Bull. Soc. Chim. Belg. vol.93/n° 2/1984

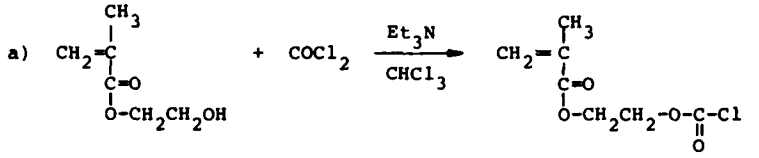
SHORT COMMUNICATION

SYNTHESIS OF 4-[N-(2-METHACRYLOYLOXY)ETHOXYCARBONYL)]AMINO-N'-[2-(DIETHYL-AMINO)ETHYL]BENZAMIDE; A NOVEL POLYMERIZABLE DERIVATIVE OF PROCAINAMIDE

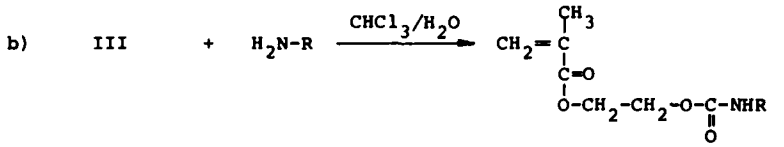
Luc RUYS and Etienne SCHACHT
Laboratory of Organic Chemistry, Rijksuniversiteit-Gent,
Krijgslaan 281 (S-4), B-9000 Gent (Belgium).

Received : 13/01/1984 - Accepted : 14/02/1984

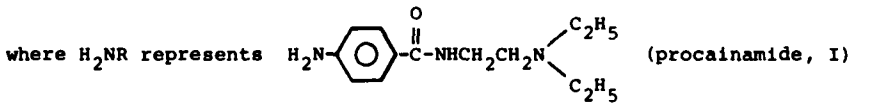
As part of a current project[1, 2] on the synthesis and evaluation of derivatives of the antiarrhythmic procainamide (I), we have prepared a novel polymerizable derivative starting from the parent drug and 2-hydroxyethylmethacrylate (II) according to the reaction scheme given below :



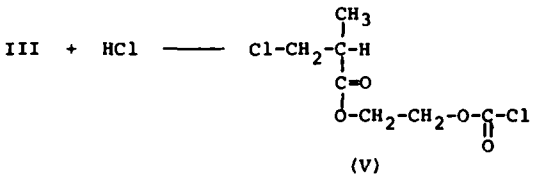
(II) (III)



(IV)



The synthesis of [(2-chlorocarbonyloxy)ethyl]methacrylate (III) starting from (2-hydroxyethyl)methacrylate and phosgene and in absence of a proton acceptor has been reported before in the literature[3]. However in our hands this method gave rather poor yields (45%). It was demonstrated that part of the reaction product further reacts with the evolved hydrogen chloride with formation of [(2'-chlorocarbonyloxy)ethyl]-2-methyl-3-chloropropionate (V).

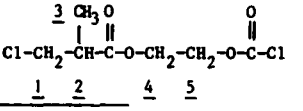


(V)

The structure of product V was identified by NMR spectroscopy (Table 1). By carrying out the reaction (a) in presence of triethylamine the yield of this reaction could be increased significantly. The reaction product was purified by distillation under reduced pressure (b.p.: 59°C/0.3 mm Hg; yield: 82%). The NMR parameters of product III are given in Table 2. The subsequent reaction of the chloroformiate with procainamide was performed in a two-phaze system (chloroform/water). The yield of the title compound (IV) after purification by repeated recrystalization from an ethanol-isopropanol mixture was 25 percent. The product was characterized by spectroscopic technics. Table 3 shows the NMR parameters of the compound.

TABLE 1.

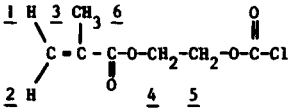
NMR parameters of product V. (90 MHz, $CDCl_3$).



Proton	H-1	H-2	H-3	H-4	H-5
ν (ppm)	3.72	2.93	1.30	4.50	

TABLE 2.

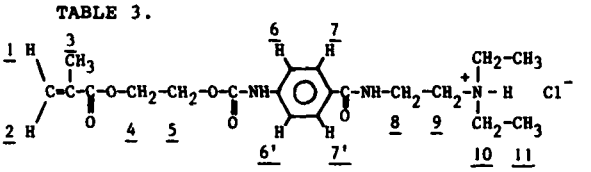
NMR parameters of product III (360 MHz, $CDCl_3$).



Proton	H-1	H-2	H-3	H-4	H-5
ν (ppm)	5.65	6.17	1.98	4.42	4.58
J (Hz)	$^2J(1,2)$: 1.5; $^4J(1,3)$: 1.5; $^4J(2,3)$: 1.1; $^3J(4,5)$: 4.5				

TABLE 3.

NMR parameters of product IV (360 MHz, D_2O).



Proton	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8	H-9	H-10	H-11
ν (ppm)	5.73	6.15	1.93	4.48		7.48	7.80	3.82	3.45	3.36	1.33
J (Hz)	$^3J(6,7)$: 8.5; $^4J(6,6')$: 2.2; $^5J(6,7')$: 2.2 ; $^3J(8,9)$: 6.3 ; $^3J(10,11)$: 7.3										

REFERENCES.

1. Ruys L., Vermeersch J., Schacht E., Goethals E., Gysselinck P., Braeckman P. and Van Severen R., Acta Pharm. Techn., 29(2), 105 (1983).
2. Ruys L., Schacht E., to be published in Bull. Soc. Chim. Belg.
3. Pinazzi C., Rabadeux J. and Pleurdeau A., Eur. Pol. J., 14, 205 (1978).