL AGENTS

Submitted by Josef E. Herz<sup>a,b</sup>, Tomasa Corro<sup>a</sup>, Maritza Velarde<sup>a</sup>  
(9/3/80) and Julieta A. Herz<sup>c</sup>

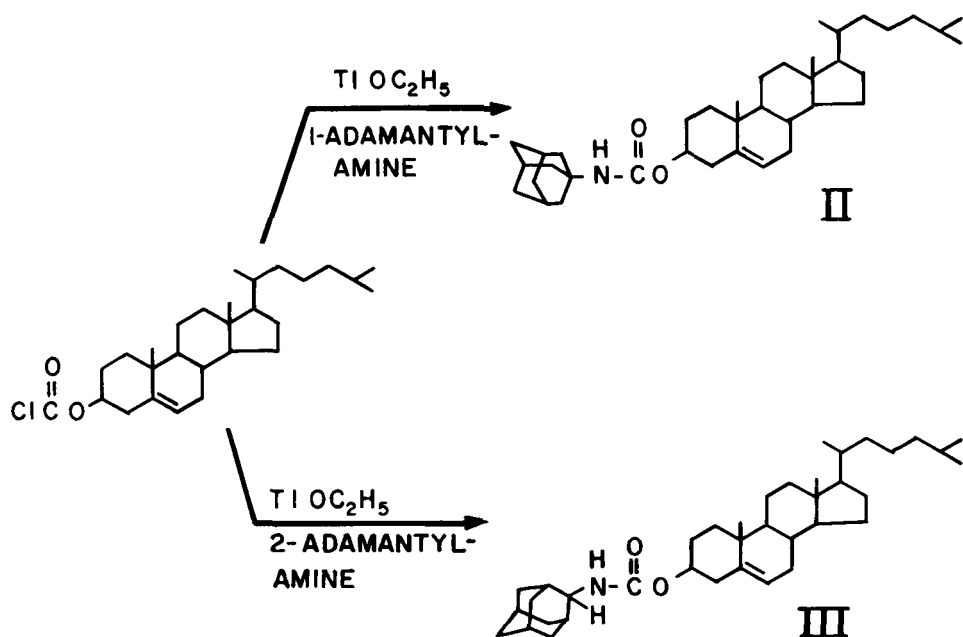
- a) Department of Chemistry, CIEA-IPN, Ap. 14-740  
Mexico 14, D.F.
- b) Department of Biotechnology, Institute for  
Biomedical Research, UNAM, Ap. 70228  
Mexico 20, D.F.
- c) Colegio de Ciencias y Humanidades, UNAM,  
Naucalpan, EM, Mexico

In previous publications<sup>1,2</sup> we reported the preparations and antiviral activities of several steroidal 1-adamantylamides. The promising results obtained induced us to synthesize additional potential antiviral compounds of a similar type. In this publication we describe the preparation of three steroidal N-(2-adamantyl)amides and of the cholesteryl carbamates of 1-amino and 2-aminoadamantane.

A number of methods for the preparation of amides<sup>1</sup> were attempted. Most gave low yields and numerous side-products. The best results were obtained when the imidazolide of the steroidal acid was prepared *in situ* and reacted without isolation with adamantylamine in a suitable solvent such as tetra-



- a)  $R_1 = R_2 = \text{H}$     b)  $R_1 = \text{OCHO}$ ,  $R_2 = \text{H}$     c)  $R_1 = R_2 = \text{OCHO}$



hydrofuran. To prepare the N-adamantylcarbamates of cholesterol the known cholesteryl chloroformate<sup>3</sup> was treated with the adamantylamine in presence of thallium(I) ethoxide according to a previously described<sup>4</sup> method for the preparation of highly hindered steroidal esters.

#### EXPERIMENTAL SECTION

N-(2-Adamantyl)amides.- Deoxycholic acid diformate (1.0 g) and N,N'-carbonyl diimidazole (500 mg) were sealed into a dry reaction flask and dry tetrahydrofuran (THF) was added with a syringe. When the formation of  $CO_2$  had ceased, 2-adamantylamine (450 mg) in 10 ml dry THF was added and the mixture heated to reflux for 2 hrs. The mixture was evaporated under vacuum, the residue taken up in ether; the ethereal solution was

washed with water, dried and evaporated. The residue was adsorbed on a silica gel dry column and eluted with benzene-ethyl acetate (60:40).

N-(2-Adamantyl)amide of lithocholic acid formate(Ia), yield 78%, mp. 148-152°,  $[\alpha]_D + 39^\circ$  (Chf). IR(CCl<sub>4</sub>): 1670 cm<sup>-1</sup> (amide), 1725 cm<sup>-1</sup> (formate), 3460 cm<sup>-1</sup> (amide). NMR(CDCl<sub>3</sub>):  $\delta$  4.0 (d, 2'-adamant), 4.8 (m, 3-CH), 5.2 (d, NH), 7.9 (s, HCOO).

