with toluene–hexane followed by repeated recrystallization from dilute ethanol raised the m. p. to 205–208°.

The experiment was repeated using ether as a solvent. This is not satisfactory because of the low solubility of the methene in ether. With no added catalyst the reaction proceeded slowly. Tripyrrylmethane X began to separate from the solution after forty minutes. The ether was evaporated on a steam-bath; yield, 97%, m. p. 191–192°.

With dioxane as solvent but with the substitution of hydrogen chloride for potassium bisulfate, only the hydrochloride of methene IX could be isolated; yield, 100% of a product melting with decomposition at 206°. This exactly parallels the cleavage of the tripyrrylmethane X which gave a copious precipitate of the salt of methene IX after five seconds and a quantitative yield when filtered after one minute.

An attempted condensation of 2,4-dimethyl-3-carbethoxy-5-formylpyrrole with 2,4-dimethyl-3-carbethoxy-pyrrole to give tripyrrylmethane X in dioxane with potassium bisulfate as catalyst was unsuccessful under the conditions which succeeded in giving tripyrrylmethane IV from the corresponding aldehyde.

Cleavage of Tripyrrylmethane IV with Hydrogen Chloride.—One and one-tenth grams of tripyrrylmethane IV was suspended in 185 cc. of dry ether and cooled in an ice-bath. Dry hydrogen chloride was passed in for ten minutes. The tripyrrylmethane dissolved with a light yellow color which rapidly gave way to orange. After two hours the solution was cherry-red. It was allowed to stand in an icebox and was wrapped with a towel to protect it from light. After two days it was deep violet but no crystals had appeared. After one month crystals had begun to appear on the walls of the vessel. The mixture was then allowed to warm up to room temperature and to stand for one year. The mother liquor was drained off and neutralized with calcium hydroxide and then chromatographed over alumina using carbon tetrachloride as solvent. The colorless fore-runs contained a dissolved oil but no crystalline derivative was obtained from it.

The crystals on the wall of the vessel were dissolved in chloroform and chromatographed over calcium hydroxide to prepare the free base of the methene. The methene solution was evaporated to dryness and taken up in a mixture of 25% chloroform and 75% carbon tetrachloride (both solvents freshly treated with lime to remove acidic decomposition products). The methene layer developed below a much darker layer on the chromatogram and was separated and eluted with purified chloroform. The solution was evaporated in a weighed flask; yield, 0.223 g. or 33%. It was identified as methene IX by its decomposition point, 187°, and by hydrogenation to 3,5,3′,5′-tetramethyl-4,4′-dicarbethoxy-dipyrrylmethane, m. p. 229°.

Summary

1. It has been discovered that dipyrrylmethenes react with pyrroles with free alpha positions to form tripyrrylmethanes.

2. Application of this reaction permits direct velocity comparisons which make it possible to study the mechanism of the formation of dipyrrylmethenes.

3. It has been demonstrated by actual isolation that a tripyrrylmethane is an intermediate in a "normal" dipyrrylmethene synthesis.

4. It is inferred from comparisons of velocity that this dipyrrylmethene is an intermediate in the formation of the tripyrrylmethane and is, therefore, an intermediate in its own formation.

5. Cleavage of a "stable" tripyrrylmethane by hydrogen chloride alone has been demonstrated.

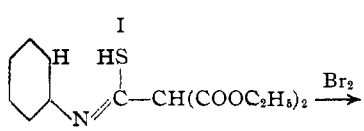
BALTIMORE, MARYLAND RECEIVED OCTOBER 23, 1939

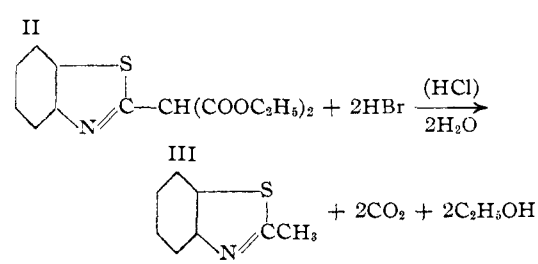
[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

The Action of Bromine on Certain Thioamides

BY DAVID E. WORRALL AND ARTHUR W. PHILLIPS

The thioamide obtained by the action of two equivalents of *p*-tolyl isothiocyanate on ethyl acetonedicarboxylate reacts spontaneously with bromine.[1] In order to present a structural interpretation of the product formed here, a study of the action of bromine on the addition product of malonic ester and phenyl isothiocyanate is here reported. The course of the reactions involved can be outlined as follows





The product resulting from the loss of hydrogen bromide, and cyclization, forms a salt with alcoholic potassium hydroxide and also acts enolic toward a Grignard reagent. With hydrochloric acid, it undergoes hydrolysis and decarboxylation, to yield the well-known 1-methylbenzothiazole.

