STUDIES ON LOCAL ANAESTHETICS

Part I

PREVIOUS work on local anæsthetics was confined for the most part to preparing esters of amino-aryl acids with different substituted alkanalamines. Substitution in the amino-

group of the acid component does not appear to have been tried. The preparation of a few derivatives of novocaine with acid chlorides of dicarboxylic acids is here reported.

Novocaine (2 mol.) was reacted in the cold with the di-acid chlorides (1 mol.) in benzene medium. The hydrochlorides of the resulting products separated out soon from which the bases were obtained by the addition of sodium carbonate solution.

TABLE I

	Acid chloride used	Formula of the compound R = —$C_6H_4COOCH_2CH_2NEt_2$	m.p. of the base	m.p. of the hydrochloride
1	Phosgene ..	$CO(NHR)_2$	103°	217–218°
2	Oxalyl chloride ..	$(CO\cdot NHR)_2$	218–19°	Chars without melting above 300°
3	Malonylchloride ..	$CH_2(CONHR)_2$	83°	149°
4	Succinylchloride ..	$(CH_2\text{-}CONHR)_2$	185°	230°
5	Glutarylchloride ..	$(CH_2)_3(CONHR)_2$	132°	172°
6	Adipyl chloride ..	$(CH_2)_4(CONHR)_2$	158°	185–90°
7	Phthalylchloride ..	$C_6H_4(CONHR)_2$	98°	118°

In the cases of (4) and (7), in addition to the normal derivative, a small trace of an insoluble cyclic product was formed by the interaction of one mol. of novocaine with one mol. of the acid chloride melting at 242°-44° and 94° respectively.

The alkylene-bis-novocaine derivatives have been prepared by heating under reflux a mixture of novocaine (4 mol.) and alkylene dibromide (1 mol.) in amyl alcohol for about 12 hours. On removal of alcohol, a dark pasty mass was left behind. It was treated with sodium carbonate solution and the liberated base taken up in benzene. The dry benzene solution on the addition of dry petroleum-ether gave a clear white precipitate.

The compounds are under pharmacological investigation.

TABLE II

	Name of the alkylene dibromide	Formula of the derivative	m.p. of the base	m.p. of the hydrochloride
1	Ethylene dibromide	$C_2H_4(NHR)_2$	185°	240°
2	Trimethylene dibromide	$(CH_2)_3(NHR)_2$	189°	261° Chars
3	Tetra methylene dibromide	$(CH_2)_4(NHR)_2$	197°	above 270°
4	Pentamethylene dibromide	$(CH_2)_5(NHR)_2$	223°	,,

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