**Decarboxylation.**—As a general procedure a mixture of aromatic anhydride (0.5 g.), crystalline barium hydroxide (2 g.) and copper-bronze (0.7 g.) was ground thoroughly in an agate mortar and was heated in a long Pyrex tube. Water of crystallization was collected up to 220°. As soon as the reaction started (about 300°), one end of the tube was fitted with a capillary and the other end was connected to water-pump suction. Heating was continued at 300–350° under reduced pressure till no more oil was evolved.

**Thiopheno-2,3:1′,2′-naphthalene (XXX).**—Decarboxylation of 0.5 g. of Xa gave 0.2 g. (55.5%) of an oil, which was treated with picric acid in ethanol; crude picrate, m. p. 135°. After crystallization from a saturated solution of picric acid in ethanol, orange needles were obtained, m. p. 141–142°.

*Anal.* Calcd. for $C_{18}H_{11}O_7N_3S$: C, 52.30; H, 2.68. Found: C, 52.32; H, 2.51.

The picrate was decomposed with dilute alkali, and a yellow oil (XXX) was formed.

*Anal.* Calcd. for $C_{12}H_8S$: C, 78.22; H, 4.38. Found: C, 78.15; H, 4.47.

**Thiopheno-2,3:3′,4′-phenanthrene (XXXIa).**—On decarboxylation of 0.5 g. of XVIII there resulted 192 mg. (50%) of an oil which solidified immediately, m. p. 70–75°. Two crystallizations from dilute ethanol afforded colorless, branched leaflets melting at 91.5–92.5°.

*Anal.* Calcd. for $C_{16}H_{10}S$: C, 82.01; H, 4.30. Found: C, 81.93; H, 4.23.

The picrate was formed in methanol and was crystallized from the same solvent as elongated orange needles, m. p. 170–171°.

*Anal.* Calcd. for $C_{22}H_{13}O_7N_3S$: C, 57.02; H, 2.82. Found: C, 57.47; H, 2.47.

**Thiopheno-2,3:3′,4′-(7′-methoxy)-phenanthrene (XXXIb).**—XV was decarboxylated to an oil which solidified; yield 44.3%. The picrate was formed in ethanol and was crystallized from a dilute solution of picric acid in ethanol as brick-red needles, m. p. 138–138.5°.

*Anal.* Calcd. for $C_{23}H_{15}O_8N_3S$: C, 55.99; H, 3.06. Found: C, 56.29; H, 2.93.

Decomposition of the picrate yielded a white solid, which crystallized from methanol in the form of needles melting at 88.5–90.0°.

*Anal.* Calcd. for $C_{17}H_{12}OS$: C, 77.24; H, 4.58. Found: C, 77.09; H, 4.30.

**Thiopheno-2,3:1′,2′-anthracene.**—Decarboxylation of XXIV afforded a red oil which solidified. This red solid was heated overnight in refluxing ethanol. The solution was clarified by filtration and used directly for picrate formation. The red picrate which formed was crystallized from methanol; dark red rods, m. p. 139–140°.

*Anal.* Calcd. for $C_{22}H_{13}O_7N_3S$: C, 57.02; H, 2.82. Found: C, 57.17; H, 2.37.

Preliminary efforts to isolate the sulfur-containing hydrocarbon by the general method, as well as by decarboxylation with quinoline and copper-bronze, were unsuccessful.

## Summary

1. Conjugation of one double bond of the thiophene nucleus and an alicyclic double bond has been found to provide an active diene system for the Diels–Alder reaction with maleic anhydride.

2. The condensation with maleic anhydride has been effected with a number of 2-thienyl- and 3-thianaphthylcycloalkenes. The hydroaromatic adducts were dehydrogenated to aromatic anhydrides.

3. Decarboxylation of several aromatic anhydrides has afforded sulfur-containing hydrocarbons, which may prove to be carcinogenic.

