Summary

There has been described a practical method of synthesis of the thiazole half of vitamin B_1.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Alkylacetanilidobarbituric Acids. II. *p*-Carbethoxy Derivatives

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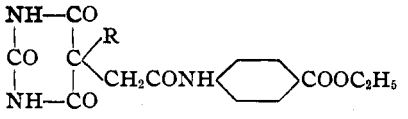
In many instances the simultaneous administration of either mixtures or addition products of hypnotic and antipyretic substances produces an analgesic effect.[2] Further, compounds have been synthesized in which groups tending to exhibit hypnotic properties and others, antipyretic properties are present within the same molecules. Hepner and Frenkenberg[2] have prepared 5,5-dialkyl derivatives of 1-phenyl-3-methylbarbituric acid. Dox and Yoder[3] have synthesized derivatives of two dialkylbarbituric acids (5-ethyl-5-propyl- and 5-isoamyl-5-propylbarbituric acids) with diethylamine, ethylaniline, acetanilide, and phenacetin, respectively, attached to the γ-carbon atom of the propyl group. Timm[4] prepared a series of 5-alkyl-5-acetanilidobarbituric acids. This work has now been extended to include a series of 5-alkyl-5-*p*-carbethoxyacetanilidobarbituric acids of the type



These compounds may be considered as derivatives of ethyl *p*-aminobenzoate, the local anesthetic.

(1) From the essay presented by John B. Howard to the Faculty of the Sheffield Scientific School of Yale University in partial fulfilment of the requirements for the degree of Bachelor of Science with Honors, June, 1936.

(2) For a review of the literature in this field see Hepner and Frenkenberg, *Ber.*, **65B**, 123 (1932).

(3) Dox and Yoder, THIS JOURNAL, **45**, 1757 (1923).

(4) Timm, *ibid.*, **57**, 1943 (1935).

Experimental Part

Barbituric Acids Containing the *p*-Carbethoxyacetanilido Group.—The method used in the synthesis of these compounds was identical with that used for the corresponding acetanilido derivatives[4] except that ethyl *p*-chloroacetaminobenzoate[5] was substituted for chloroacetanilide. The products were recrystallized from 90% ethyl alcohol except in the cases of the allyl and the isopropyl derivatives in which cases absolute alcohol was used to avoid the formation of hydrates. All melt with decomposition at temperatures above 225°.

TABLE I

Barbituric acid, 5-*p*-carbethoxyacetanilido-	Yield, %	N Analysis, % Calcd.	Found	
5-Ethyl-	40	11.63	11.54	11.60
5-Isopropyl-	9	11.20	11.22	11.24
5-*n*-Butyl-	13	10.79	10.78	10.81
5-Isobutyl-	25	10.79	10.73	10.77
5-Isoamyl-	43	10.42	10.41	10.43
5-Allyl-	20	11.25	11.18	11.22

Summary

The following 5-*p*-carbethoxyacetanilidobarbituric acids have been prepared: 5-ethyl-, 5-isopropyl-, 5-*n*-butyl-, 5-isobutyl-, 5-isoamyl- and 5-allyl-.

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(5) This compound has been prepared in this Laboratory by Ruth Watts. Its preparation and properties will be reported shortly.