

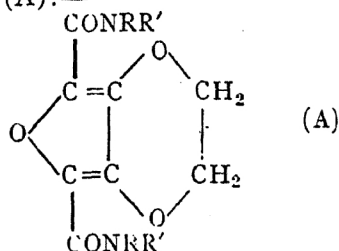
STUDIES ON ANÆSTHETICS AND
LOCAL ANÆSTHETICS

Amides and Esters of 2:5-Dicarboxy-furo-
(3:4)-*p*-dioxan

GILMAN¹ observed that β -diethylamino ethyl esters of acids containing aminobenzene, benzene, pyrrole, thiophene and furan rings possess low local anæsthetic action. Cook and Kreke,² from a comparison of the local anæsthetic actions as exhibited by the diethylamino ethyl esters of benzoic and furoic acids, showed that furoates are frequently somewhat superior. Degan and Pope³ prepared large number of N-alkyl N-aryl furaminines, and made the interesting observation that N-*n*-butyl N'-*p*-phenethylfuramidine hydrochloride is more than three times as active as cocaine, and it is not

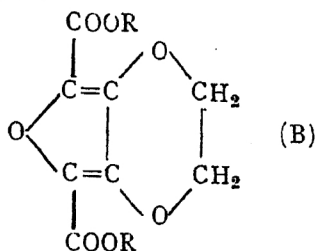
irritating to the cornea of the eye. It seemed very reasonable, therefore, that a search for new and efficient local anaesthetics in the differently (alkyl and aryl) substituted esters, amides and amidines might lead to some very interesting results.

2:5-Dicarboxy-furo-(3:4)-*p*-dioxan has been prepared starting from diglycollic acid by five steps.¹ This di-acid gave the acidchloride, m.p. 154°; yield 80 per cent. The di-acid chloride by reacting with varieties of aliphatic and aromatic amines have given the following diamides (A):—



- (1) R = H; R' = H; m.p. 333-35°
- (2) R = H; R' = Me; m.p. 260°
- (3) R = Et, R' = Et; m.p. 102°
- (4) R = H; R' = Ph; m.p. 103°
- (5) R = H; R' = *p*-methoxy-phenyl; m.p. 226°
- (6) R = H; R' = *o*-methoxy-phenyl; m.p. 339°
- (7) R = H; R' = *o*-tolyl; m.p. 322°
- (8) R = H; R' = *p*-tolyl; m.p. 257°
- (9) R = H; R' = *m*-tolyl; m.p. 271°
- (10) R = H; R' = benzyl; m.p. 86°
- (11) R = H; R' = C₆H₄·SO₂NH₂; 270° (decomp.)

The following four diesters (B) have been prepared:—



- (1) R = benzyl; m.p. 126°
- (2) R = CH₂·CH₂·N(C₂H₅)₂; m.p. 271°
- (3) R = CH₂ - CH = CH·C₆H₅; m.p. 169-71°
- (4) Ethyl-thio-ester, m.p. 182°

Further work on the preparation of some more esters, amides and amidines of this series, as also on the preparation of esters, amides and amidines with the diacid chlorides of 2:5-dicarboxythieno-(3:4)-*p*-dioxan, and pyrro-(3:4)-*p*-dioxans is in progress.

The above compounds are under pharmacological examination.

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1. *J. Amer. Chem. Soc.*, 1925, **47**, 245. 2. *Ibid.*, 1940, **62**, 1951. 3. *Ibid.*, 1940, **62**, 1960. 4. *J. Indian Inst. Sci.*, 1938, **21A**, 115.