In the preparation of cyclohexyl thiocyanate ammonium thiocyanate was used instead of the potassium salt. This proved to be unsatisfactory due to some of it being carried into the ether extract; it may have been responsible for the low yield.

The thiocyanates are water-white liquids with an ethereal odor, quite strong in the amyl and cyclohexyl but faint in the tridecyl compound.

They are insoluble in water, but readily soluble in ether, carbon tetrachloride, benzene, absolute methyl and ethyl alcohols, glacial acetic acid and ethyl acetate. The mutual solubility with 96% ethanol appears to decrease with increasing molecular weight of the thiocyanate.

## Summary

The series of normal aliphatic thiocyanates has been completed through the thirteen carbon member; cyclohexyl thiocyanate has been prepared.

ANNAPOLIS, MARYLAND RECEIVED NOVEMBER 3, 1934

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[CONTRIBUTION FROM THE ORGANIC CHEMICAL LABORATORY OF THE UNIVERSITY OF FLORIDA]

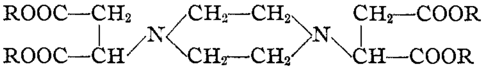
# Derivatives of Piperazine. III. Reactions with Unsaturated Esters, Part 1

BY C. B. POLLARD, J. P. BAIN AND DAVID E. ADELSON

Reference to previous work on the addition of amines to esters of fumaric and maleic acids reveals that only two cases have been reported wherein the amine adds to the ethenoid linkage. These are ammonia and methylamine, which yield under drastic conditions aspartic ester and methylaspartic ester, respectively.[1]

More recently Clemo and Graham[2] have reported that methyl maleate is isomerized into the corresponding fumarate in the presence of a variety of primary and secondary amines, including piperazine. They state that no additive complexes involving the ethenoid linkage and the catalyst could be isolated, although they admit that there is no adequate reason why some of the additive complexes should not reach a stable maturity. These authors postulate a mechanism involving a coördinate link between the hydrogen atom of the base and the carbonyl oxygens of the ester. This would lead to an uncertain electronic system and thus to a very unstable complex. In this fashion Clemo and Graham attempt to account for the non-isolation of an intermediate additive compound.

In this paper stable compounds involving the addition of piperazine to the ethenoid linkage of a series of esters of fumaric and maleic acids are described (Table I). The mechanism of the reaction between piperazine and the maleic ester seems to involve two consecutive stages, first, a conversion of the ester from the maleinoid to the fumaroid form, and, second, the addition of the piperazine to the ethenoid linkage of the fumarate. When one mole of anhydrous piperazine is added to two moles of methyl maleate, the latter isomerizes instantly to the fumarate. A mixed melting point determination indicates that a mixture of piperazine and methyl fumarate is now present. Likewise, piperazine can be identified in the mixture by conversion into the 1,4-dinitroso compound.[3] Upon heating this mixture to 100° and subsequently extracting with dioxane, pure piperazino-1,4-bis-(methyl succinate) crystallizes out. When the ester is initially in the fumaroid form, the addition takes place directly. In either case identical compounds are formed resulting from the addition of one molecule of piperazine to two molecules of the ester



$$\begin{array}{lllll} ROOC-CH_2 & & CH_2-CH_2 & & CH_2-COOR \\ \quad | & N & & N & \quad | \\ ROOC-CH & & CH_2-CH_2 & & CH-COOR \end{array}$$

Piperazino-1,4-bis-(alkyl succinate)

The reactions are definitely exothermic.

The authors have duplicated the experimental work of Clemo and Graham[2] with special attention to the conversion taking place in the presence of piperazine. That this isomerization does not concern the formation of an additive compound involving the ethenoid linkage is shown by the fact that the type of compound described below does not cause the transformation of pure methyl maleate into the fumarate.

These syntheses are effected by refluxing for a short time 0.05 mole of piperazine and 0.1 mole of the ester in 100 cc. of the appropriate solvent. Upon cooling, the pure additive compound crystallizes out. These compounds can also be made in the proper solvent at room temperature. Either the hexahydrate or the anhydrous form of piperazine may be used, although the latter is preferable in most cases. Anhydrous piperazine may easily be prepared by placing the hexahydrate *in vacuo* over solid potassium hydroxide for one week. The average yield of

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[1] Körner and Menozzi, *Ber.*, **21R**, 86 (1888); **22R**, 735 (1889).

[2] Clemo and Graham, *J. Chem. Soc.*, 213 (1930).

[3] Ladenburg, *Ber.*, **24**, 2401 (1891).

the piperazino-1,4-bis-(alkyl succinate) is 65 to 70% of the theoretical. These derivatives are soluble in dilute hydrochloric acid and are reprecipitated unchanged by the addition of alkali.

