with the Beckmann spectrophotometer. The absorption maxima are given in Table I, together with those of xanthopterin and isoxanthopterin determined in the same way.

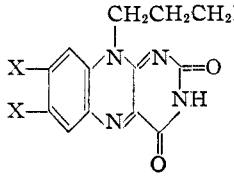
The authors wish to express their gratitude to Mr. Samuel W. Blackman for the microanalyses recorded here.

THE WELLCOME RESEARCH LABORATORIES
TUCKAHOE 7, NEW YORK RECEIVED JUNE 14, 1947

## Basically-substituted Isoalloxazines

BY HOWARD BURKETT

The structural similarity of atebrin to riboflavin suggested the synthesis of basically-substituted isoalloxazine derivatives, such as I, II and III, as possible antimalarials.



I, X = $CH_3$—
II, X = $CH_3O$—
III, X = Cl—

After this work was begun, other series of compounds very closely related to these were reported.[1,2,3] As a result the preparation of related compounds which had been planned was not carried out. The synthesis of compound III was attempted using a procedure similar to that employed for I and II and also according to the method of Kuhn and Weygand,[4] in which acetic acid served as the solvent and boric acid as the catalyst. That the product in very dilute solution gave a yellow-green fluorescence, typical of isoalloxazines, would indicate that the desired product was present, but the analyses indicated considerable contamination and cast some doubt that the expected compound was obtained. Consequently, this product was not submitted for biological testing and it is not reported in this note.

Compounds I and II were devoid of antimalarial activity, when tested on ducks infected with *Plasmodium lophurae*.

The author thanks Dr. K. K. Chen and Dr. C. L. Rose of Eli Lilly and Company for the pharmacological tests, Mr. Howard Hunter also of Eli Lilly and Company for the microanalyses and Eli Lilly and Company for financial assistance.

### Experimental

**7,8-Dimethoxy-10-(γ-diethylaminopropyl)-isoalloxazine Hydrochloride.**—Four grams of 4,5-dinitroveratrole[5] was mixed with 4 ml. of γ-diethylaminopropylamine and 5 ml. of ethanol. After the mixture had refluxed for twenty hours, it was poured into water and acidified with hydrochloric acid. This solution was extracted with ether. The aqueous solution was made basic with sodium hydroxide and extracted with ether. The ethereal solution was dried over anhydrous magnesium sulfate, filtered and saturated with anhydrous hydrogen chloride, forming an oily precipitate of crude 4-nitro-5-(γ-diethylaminopropylamino)-veratrole hydrochloride,[6] which could not be made to crystallize. The hydrobromide, sulfate and free-base could not be obtained in solid form and the base could not be distilled. Consequently, the oily hydrochloride was dissolved in 40 ml. of methanol and hydrogenated at atmospheric pressure and room temperature, using 0.10 g. of Adams platinum oxide catalyst. After the catalyst had been removed by filtration, the methanol was evaporated under reduced pressure with slight warming. Twenty milliliters of methanol was added and again evaporated. Ether was added to the residue and the mixture was saturated with anhydrous hydrogen chloride. After the ether had been decanted, the oil which remained was dissolved in 40 ml. of boiling methanol and 2.5 g. of alloxan monohydrate in 15 ml. of methanol was added. After refluxing for thirty minutes, the mixture was cooled and filtered. Recrystallization of the yellow solid from a water–acetone solution gave 1.04 g. (13.1%) of product melting at 220–222° with decomposition.

*Anal.* Calcd. for $C_{19}H_{25}N_5O_4 \cdot HCl \cdot 2H_2O$: C, 49.70; H, 6.58; N, 15.25. Found: C, 49.76; H, 6.22; N, 15.70.

**4-Nitro-5-(γ-diethylaminopropylamino)-*o*-xylene.**—Three grams of 4,5-dinitro-*o*-xylene,[7] 4 ml. of γ-diethylaminopropylamine and 8 ml. of ethanol were refluxed on the steam-bath for four days. The reaction mixture was cooled, poured into water, acidified with concentrated hydrochloric acid and extracted with ether. In a short time, as the dissolved ether evaporated spontaneously from the aqueous solution, yellow needles precipitated. Filtering and washing with a small amount of water yielded 2.89 g. of product melting at 211–212.5°.

*Anal.* Calcd. for $C_{15}H_{25}N_3O_2$: C, 57.00; H, 7.99; N, 13.33. Found: C, 56.73; H, 8.03; N, 13.17.

Evaporation of the filtrate to two-thirds of its original volume and cooling yielded an additional 0.4 g. of slightly less pure product, making the total yield 3.29 g. (77%).

**7,8-Dimethyl-10-(γ-diethylaminopropyl)-isoalloxazine Hydrochloride.**—Treatment of the 4-nitro-5-(γ-diethylaminopropylamino)-*o*-xylene in the same way as the 4-nitro-5-(γ-diethylaminopropylamino)-veratrole hydrochloride was treated above, yielded 37.5% of a yellow, crystalline product melting at 289–289.5° with decomposition.

*Anal.* Calcd. for $C_{19}H_{25}N_5O_2 \cdot HCl \cdot 2.5H_2O$: C, 52.20; H, 6.86; N, 16.01. Found: C, 52.26; H, 6.66; N, 16.23.

(1) Adams, Weisel and Mosher, THIS JOURNAL, **68**, 883 (1946).
(2) King and Acheson, *J. Chem. Soc.*, 681 (1946).
(3) Kipnis, Weiner and Spoerri, THIS JOURNAL, **69**, 799 (1947).
(4) Kuhn and Weygand, *Ber.*, **68**, 1282 (1935).
(5) Prepared according to the method of Vermeulen, *Rec. trav. chim.*, **48**, 969 (1929).
(6) The procedure for the synthesis of this compound has been discussed by Parijs, *Rec. trav. chim.*, **49**, 45 (1930), and by Kipnis, Weiner and Spoerri, THIS JOURNAL, **66**, 1446 (1944). The latter authors give other references to applications of this reaction.
(7) Prepared according to the method of Crossley and Renouf, *J. Chem. Soc.*, **95**, 212 (1909).

DEPARTMENT OF CHEMISTRY
DEPAUW UNIVERSITY
GREENCASTLE, INDIANA RECEIVED MAY 7, 1947

## The Reduction of Allylic Quaternary Ammonium Bromides

BY DAVID R. HOWTON

In connection with other work, we have studied the reduction of 2-cyclohexenyltrimethylammonium bromide (I). The catalytic hydrogenation of I at room temperature and atmospheric pressure over Adams platinum, Raney nickel, palladium-on-barium-sulfate, or palladium-on-charcoal proceeds with the uptake of more than one molecular equivalent of hydrogen and the forma-