

From the acid chloride of the above pure mono acids, the following new N-substituted amides, which are likely to possess anæsthetic action, have been prepared.

- (1) Picolinic acid *p*-anisidide, m.p. 88°;
- (2) Picolinic acid *o*-anisidide, m.p. 110°;
- (3) Nicotinic acid *p*-anisidide, m.p. 141°;
- (4) Isonicotinic acid *p*-anisidide, m.p. 153°;
- (5) Picolinic acid benzyl amide (semi-solid).

$\beta$ -Chlorethyl picolinate,  $C_{11}H_{14}N-CO_2-CH_2-CH_2-Cl$  (b.p. 136-138°/5-7 mm.) and  $\beta$ -chlorethyl nicotinate (b.p. 167-69°/45 mm.), have been prepared from the corresponding acid chlorides by the action of ethylene chlorhydrin. *p*-Methoxyphenylaminoethyl picolinate,  $C_{17}H_{19}N-COO-CH_2-CH_2-NHC_6H_4OCH_3$ , was prepared from the chlorethyl ester by the action of *p*-anisidine; acetyl derivative, m.p. 170°. Further work on the preparation of some typical esters and amides of this series is in progress. The compounds prepared await pharmacological examination.

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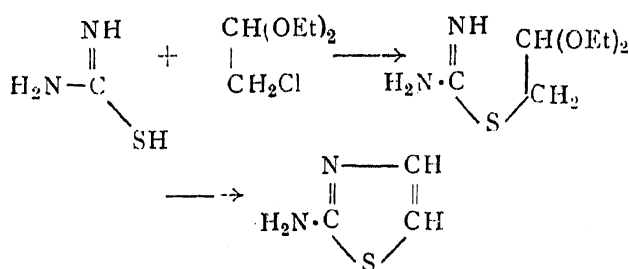
1. *Indian Med. Gaz.*, 1942, **77**, 98. 2. *J. Amer. Pharm. Assoc.*, 1944, **33**, 72. 3. *J. Amer. Chem. Soc.* 1942, **64**, 1721.

## N<sup>1</sup> AND N<sup>4</sup> SUBSTITUTED SULPHANILAMIDES

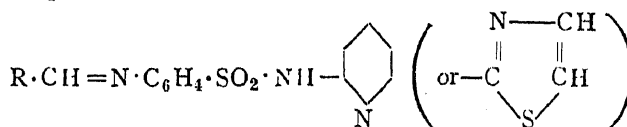
### Part I. Schiff's Base of Sulpha-pyridine and Sulpha-thiazole

ALTHOUGH a number of Schiff's bases of sulphanilamide have been prepared and they have shown to be therapeutically active, no systematic investigation seems to have been undertaken on the preparation of Schiff's bases of the two well-reputed sulphanilamide drugs, viz., of sulpha-pyridine and sulpha-thiazole. The three anils of sulpha-pyridine<sup>1</sup> known so far have been prepared by the action of benzaldehyde, *p*-methoxy-benzaldehyde and cinnamic aldehyde, and they have been found to possess good therapeutic properties. No anil (Schiff's base) seem to have been prepared from sulpha-thiazole.

Aminothiazole to be used for the preparation of sulphathiazole required as the starting material for our work was prepared by the action of chloracetal (prepared in this laboratory in satisfactory yield<sup>2</sup>) on thiourea. The method (English patent, E.P. 540,032, by the British Drug House, Ltd., by the action of brominated alcohol on thiourea; and the Indian Patent, 29,345, by the Director, Haffkine Institute, Bombay) by the action of chlorinated alcohol (in none of which details are given) came to our notice after the new method of preparation of aminothiazole was established in this laboratory. The reaction proceeds as follows:—



The following anils of sulpha-pyridine and sulpha-thiazole have been prepared:—



R	Melting point of anils of sulpha-pyridine	M.P. of anils of sulpha-thiazole
$C_6H_5$	240°	202°
<i>p</i> - $OCH_3 \cdot C_6H_4$	205°	160°
3- $OH$ , 4- $OCH_3 \cdot C_6H_3$	146-47°	245°
3, 4, $(OCH_3)_2 \cdot C_6H_3$	210°	138°
$C_6H_5 \cdot CH = CH$	210°	260°
$C_4H_3O$ (furfuraldehyde)	214°	chars at 210°
<i>m</i> - $NO_2 \cdot C_6H_4$	254°	231°
<i>m</i> - $Cl \cdot C_6H_4$	101°	124°
$C_6H_5 \cdot CH_2$	decomposes at 100°	164°

Fuller details will be published elsewhere. These compounds await pharmacological examination.

Work on the preparation of some more anils as also some acyl and sulphanil derivatives, is in progress.

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1. Kalloff, H. G., and Hunter, J. H., *J. Amer. Chem. Soc.*, 1940, **62**, 158. 2. *vide Curr. Sci.*, 1943, **12**, 82.

