

graphs of specimens with greater "thickness" will be of special interest.

Work is in progress to accomplish electron radiography by transmission on a quantitative basis. The uniform intensity of the sources was measured by the methods of absolute  $\beta$ -counting. These values can be compared with the electron intensities in the betagraph, determined with a microdensitometer. The results represent a measure for the absorption of electrons of a given mean velocity in small areas (limit, 30  $\mu$  diameter) which is related to the "thickness" of the structure of the specimen.

The application of  $\alpha$ -emitting monolayers (radium, polonium, plutonium) opens up new possibilities for studies of specimens in  $\alpha$  light. Pictures of butterfly wings depicted in the radiation from a radium stearate source show about the same shades as the betagraph in Fig. 2.

Descriptions of other applications of radioactive monomolecular films will appear elsewhere.

#### References

1. BEISCHER, D. E. Radioactive monomolecular layers. Project No. NM 000 007, Rep. No. 1, 1949.
2. BLODGETT, K. *J. Am. Chem. Soc.*, **57**, 1007 (1935).

## Dicarboxylic Acid Bis-( $\beta$ -Tertiaryaminoalkyl) Amides as Curare Substitutes

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A series of bis-( $\beta$ -dimethylaminoethyl) esters of dicarboxylic acids was recently reported (1) to possess powerful curarelike activity. Concurrently with the esters, a group of bis-( $\beta$ -tertiaryaminoalkyl) amides of the dicarboxylic acids was prepared and examined for curariform action.

The bis-amides were obtained in excellent yields by brief refluxing of a slight excess of the unsymmetrical disubstituted ethylene diamines with the dimethyl or diethyl esters of the dicarboxylic acids. In most cases the bis-amides were crystalline solids readily recrystallized from organic solvents. The bis-tertiary amino amides were transformed into bis-quaternary ammonium salts by refluxing in methanol solution with an excess of the appropriate alkyl halide, most commonly methyl or ethyl iodide.

Examples of the types of products made are: bis-dimethylaminoethyl oxamide (mp, 123°–124°; calcd.: C, 52.1; H, 9.6. Found: C, 52.1; H, 9.6); its bis-methiodide (mp, 288°–290°; calcd.: C, 28.0; H, 5.5. Found: C, 28.2; H, 5.5); bis-dimethylaminoethyl succinamide (mp, 134°–135°; calcd.: C, 55.8; H, 10.1. Found: C, 55.6; H, 9.9); its bis-methiodide (mp, 251°–252°; calcd.: C, 31.0; H, 5.9. Found: C, 31.1; H, 5.9); its bis-ethiodide (mp, 189°–190°; calcd.: C, 33.7; H, 6.4. Found: C, 33.7; H, 6.1); bis-diethylaminoethyl adipamide bis-methiodide (mp, 134°–135°; calcd.: C, 38.4; H, 7.1. Found: C, 38.9; H, 6.8); bis-morpholinoethyl malonamide

(mp, 127°–128°; calcd.: C, 54.8; H, 8.6. Found: C, 54.8; H, 8.4); and its bis-methiodide (mp, 153°–154°; calcd.: C, 33.3; H, 5.6. Found: C, 33.7; H, 5.4).

Interestingly, both the bis-tertiary amino amides and the derived quaternary salts were relatively devoid of curarelike activity, requiring huge doses to produce any perceptible block of neuromuscular transmission in the cat. However, both in the tertiary and quaternary form these compounds have been found to possess the remarkable ability, anticholinesteraselike, to prolong the duration of the block produced in the cat by the bis-esters (1) as much as four or five times. Details of the pharmacological results will be published elsewhere by E. J. de Beer and J. C. Castillo of these laboratories. Further work along these lines will be reported later.

#### Reference

1. PHILLIPS, A. P. *J. Am. Chem. Soc.*, **71**, 3264 (1949).

## The Enzymatic Dehydrogenation of Estradiol to Estrone<sup>1</sup>

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An enzyme system that catalyzes the conversion of  $\alpha$ -estradiol to estrone, *in vitro*, was demonstrated by using a purified protein fraction of beef liver and rat tissue homogenates as enzyme sources.

A 2-mg sample of a crudely purified preparation from the acetone-insoluble, water-soluble fraction of beef liver was tested for ketosteroid and found to be negative (1). A 5-mg sample of crystalline  $\alpha$ -estradiol<sup>3</sup> was likewise negative.

Five mg of the estradiol was added to 0.2 mg of the purified beef liver preparation in 20 ml of water and incubated for 12 hr under conditions previously found to be within the range of maximal enzymatic activity. Twenty ml of a 0.1% solution of 2-hydroxy-3-naphthoic acid hydrazide, containing 50% ethyl alcohol and 5% acetic acid, was stirred into the mixture, brought to boiling, and cooled to room temperature. The yellow precipitate formed was separated from both the excess hydrazide and any estradiol present by centrifugation, repeatedly washed with 50% ethyl alcohol, and refluxed with pyruvic acid for 30 min. Distilled water was added to saturation, and a white crystalline precipitate was formed on cooling (3). The crystals were purified by repeated washings with warm 5% sodium bicarbonate solution and warm distilled water. After drying in air, the crystals were examined microscopically and found to be colorless plates similar in form to estrone. The mp was 252°–254° C. When some of the crystals were mixed with a known sample of crystalline estrone<sup>3</sup> (mp 253°–

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