Ac NH·C_6H_4-SO_2-N R′-C(:NH)·SR″ (II)

1. R′ = Phenyl ; R″ = Ethyl ; m.p 209-10°
2. The free base ; m p. 192-93°
3. R′ = Phenyl ; R″ = Propyl ; m.p. 206-7°
4. The free base ; m.p. 195-96°
5. R′ = Phenyl ; R″ = Butyl ; m p. 207-8°
6. The free base ; m.p. 191-92°
7. R′ = Phenyl ; R″ = Allyl ; m.p. 204°
8. The free base ; m.p. 193-94°
9. R′ = Phenyl ; R″ = Benzyl ; m.p. 205-6°
10. The free base ; m.p. 190°
11. R′ = Phenyl ; R″ = p-nitro-benzyl ; m.p. 201°
12. The free base ; m.p. 166° (decomp.)
13. R′ = p-tolyl ; R″ = Ethyl ; m.p. 204-6°
14. The free base ; m.p. 188-89°
15. R′ = p-methoxy-phenyl ; R″ = ethyl ; m.p. 200-1°
16. The free base ; m.p. 194°
17. R′ = β-naphthyl ; R″ = ethyl ; m.p. 201-2°
18. The free base ; m.p. 186-88°

These compounds await pharmacological examination.

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August 9, 1944. V. MAHADEVAN

1 *Curr. Sci.*, 1943, **12**, 325.

SYNTHESIS OF SULPHANILAMIDE COMPOUNDS CONTAINING ALKYL-THIOL-1-SUBSTITUTED THIOSEMICARBAZIDES

IN a previous communication[1] sulphanilamide compounds with thiosemicarbazide, and 4-phenyl-thiosemicarbazide have been described. Due to the pronounced basic character of the hydrazino group (-NH.NH_2) in all these cases acetamino benzene suphonylchloride reacted with the nitrogen in position 1. It seemed to be interesting to prepare sulphanilamido derivatives of 1-N-aryl thiosemicarbazides. There being no basic group like (.NH.NH_2) present in 1-substituted aryl-thiosemicarbazides they did not react with the sulphochloride. But 1-N-aryl-thiosemicarbazides reacted readily with alkyl halides to give the corresponding alkyl-thiol derivatives which reacted readily with acetaminophenylsulphochloride to give the compounds of the general formula (I) or (II)

Ac·NH·C_6H_4·SO_2-N = C-NH·NH·Ph (I)
|
SR

Ac·NH·C_6H_4-SO_2-N———C : NH (II)
| |
NHPh SR

1. R = Ethyl ; m p. 104-7°
2. R = Propyl ; m.p. 91°
3. R = Butyl ; m p. 110°
4. R = Allyl ; m.p. 83-6°
5. R = Benzyl ; m.p. 62-7°
6. R = p-nitrobenzyl ; m.p. 125°

Further work is in progress to elucidate as to whether the sulphanilamide compounds possess the structure (I) or (II).

The pharmacological studies of these compounds are in progress.

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1. *Curr. Sci.*, 1943, **12**, 150.

STUDIES ON ANÆSTHETICS AND LOCAL ANÆSTHETICS

N-Substituted Amides and Esters of Nicotinic, Picolinic, and *Iso*-Nicotinic Acids

OF the three isomeric pyridine monocarboxylic acids, the β-variety, *viz.*, nicotinic acid has, in recent years, assumed great importance as an accessory food factor belonging to the vitamin B complex[1] with great therapeutic possibilities. Further its diethylamide, familiarly known as 'Coramine', is a reputed cardio-respiratory stimulant.[2] A further point of interest in this acid is that its N-substitued ethanolamine and homologous esters have been shown to possess local anæsthetic activity.[3]

The present work, therefore, involves the preparation of the three isomeric acids from β- and γ-picolines isolated from the middle oil fraction of Indian coal-tar, and the α-acid from a sample of α-picoline. The β-acid was also prepared by the decarboxylation of quinolinic acid obtained by the oxidation of qinoline (*i*) isolated from Indian coal-tar, and (*ii*) synthesised by Scraup's method.