(1) Worrall, THIS JOURNAL, 61, 2966 (1939).

Experimental

Benzothiazole-1-diethyl Malonate.—To 10 g. of I, prepared from malonic ester and phenyl isothiocyanate dissolved in glacial acetic acid, was added slowly the molar equivalent of bromine in acetic acid. The mixture, which became turbid from the separation of small amounts of sulfur and other decomposition products, was immediately poured into water. After three crystallizations from alcohol, the new product was obtained in small needles, m. p. 138–139°; yield approximately 5 g.

Anal. Calcd. for $C_{14}H_{15}NO_4S$: C, 57.3; H, 5.1. Found: C, 56.9; H, 5.1.

II was soluble in cold concd. hydrochloric acid, separating unchanged on dilution with water. It changed into a powder in the presence of alcoholic potassium hydroxide, which was soluble in water and which was changed by hydrochloric acid into the original substance. A precipitate was formed and bubbles of gas escaped when an ether solution of the thiazole was mixed with methylmagnesium iodide from which the same thiazole was recovered on the addition of water.

1-Methylbenzothiazole from II.—Ten grams of II was heated for two hours with concd. hydrochloric acid, the mixture was diluted with water, filtered and steam distilled until the distillate was clear. Then an excess of alkali was added and steam distillation resumed. A colorless oil with a strong pyridine-like odor resulted. Its identity with an authentic sample of 1-methylbenzothiazole was confirmed by a boiling point determination, and an analysis.

1-Benzothiazoylacetylacetone.—The thiazole prepared from acetylacetone and phenyl isothiocyanate separated from ligroin in silky needles, m. p. 155°. It was rapidly changed by hot alkali, more slowly by acid, into methyl benzothiazole.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.8; H, 4.7. Found: C, 62.1; H, 4.5.

Summary

It has been shown that bromine converts the monothioanilide of carbethoxyethylmalonate into benzothiazoylmalonic ester, which is changed by hydrolysis into methylbenzothiazole.

MEDFORD, MASS. RECEIVED OCTOBER 9, 1939

[CONTRIBUTION FROM THE BURROUGHS WELLCOME & CO. U. S. A. EXPERIMENTAL RESEARCH LABORATORIES]

3-Methyl-3,4-dihydroisoquinolines and 3-Methyl-1,2,3,4-tetrahydroisoquinolines[1]

BY WALTER S. IDE AND JOHANNES S. BUCK

Work in progress on the pharmacological effects of various substituting groups in the isoquinoline nucleus necessitated the preparation of a series of 3-methyl-3,4-dihydroisoquinolines and 3-methyl-1,2,3,4-tetrahydroisoquinolines (analogous to norhydrastinine and dihydronorhydrastinine). There are a number of scattered isoquinoline compounds with a 3-methyl group in the literature, but the methods of preparation vary widely and in many cases essential details are lacking. Most of the compounds are also substituted in the 1-position.

The authors therefore set out to devise a series of general reactions for the preparation of the desired 3-methylisoquinoline derivatives. By the method selected three series of compounds, containing as substituents 6,7-dimethoxyl, 6,7-methylenedioxyl and 6,7-dihydroxyl, were prepared and other series doubtless could be made in a similar way. The isoquinolines were prepared by cyclizing formyl-β-phenylisopropylamines (Bischler–Napieralski reaction). This required fairly large amounts of β-phenylisopropylamines. The methods of Mannich and Jacobsohn[2] and of Merck[3] for the preparation of these amines were not investigated since they depend on naturally-occurring materials and are therefore not general. The nitropropenyl method of Alles[4] also was not investigated. The most feasible route appeared to be a series of reactions similar to those used for phenethylamines[5,6] but attempts to prepare disubstituted α-methylcinnamic acids by the method of Bogert and Davidson[7] failed, the condensation of disubstituted benzaldehydes with methyl ethyl ketone not proceeding in the desired way. Recourse therefore was had to the Reformatsky reaction and the required α-methylcinnamic acids were prepared by condensing ethyl α-bromopropionate with the aldehyde, followed by the dehydration and saponification of the product. An alternative method used was the Claisen condensation of the aldehyde with ethyl propionate, followed by saponification. The α-methylcin-

(1) This work is part of a joint research being carried out in collaboration with a pharmacological group at the above laboratories.

(2) Mannich and Jacobsohn, *Ber.*, **43**, 189 (1910).
(3) German Patent 274,350.
(4) United States Patent 1,879,003.
(5) Buck, THIS JOURNAL, **54**, 3661 (1932).
(6) Woodruff and Conger, *ibid.*, **60**, 465 (1938).
(7) Bogert and Davidson, *ibid.*, **54**, 334 (1932).