CAMBRIDGE 38, MASSACHUSETTS RECEIVED JULY 29, 1949

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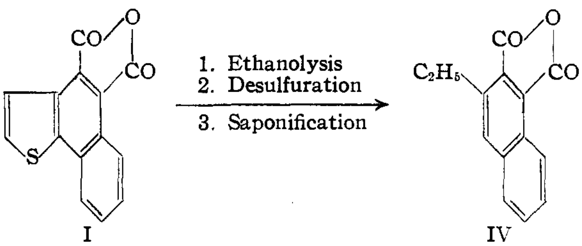
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

# Preparation of Substituted Aromatic Anhydrides by Reductive Desulfuration

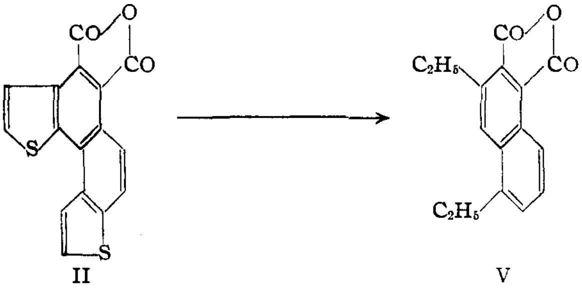
BY EDWARD J. MODEST[1] AND JACOB SZMUSZKOVICZ[2]

The desulfuration reaction with Raney nickel has already been applied to certain derivatives of thiophene. Bougault and co-workers[3] have reported a method for the removal of undesired thiophene derivatives from aromatic hydrocarbons by means of Raney nickel; and du Vigneaud and associates,[4] in their work on the elucidation of the structure of biotin, desulfurized a tetrahydrothiophene ring. In a recent article Blicke and Sheets[5] describe the desulfuration of thianaphthenecarboxylic acids.

Reductive desulfuration of the sulfur-containing aromatic anhydrides I, II, IIIa and IIIb[6] afforded naphthalene and phenanthrene derivatives. During treatment with Raney nickel the thiophene nucleus is cleaved and converted into an ethyl group with loss of sulfur.



I IV



II V

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[1] Harvard University Ph.D. 1949; present address: Children's Medical Center, Boston, Mass.

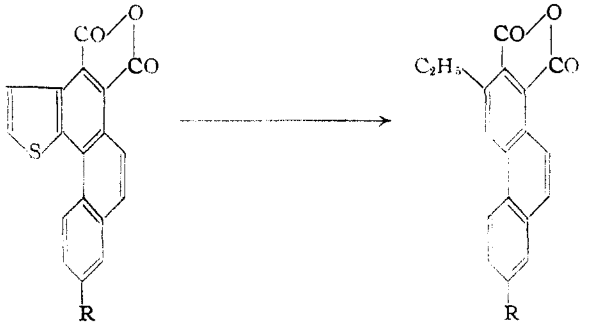
[2] Harvard University Postdoctoral Fellow 1947–1948; on leave of absence from the Weizmann Institute of Science, Rehovoth, Israel.

[3] Bougault, Cattelain and Chabrier, *Bull. soc. chim.*, [5] **7**, 780 (1940).

[4] du Vigneaud, *et al.*, *J. Biol. Chem.*, **146**, 475 (1942).

[5] Blicke and Sheets, THIS JOURNAL, **70**, 3768 (1948). Our investigation was completed before publication of this article.

[6] Szmuszkovicz and Modest, *ibid.*, **72**, 571 (1950).



III a, R = H
b, R = $OCH_3$

VI

The desulfuration probably proceeds either by rupture of the thiophene ring followed by hydrogenation of the newly formed vinyl group, or by prior formation of a dihydrothiophene nucleus and abstraction of the sulfur atom. The infrared absorption spectra[7] of naphthalene-1,2-dicarboxylic acid anhydride and of IV and V (Figs. 1, 2, 3) display a striking similarity and support the structures assigned to the latter two compounds.