Though there is considerable literature on the oxidation of the picolines and quinoline, the available information was found to be very inadequate, and the detailed conditions for their convenient preparation had to be worked out using $KMnO_4$ solution at temperatures below 100° C., and isolation of the acids through the copper salts. Results of our experiments are given below:—

Raw material used	Acid obtained	Yield (% on theory)	M.P	Equivalent
1. α-Picoline B.P. 124-29°	Picolinic acid	25	135-136°	123·4
2 Mixture of β & γ-picoline B.P. 140-47°	*{ Nicotinic acid	11	225-226°	125·5
	*{ Isonicotinic acid	12·5	305-306°	122·1
3. Quinoline B.P. 230-35°	Quinolinic acid	33	180° (decomp	83·9
4. Quinolinic acid	Nicotinic acid	80	232°	125·2

* Separated from the oxidation product by repeated crystallisation from absolute alcohol.

Coramine (b.p. 172-173°/19 mm.) has been prepared (yield, 68·8 per cent.) from nicotinic acid, *via.* its acid chloride, by the action of diethylamine also prepared in this laboratory.

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).

β-Chlorethyl picolinate, C_5H_4N-CO_2-CH_2.CH_2.Cl (b.p. 136-138°/5-7 mm.) and β-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_5H_4N-$COO.CH_2$.$CH_2.NHC_6H_4.OCH_3$, 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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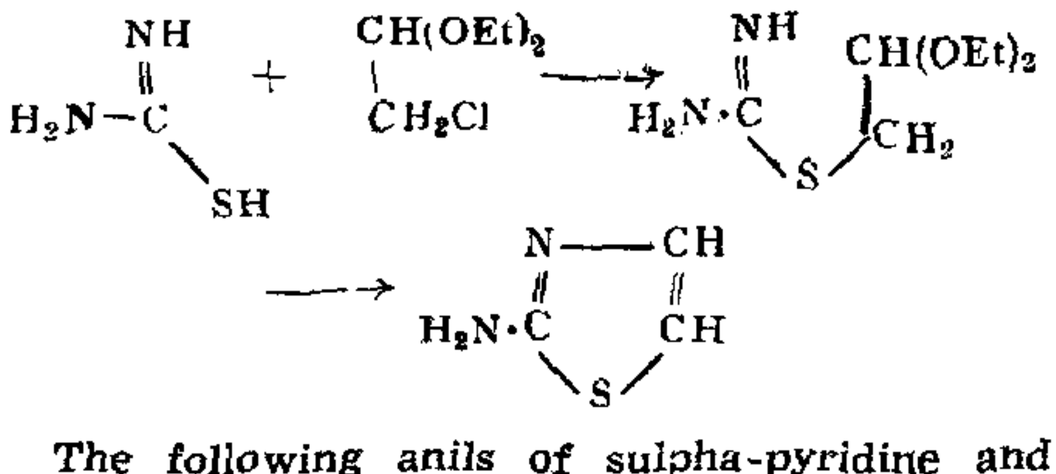
1 *Indian Med. Gaz.*, 1942, **77**, 98. 2. *J Amer. Pharm. Assoc.*, 1944, **33**, 72. 3. *J. Amer. Chem. Soc.* 1942, **64**, 1721.

N¹ AND N⁴ SUBSTITUTED SULPHANILAMIDES

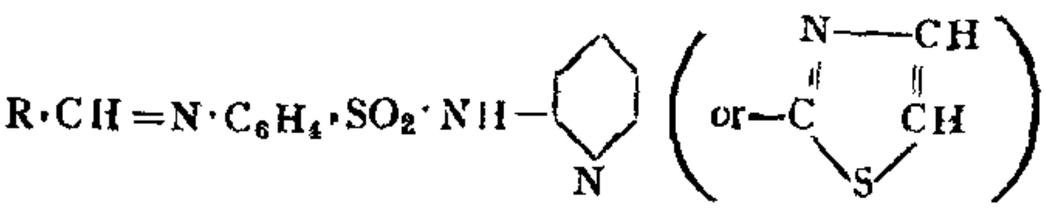
Part I. Schiff's Base of Sulpha-pyridine and Sulpha-thiazole

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[1] 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[2]) 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 sulphapyridine	M.P. of anils of sulphathiazole
C_6H_5	240°	202°
p-$OCH_3 \cdot C_6H_4$	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°
m-$NO_2 \cdot C_6H_4$	254°	231°
m-$Cl \cdot C_6H_4$	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 sulphanyl derivatives, is in progress.

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August 9, 1944. K. R. DORASWAMI.

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[1] 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. Degnan and Pope[3] prepared large number of N-alkyl N-aryl furaminines, and made the interesting observation that N-*n*-butyl N'-*p*-phenetylfuramidine hydrochloride is more than three times as active as cocaine, and it is not