Anal. Calcd. for C<sub>35</sub>H<sub>55</sub>NO<sub>3</sub>: C, 78.16; H, 10.31; N, 2.60.

Found: C, 78.31; H, 10.26; N, 2.38.

N-(2-Adamantyl)amide of deoxycholic acid diformate(Ib), yield 73%, mp. 175-177°,  $[\alpha]_D + 71.5^\circ$  (Chf). IR(CCl<sub>4</sub>): 1660 cm<sup>-1</sup> (amide), 1720 cm<sup>-1</sup> (formate), 3460 cm<sup>-1</sup> (amide). NMR(CDCl<sub>3</sub>):  $\delta$  3.8 (d, 2'-adamant), 4.8 (m, NH, 3 $\beta$  CH), 5.2 (s, 12 $\beta$  CH), 8.0 (s), 8.15 (s, HCOO).

Anal. Calcd. for C<sub>36</sub>H<sub>55</sub>NO<sub>5</sub>: C, 74.31; H, 9.53; N, 2.41.

Found: C, 74.27; H, 9.50; N, 2.26.

N-(2-Adamantyl)amide of cholic acid triformate(Ic), yield 67%, mp. 131-133°,  $[\alpha]_D + 56.75^\circ$  (Chf). IR(CCl<sub>4</sub>): 1660 cm<sup>-1</sup> (amide), 1715 cm<sup>-1</sup> (HCOO), 3460 cm<sup>-1</sup> (amide). NMR(CDCl<sub>3</sub>):  $\delta$  3.8 (d, 2'-adamant), 4.8 (b, 3 $\beta$  CH), 5.0 (d, NH), 5.3 (m, 7 $\beta$ , 12 $\beta$  CH), 7.8 (s), 8.0 (s), 8.15 (s, HCOO).

Anal. Calcd. for C<sub>37</sub>H<sub>55</sub>NO<sub>7</sub>: C, 71.02; H, 8.86; N, 2.23.

Found: C, 70.84; H, 8.83; N, 2.22.

Preparation of N-Adamantylcarbamates of Cholesterol.- The adamantylamine (600 mg) was dissolved in about 150 ml dry benzene under nitrogen and with exclusion of moisture. A solution of 1.0 g thallium(I) ethoxide in 10 ml benzene was added. To facilitate the formation of the thallium salt of the amine, the

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$C_6H_6-C_2H_5OH$  mixture was concentrated to a small volume (distillation) and replaced by fresh anhydrous benzene. This procedure was repeated 3-4 times. Finally, a solution of 1.8 g cholesteryl chloroformate<sup>3</sup> in 20 ml dry benzene was added dropwise with stirring and heating. A white precipitate formed almost immediately. After 2 hrs of heating at reflux the mixture was cooled to room temperature and filtered through a layer of Celite. The benzene solution was washed with water, dried and evaporated. The product was crystallized from benzene-ethyl acetate (98:2).

N-(1-Adamantyl)carbamate of cholesterol(II), yield 76%, mp. 201-203<sup>o</sup>,  $[\alpha] - 106^o$  (Chf), IR( $CCl_4$ ): 1735, 3460  $cm^{-1}$  (urethane), NMR( $CDCl_3$ ):  $\delta$  4.3 (s, 3 $\alpha$ -CH, cholest.), 4.9 (d, NH), 5.25 (m,  $\Delta^5$ ).

Anal. Calcd. for  $C_{38}H_{61}NO_2$ : C, 80.94; H, 10.90; N, 2.48.

Found: C, 81.01; H, 11.14; N, 2.41.

N-(2-Adamantyl)carbamate of cholesterol(III), yield 81%, mp. 214-217<sup>o</sup>,  $[\alpha]_D + 38^o$  (Chf), IR( $CCl_4$ ): 1730, 3480  $cm^{-1}$  (urethane), NMR( $CDCl_3$ ):  $\delta$  3.8 (d, CH, 2'-adamantane), 4.4 (s, 3 $\alpha$ -CH, cholest), 4.9 (d, NH), 5.3 (m,  $\Delta^5$ ).

Anal. Calcd. for  $C_{38}H_{61}NO_2$ : C, 80.94; H, 10.90; N, 2.48.

Found: C, 80.72; H, 10.70; N, 2.28.

Microanalyses were carried out by Butterworth Laboratories, Teddington, ENGLAND.

REFERENCES

1. J. E. Herz and R. E. Mantecon, Org. Prep. Proced. Int., 4, 129 (1972).

2. A. Kreutzberger, J. E. Herz, R. E. Mantecon, A. Murillo, Chemiker Zeitg., 100, 195 (1976).
3. S. Nakanishi and E. V. Jensen, Chem. Pharm. Bull., 25 3398 (1977).
4. J. E. Herz, S. Cruz, J. V. Torres, A. Murillo, Synth. Comm., 7, 383 (1977)