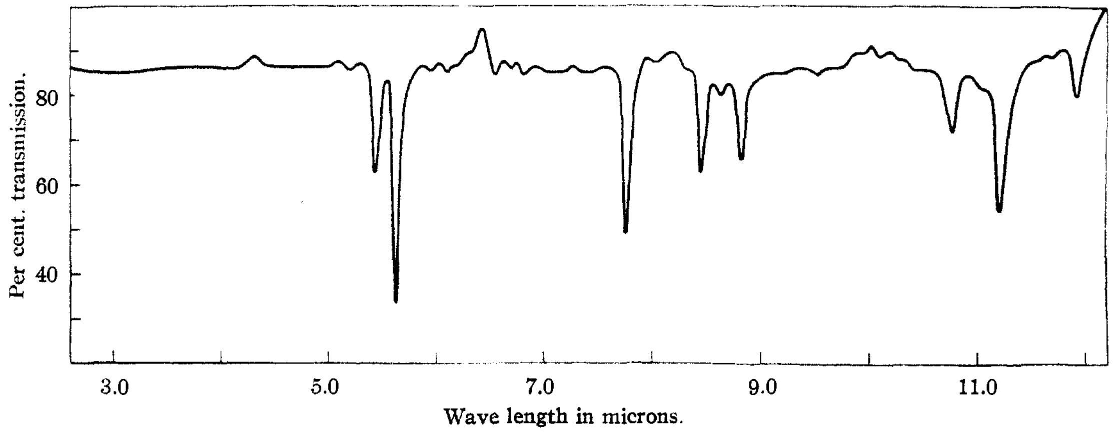


Fig. 1.—Infrared absorption spectrum of naphthalene-1,2-dicarboxylic acid anhydride, 1.0% solution in carbon tetrachloride; absorption bands: 5.41 and 5.61μ, anhydride group.

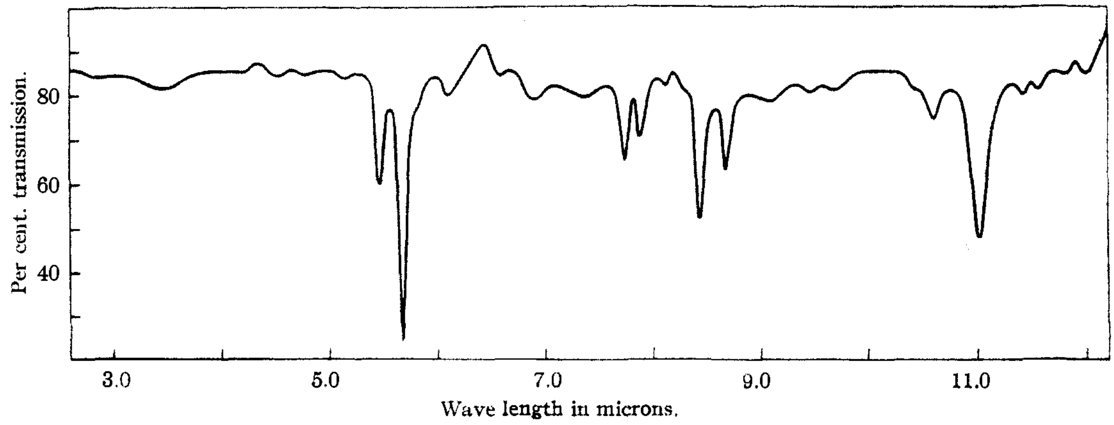


Fig. 2.—Infrared absorption spectrum of 3-ethylnaphthalene-1,2-dicarboxylic acid anhydride, 1.0% solution in carbon tetrachloride; absorption bands: 3.40μ, aliphatic carbon-hydrogen bond; 5.42 and 5.62μ, anhydride group.

The experimental method involves dissolution of the sulfur-containing aromatic anhydride in ethanol, desulfuration with Raney nickel, and isolation of the product by Soxhlet extraction; no nuclear hydrogenation was observed.

**Acknowledgment.**—The authors wish to express their appreciation to Professor Louis F. Fieser for his support and interest. This investigation of the desulfuration reaction was undertaken at his suggestion. The microanalyses were performed by Mrs. Shirley R. Golden.

## Experimental[8]

The following procedure for desulfuration is generally applicable and is based upon numerous trial runs. A mixture of 500 mg. of sulfur-containing aromatic anhydride and 150 cc. of absolute ethanol, in a 500-cc. three-necked flask equipped with a mercury-sealed stirrer and a condenser, was refluxed for twenty-four hours. The clear yellow solution was cooled and approximately 5 g. of Raney

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(7) All measurements were made with 1.0% carbon tetrachloride solutions on an infrared recording spectrophotometer manufactured by Baird Associates, Inc., Cambridge, Mass.

(8) All melting points are corrected.

