[CONTRIBUTION FROM THE GEORGE WASHINGTON UNIVERSITY]

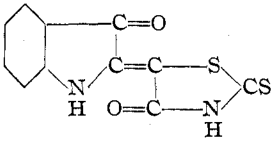
THE CONDENSATION OF RHODANIC ACIDS WITH ISATIN. 3-ARYL-RHODANAL-$\Delta^{5,3'}$-OXINDOLES[1]

BY RAYMOND M. HANN

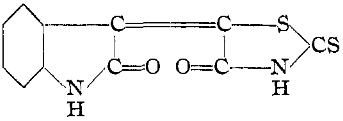
RECEIVED FEBRUARY 9, 1925 PUBLISHED APRIL 4, 1925

A recently published article[2] dealing with the condensation of isatin and isatin-α-chloride with certain hydantoins has suggested the advisability of publishing the work in the same field, carried on in this university, in an effort to prevent possible duplication of the study of reactions herein discussed. The compounds now described were prepared as part of an investigation of the effect of constitutional variation upon absorption. The physical measurements are as yet incomplete and are reserved for a later publication.

The first recorded condensation of an isatin derivative with rhodanic acid was by Felix and Friedlaender[3] who prepared "5-thiazolthiol-2-indole indigo" from rhodanic acid and α-isatin-anilide. Sometime later Andreasch[4] condensed isatin with rhodanic and phenyl-rhodanic acids and obtained what he believed to be 5-ψ-indoxy-rhodanine I and 3-phenyl-5-ψ-indoxylidene-rhodanine, assuming the former derivative to be identical with the compound of Felix and Friedlaender. Recently it has been conclusively shown, however, by Granacher and Mahal[5] that the condensation takes place in the 3-position to give β-rhodanal-oxindole II. This compound gives a characteristic pyridine derivative and upon treatment with sodium hydroxide gives indoxyl-β-sulfhydrylic acid, which is readily reduced to oxindole-β-acetic acid by zinc and concd. hydrochloric acid. The isomeric-α-rhodanal-oxindole derivatives result from the interaction of rhodanines with isatin chloride and isatin-anilide as reported by Felix and Friedlaender.[3] These substances yield oxindole-α-sulfhydrylic acids upon treatment with alkalies.



I



II

Within the past few months Hill and Henze[2] have condensed isatin chloride and isatin with hydantoins and thiohydantoins and obtained both the

---

[1] This problem was suggested by Professor Marston T. Bogert, Columbia University, at the Washington meeting of the American Chemical Society, 1924.

[2] Hill and Henze, THIS JOURNAL, **46**, 2806 (1924).

[3] Felix and Friedlaender, *Monatsh.*, **31**, 55 (1910).

[4] Andreasch, *ibid.*, **38**, 121 (1917).

[5] Granacher and Mahal, *Helvetica Chim. Acta*, **6**, 467 (1923).

alpha and the beta isomers of hydantoin-oxindole and of 3-phenyl-2-thiohydantoin-oxindole.

The condensation of rhodanic acids with isatin-α-chloride and isatin-anilide is now being studied in an effort to determine the effect of selective condensation of the 2- and 3-positions of the isatin ring upon the absorption spectra of the isomeric compounds.

Experimental Part

The general method of preparation was to dissolve about 3 g. of the rhodanic acid in 50 cc. of hot glacial acetic acid containing 5 g. of fused sodium acetate, add the molecular quantity of isatin dissolved in 25 cc. of glacial acetic acid, and heat the mixture under a reflux condenser until condensation took place. The condensation product separated as a red, crystalline material. When the mixture had cooled, the condenser was washed down with water, and an excess of water was added to the reaction mixture. The separated β-rhodanal-oxindole was then filtered off, washed, and recrystallized from acetic acid. The yields were usually 95–100%.

All the derivatives were red, crystalline or microcrystalline compounds, soluble in hot glacial acetic acid, sparingly soluble in cold glacial acetic acid, insoluble in water and most organic solvents. They dissolve in concd. sulfuric acid with formation of deep red solutions. With the exception of the ψ-cumidyl derivative (m. p., 218–219°), all melt above 300°.