In an attempt at proof of structure, anhydrous piperazine and methyl bromosuccinate, prepared by the method of Volhard,[4] were refluxed in dioxane. Only piperazine dihydrobromide and methyl fumarate were formed. The former was identified by conversion into 1,4-dinitrosopiperazine[3] and the latter by a mixed melting point determination with an authentic sample. Piperazino-1,4-bis-(methyl succinate) was refluxed with excess alcoholic potassium hydroxide for an hour, piperazino-1,4-bis-(potassium succinate) crystallizing out from the hot solution. This potassium salt was boiled successively with alcohol and dioxane and dried for four hours at 105°. Subsequent analyses justified the formula assigned to the salt, and hence corroborated the structure of the piperazino esters.

TABLE I

PHYSICAL CONSTANTS AND ANALYSES OF THE PIPERAZINO-1,4-BIS-(ALKYL SUCCINATES)

| Ester | M. p., °C., corr. | Solvent cryst. | Nitrogen analyses, % Calcd. | Found |
|---|---|---|---|---|
| Methyl | 158.5–159 | Dioxane | 7.49 | 7.45 |
| Ethyl | 96–96.5 | Dioxane | 6.51 | 6.53 |
| Isopropyl | 90–90.5 | Heptane | 5.76 | 5.72 |
| *n*-Propyl | 88 | Hexane | 5.76 | 5.65 |
| *n*-Butyl | 48–48.5 | Hexane | 5.17 | 5.12 |
| Benzyl | 112–113 | Methanol | 4.13 | 4.11 |
| Cyclohexyl | 121 | Hexane | 4.33 | 4.20 |
| Potassium (salt) | K, 33.24 | 33.04 | 5.95 | 6.04 |

The authors wish to express their appreciation to Dr. H. G. Shaw and Mr. G. A. Barber for considerable analytical data presented in this paper.

## Summary

1. The preparation and properties of compounds arising from the addition of piperazine to the ethenoid linkage of ethylene dicarboxylic esters have been described.

2. Syntheses involving mono-substituted piperazines and other amines with these and other unsaturated esters are in progress.

3. The reaction velocities of these syntheses are being studied.

GAINESVILLE, FLORIDA RECEIVED NOVEMBER 8, 1934

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(4) Volhard, *Ann.*, **242**, 148 (1887).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

# The Mechanism of Carbohydrate Oxidation. XVII.[1] The Preparation and Structure of Alpha-Methyl-*l*-arabinomethyloside[2]

BY DONALD ROBERT SWAN AND WM. LLOYD EVANS

The chemistry of the methyltetroses is far from complete. Of the eight possible configurations in this series only three have been reported in the literature. Ruff[3] prepared *l*-arabinomethylose[4] by the degradation of calcium rhamnonate with hydrogen peroxide and basic ferric acetate. This sugar was also reported by Fischer[5] as a degradation product of rhamnose (*l*-mannomethylose) by the Wohl reaction. Votoček[6,7] prepared *d*-arabinomethylose from isorhodeose (*d*-glucomethylose) by the Ruff reaction mentioned above, and *d*-lyxomethylose from rhodeose (*d*-galactomethylose, *d*-fucose) by the Wohl reaction. Deulofeu[8] obtained *l*-arabinomethylose osazone from rhamnonic amide by the Weerman degradation, but reported no data with reference to the yield.

None of these sugars have ever been obtained in crystalline form nor has a glycoside of any of them been reported previously. Likewise, the ring structure, although practically certain to be of the butylene oxide type, has not been proved.

In quantitative experiments carried out by us, $\alpha$-methyl-*l*-arabinomethyloside showed the rapid hydrolysis characteristic of $\gamma$-glycosides[9] (Fig. 1). This new glycoside is of interest in that it is a key compound in the scheme of ring structure proof developed by Hirst, Haworth and others,[10] because a pyranose structure is excluded. We

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(1) Contribution XVI of this series, THIS JOURNAL, **55**, 4957 (1933).

(2) This paper was abstracted from the dissertation submitted in the Autumn, 1934, by D. R. Swan to the Graduate School of The Ohio State University for the Ph.D. degree. It was reported at the Cleveland Meeting of the American Chemical Society, September, 1934 (W. L. E.).

(3) O. Ruff, *Ber.*, **35**, 2362 (1902).

(4) According to the nomenclature proposed by Votoček for the methylpentoses [*Bull. soc. chim.*, [4] **43**, 18 (1928)] and extended by Micheel to the methyltetroses [*Ber.*, **63**, 347 (1930)], the methyltetrose having the *l*-arabinose configuration is named *l*-arabinomethylose. On this basis we have named the glycoside $\alpha$-methyl-*l*-arabinomethyloside.

(5) Emil Fischer, *ibid.*, **29**, 1381 (1896).

(6) E. Votoček and C. Krauz, *ibid.*, **44**, 3287 (1911).

(7) E. Votoček, *ibid.*, **50**, 35 (1917).

(8) Deulofeu, *J. Chem. Soc.*, 2605 (1930).

(9) W. N. Haworth, *Ber.*, **65A**, 43 (1932).

(10) W. N. Haworth, "The Constitution of Sugars," Longmans, Green and Co., New York, 1929.