

ing the mechanism of the reaction involved has been further acknowledged by Buck.⁵

The only instance of the preparation of oxazoles linked to the naphthalene ring recorded in literature is that regarding the synthesis of 2- α -naphthyl, 5-phenyl oxazole and 2-phenyl, 5- α -naphthyl oxazole by Lister and Robinson⁶ who obtained them by the action of conc. H_2SO_4 on α -naphthoyl, ω -amino acetoveratrone and N-benzol, ω -amino, α -acetonaphthone respectively. The two naphthyl oxazole derivatives were feeble bases and exhibited fluorescence more intense than those of other oxazoles in solutions, a property which was supposed to be dependent on the long uninterrupted chains of conjugate double linkages connecting the aromatic nuclei through the oxazole ring.^{6,7}

We have carefully repeated the preparation of 2-phenyl 5- α -naphthyl oxazole using concentrated sulphuric acid as directed by Lister and Robinson as well as phosphorous oxychloride both with and without the addition of toluene as the cyclising agents. Although according to Lister and Robinson the cyclising agent of choice in the synthesis of 2-naphthyl, 5-phenyl oxazole is conc. H_2SO_4 , the cyclisation of N-benzil, ω -amino, α -acetonaphthone is best effected by employment of phosphoryl chloride. We have also studied the action of conc. H_2SO_4 on the amides III, V and VII. A solution of III in five parts of conc. H_2SO_4 , after heating at 100° for 5 minutes and dilution with ice-water gave in addition to resinous matter only a trace of basic matter which could not be characterised. The action of H_2SO_4 on the amides V and VII at room temperature was nil, the original amides being completely recoverable at the conclusion of the experiments. However, the action of sulphuric acid at 100° for 5 minutes on VII gave rise to a pale yellow solid separating from alcoholic-acetic acid as a pale yellow crystalline powder exhibiting violet fluorescence in alcoholic or sulphuric acid solution and melting at 308-09° dec. The same product is also obtainable from VIII by similar action of H_2SO_4 . The substance appears to be acidic in character and has not yet been fully investigated.

Although it is usual to consider oxazoles as capable of breaking down to acids and amides on evaporation with hydrochloric acid and that oxidants and reducing agents frequently rupture the oxazole ring with great ease,⁸ the oxazoles derived from naphthalene should be considered as fairly stable. We had formerly reported¹ that oxidising agents such as alkaline hydrogen peroxide, dilute nitric acid and potassium permanganate in acetone solution had no action on the base VIII and that all the substances (II, IV, VI and VIII) then synthesised were resistant to reduction by the usual chemical methods. Some of the reducing agents used were zinc dust and sulphuric acid, amalgamated zinc and hydrochloric acid and tin and hydrochloric acid. The action of a few mineral acids on the above bodies has now been studied. The base IV by heating with con. HCl at 150-60° for 4 hours gave rise to intractable tarry matter, while simple refluxion with a mixture of acetic and hydrobromic acids for 5 hours resulted only in the

recovery of IV. The action of acetic acid-hydrobromic acid on VIII yielded an acidic principle, separating from alcohol in pale yellow needles, m.p. 193-95° after softening at 191° and exhibiting violet fluorescence in alcoholic solution. Hydrobromic acid had no action whatsoever on 2-phenyl, 5- α naphthyl oxazole.

Although conclusive evidence by degradation studies is as yet unavailable, there can be no doubt that from their method of formation and properties of feeble basicity and intense violet fluorescence in neutral organic solvents,^{4,6,7,9,10} the substances hitherto considered to be benzoisoquinolones, possess in reality the naphthalenic oxazole structures. The names of the compounds II, IV, VI and VIII, viz., 1-methyl, 3:4-dihydro, 4-keto, 5:6-1-methyl, 3:4-dihydro, 4-keto, 7:8-, 1-methyl, 3:4-dihydro, 4-keto, 7-methoxy, 5:6- and 1-phenyl, 3:4-dihydro, 4-keto, 7-methoxy, 5:6-benzoisoquinolines, therefore, should be corrected as 2-methyl, 5- α , naphthyl-, 2-methyl, 5- β , naphthyl-, 2-methyl, 5-(4', methoxy), naphthyl- and 2-phenyl, 5-(4', methoxy-) naphthyl oxazoles respectively.

Presidency College,
Madras,
July 26, 1944.

B. B. DEY.
S. RAJAGOPALAN.

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N¹-SULPHANILYL-ISOTHIOUREAS

In continuation of the work already reported,¹ the following compounds of the general formula (I) have been made:—



1. R = $CH_2 \cdot CH_2 \cdot CH(CH_3)_2$; m.p. 186°
2. The free base, m.p. 145-46°
3. R = $CH_2 \cdot C_6H_5$; m.p. 173°
4. The free base, m.p. 143-46°
5. R = $CH_2 \cdot C_6H_4 \cdot NO_2(p)$; m.p. 214-25°
6. The free base, m.p. 153-55°
7. R = $CH_2 \cdot C_6H_4 \cdot OCH_3$; m.p. 138-40°
8. The free base, m.p. 89-92°
9. $Ac \cdot NH \cdot C_6H_4 \cdot SO_2 \cdot NH \cdot C(:NH)S \cdot CH_2$
 $Ac \cdot NH \cdot C_6H_4 \cdot SO_2 \cdot NH \cdot C(:NH)S \cdot CH_2$
m.p. 255°
10. The free base; m.p. 175-77°

The compound No. 1 was hydrolysed with 10 per cent. aqueous HCl, to get the corresponding free base No. 2, and compounds Nos. 3, 5, 7 and 9 were hydrolysed with alcoholic HCl to get the corresponding free bases.

The following sulphanilamide derivatives of N-aryl substituted pseudo-thioureas of the general formula (II) have been made:—

- Ac·NH·C₆H₄·SO₂·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.

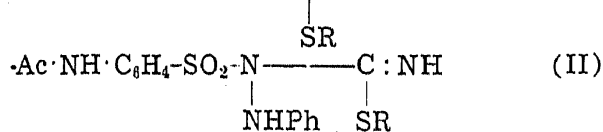
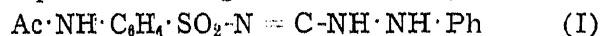
Organic Chemistry Laboratories,
Dept. of Pure & Applied Chemistry,
Indian Institute of Science,
Bangalore,
August 9, 1944.

P. C. GUHA.
V. MAHADEVAN

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

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

In a previous communication¹ sulphanilamide compounds with thiosemicarbazide, and 4-phenyl-thiosemicarbazide have been described. Due to the pronounced basic character of the hydrazino group (-NH.NH.) in all these cases acetamino benzene sulphonylchloride 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.) 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).



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.

Organic Chemistry Laboratories,
Dept. of Pure & Applied Chemistry,
Indian Institute of Science,
Bangalore,
August 9, 1944.

P. C. GUHA.
V. MAHADEVAN

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 complex¹ 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-substituted 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 quinoline (i) isolated from Indian coal-tar, and (ii) synthesised by Scaup'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 KMnO₄ 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 Isonicotinic acid	{ 11 12.5	{ 225-226° 305-306°	{ 125.5 122.1
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, viz. its acid chloride, by the action of diethylamine also prepared in this laboratory.