The data thus far obtained are given in Table I.

TABLE I

DATA ON 3-ARYL-RHODANAL-$\Delta^{5,3'}$-OXINDOLES

	Analysis			
	Kjeldahl-Gunning-Arnold method			
			Nitrogen	
3-Aryl-Rhodanal- -$\Delta^{5,3'}$ Oxindole	Weight G.	0.1 N acid consumed Cc.	Calcd. %	Found %
Phenyl	0.1000	5.9	8.31	8.26
o-Tolyl	.0993	5.4	7.66	7.72
m-Tolyl	.1153	6.3	7.66	7.65
p-Tolyl	.1129	6.2	7.66	7.69
ψ-Cumidyl	.1068	5.3	7.23	6.95
o-Anisidyl	.1041	5.5	7.60	7.40
p-Anisidyl	.1018	5.5	7.60	7.56
4-*m*-Xylidyl	.1385	7.5	7.64	7.58
2-*p*-Xylidyl	.1037	5.6	7.64	7.57
α-Naphthyl	.1823	9.5	7.21	7.20
β-Naphthyl	.1066	5.4	7.21	7.10

Approximate measurements of the absorption of the phenyl and *p*-tolyl compounds with a Hilger wave-length spectrometer provided with a Nutting photometer have been made by W. C. Holmes, of the Color Laboratory of the Bureau of Chemistry. In concentrations of one part in 20,000 in glacial acetic acid these derivatives show maximum absorption at 430 and 433 $\mu\mu$, respectively.

Summary

Isatin has been condensed with phenyl, *o*-, *m*-, and *p*-tolyl-, ψ-cumidyl-, *o*- and *p*-anisidyl-, 4-*m*- and 2-*p*-xylidyl-, α- and β-naphthyl-rhodanic acids to yield the corresponding 3-aryl-rhodanal-$\Delta^{5,3'}$-oxindoles.

WASHINGTON, D. C.

NOTES

Glucosides of the Navel Orange.[1]—Hesperidin has long been known to be a constituent of many varieties of citrus fruits. Chemically, it is a member of the large group of glucosides built around phenolic nuclei. As far as we are aware, no satisfactory explanation has yet been offered as to the physiological functions of members of this group.

The relative proportion of hesperidin present in unripe oranges is greater than in ripe fruit, but O. Tunmann[2] points out that it forms in the young plant and persists throughout its life. The total quantity of hesperidin in a given orange probably does not decrease upon ripening of the fruit, although its percentage decreases due to the increase in the weight of the fruit.

W. Pfeffer[3] reported the occurrence of hesperidin in practically all parts of *Citrus Aurantium* Risso except the seeds and oil cells. He mounted sections in alcohol, whereupon the hesperidin crystals became visible. He states that hesperidin occurs *in solution in the living cell* but raises the question as to the conditions under which this is possible, since the glucoside is nearly insoluble in water and dilute acids.

It is the purpose of this note to present certain evidence bearing on the mode of occurrence of hesperidin in the plant, and its possible physiological function.

Precipitation of Hesperidin in Frozen Oranges.—Navel and Valenica oranges, within a few days after freezing on the tree, develop small, white crystalline aggregates imbedded in the endocarp or section covering tissue. These have been called hesperidin.[4] Further, in the case of navel oranges, these aggregates disappear usually within three months after freezing. In Valencia oranges we have found them eight months after freezing.

---

[1] The following observations were made in the course of related work on certain constituents of the Navel Orange. Their incomplete nature is fully recognized. However, the problems presented appear to be of sufficient biochemical interest to warrant the publication of this note with a view to opening a field whose further investigation may prove inviting. Other demands on the writer's time prevent his following the work further at present.

[2] Tunmann, "Pflanzenmicrochemie, Gebrüder Borntraeger chemie," Berlin, **1913**.

[3] Pfeffer, *Bot. Z.*, **32,** 529 (1874).

[4] Univ. California Agr. Expt. Sta., *Bull.*, **304,** 257 (1919).