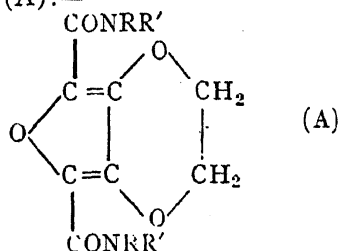
## STUDIES ON ANÆSTHETICS AND LOCAL ANÆSTHETICS

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

GILMAN<sup>1</sup> observed that  $\beta$ -diethylamino ethyl esters of acids containing aminobenzene, benzene, pyrrole, thiophene and furan rings possess low local anæsthetic action. Cook and Kreke,<sup>2</sup> 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. Degnan and Pope<sup>3</sup> prepared large number of N-alkyl N-aryl furaminines, and made the interesting observation that N-*n*-butyl N'-*p*-phenetylfuramide hydrochloride is more than three times as active as cocaine, and it is not

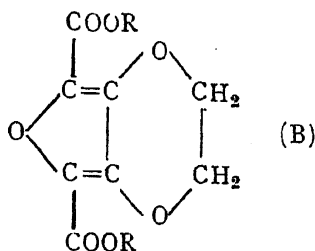
irritating to the cornea of the eye. It seemed very reasonable, therefore, that a search for new and efficient local anaesthetics in the differently (alkyl and aryl) substituted esters, amides and amidines might lead to some very interesting results.

2:5-Dicarboxy-furo-(3:4)-*p*-dioxan has been prepared starting from diglycollic acid by five steps.<sup>1</sup> 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' = C<sub>6</sub>H<sub>4</sub>·SO<sub>2</sub>NH<sub>2</sub>; 270° (decomp.)

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



- (1) R = benzyl; m.p. 126°
- (2) R = CH<sub>2</sub>·CH<sub>2</sub>·N(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>; m.p. 271°
- (3) R = CH<sub>2</sub>—CH=CH·C<sub>6</sub>H<sub>5</sub>; 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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## CHEMICAL NON-HOMOGENEITY IN CHROMITES AND ITS POSSIBLE USEFULNESS IN INDUSTRY

In the course of my investigations on the conversion of the Cr<sub>2</sub>O<sub>3</sub> of chromite to chromate, I found that, in almost all experiments, the undecomposed portion of the chromite had a higher value for the ratio Cr/Fe than the chromite as a whole. This indicated that the chromite might not be chemically homogeneous and, to test this point, two samples of chrome ore were systematically investigated.

The ores had to be repeatedly fused with Na<sub>2</sub>CO<sub>3</sub> and dissolved in sulphuric acid before they could be brought into complete solution. Eight such fusions were necessary in the case of one sample and seven in the case of the other. Even then small residues were left, which were rejected. The ores and the successive residues were mixed with their own weight of Na<sub>2</sub>CO<sub>3</sub> and heated in a platinum crucible, kept slanting, with the lid on the crucible leaving a small opening, over the full flame of a Bunsen burner for two hours. I have repeatedly found that Na<sub>2</sub>CO<sub>3</sub> fusion of chrome ore does not bring about complete solution of the ore at the first fusion or even after three or four fusions although strong heat is applied for a longer period. But this necessity for repeated fusion was an advantage in this investigation. The solution obtained after each fusion was separately analysed.

In Table I are given the percentages of Cr<sub>2</sub>O<sub>3</sub> and Fe actually obtained, the percentage of Cr<sub>2</sub>O<sub>3</sub> calculated as the percentage of the total Cr<sub>2</sub>O<sub>3</sub> and the value of the Cr/Fe ratio for each solution. The samples are numbered 1764 and 1926. Total Cr<sub>2</sub>O<sub>3</sub> per cent., total Fe per cent., and the value of the ratio Cr/Fe are respectively 49.60, 15.48 and 2.192 for 1764 and 48.29, 13.88 and 2.38 for 1926.

All the solutions of sample 1926 and only the last four solutions of 1764 were analysed for Al<sub>2</sub>O<sub>3</sub> and MgO also, besides Cr<sub>2</sub>O<sub>3</sub> and Fe. To make out the non-homogeneity more clearly, the sum of the compositions of solutions 2, 3 and 4, of 5, 6 and 7, and of all the six solutions of 1926, expressed in terms of the four molecules, MgO·Al<sub>2</sub>O<sub>3</sub>, MgO·Cr<sub>2</sub>O<sub>3</sub>, FeO, Cr<sub>2</sub>O<sub>3</sub> and FeO·Fe<sub>2</sub>O<sub>3</sub>, and calculated to 100, are given in the bottom of Table II under columns 4, 5 and 6 respectively. The actual compositions in terms of the constituents Cr<sub>2</sub>O<sub>3</sub>, Al<sub>2</sub>O<sub>3</sub>, Fe<sub>2</sub>O<sub>3</sub>, Fe and MgO are also given in the top of the table. The composition of the first solution was not taken for calculation as it contained all the magnesium silicate mixed in the ore. In the case of 1764 the pure chromite mineral present in it was 80 per cent. of the ore. The mixed magnesium silicate was freed from it by heating with a mixture of HF and H<sub>2</sub>SO<sub>4</sub> acids in which it dissolved. The percentages of Cr<sub>2</sub>O<sub>3</sub>, Al<sub>2</sub>O<sub>3</sub>, Fe and MgO present in this 80 per cent. of mineral were determined. The compositions of this, of the sum of the four solutions 5, 6, 7 and 8, and of the difference between these two are expressed and calculated in the same way as for 1926 and given in the bottom of Table II under

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.