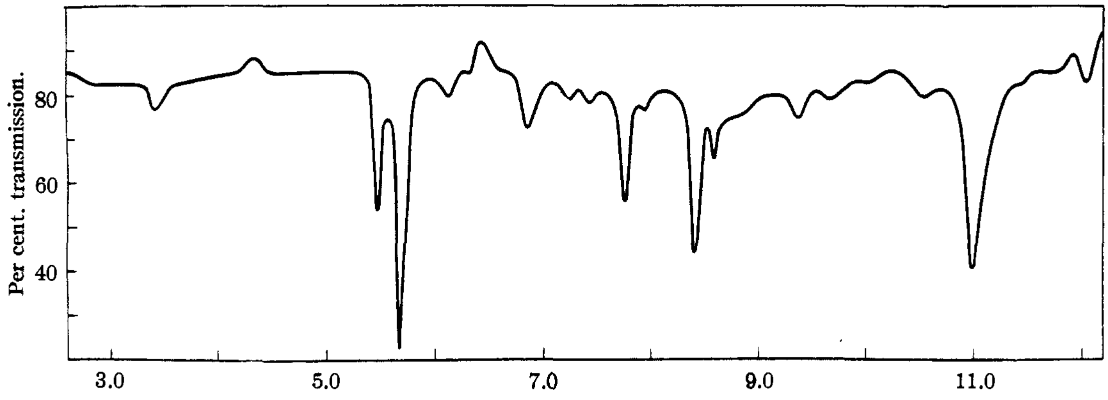

Fig. 3.—Infrared absorption spectrum of 3,5-diethylnaphthalene-1,2-dicarboxylic acid anhydride, 1.0% solution in carbon tetrachloride; absorption bands: 3.40μ, aliphatic carbon–hydrogen bond; 5.42 and 5.62μ, anhydride group.

nickel[9] added. (The ratio of Raney nickel to sulfur-containing anhydride was 10*n*:1 by weight, where *n* = number of atoms of sulfur in the compound.) Desulfuration was carried out with vigorous stirring for five hours at the reflux temperature. Since the desulfurized product was found to be highly adsorbed on the finely divided nickel, Soxhlet extraction was employed in the isolation procedure. The nickel was allowed to settle, and the supernatant liquid was filtered through a Soxhlet thimble into the receiver of a Soxhlet extraction apparatus. The moist Raney nickel was transferred into the thimble with the aid of absolute ethanol and extracted for twenty-four hours. After evaporation of the solvent the residual monoester (a pale yellow solid) was dissolved in a solution of 2 g. of sodium hydroxide in 20 cc. of ethanol and 20 cc. of water, and the solution was refluxed for one-half hour. A small amount of inorganic matter was removed by filtration. Ethanol was completely removed by distillation at diminished pressure and the aqueous solution was heated for one hour at steam-bath temperature. Acidification with concentrated hydrochloric acid caused precipitation of the desulfurized anhydride, which exhibits a strong blue fluorescence in dilute ethanolic solution.

Compounds IV and VIa fail to decolorize dilute solutions of potassium permanganate in water and bromine in carbon tetrachloride.

TABLE I

DESULFURIZED ANHYDRIDES

| Compound | M. p., °C.[a] | Yield,[b] % | Formula | Analyses, % Calcd. C | H | Found C | H |
|---|---|---|---|---|---|---|---|
| IV | 153.5–158 | 49.7 | $C_{14}H_{10}O_3$ | 74.33 | 4.46 | 74.14 | 4.54 |
| V | 159.5–162 | 39.0 | $C_{16}H_{14}O_3$ | 75.57 | 5.55 | 75.85 | 5.56 |
| VIa[c] | 243.7–244.7 | 87.8 | $C_{18}H_{12}O_3$ | 78.25 | 4.38 | 78.36 | 4.40 |
| VIb[c] | 214–216 | 67.4 | $C_{19}H_{14}O_4$ | 74.50 | 4.67 | 74.25 | 4.60 |

[a] All desulfurized products crystallized as pale yellow needles from acetic acid. [b] Yields based on crude products. [c] Analytical sample dried for three hours at 110°; very hygroscopic.

## Summary

1. The desulfuration reaction with Raney nickel has been applied to some aromatic sulfur-containing compounds.

2. A novel synthetic route is described for the preparation of certain naphthalene and phenanthrene derivatives.

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[9] Prepared by the procedure of Mozingo, "Organic Syntheses," **21**, 15 (1941), and washed according to Pavlic and Adkins, THIS JOURNAL, **68**, 1471 (1946).

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

# Steroids Labeled with Isotopic Carbon: Cholestenone and Testosterone[1]

BY RICHARD B. TURNER*

Involvement of various endocrine secretions in the etiology of cancer has been recognized since 1916 when Lathrop and Loeb[2] observed that castration of female mice of certain strains results in a marked decrease in the incidence of spontaneous mammary cancer in these animals. Subsequently Lacassagne,[3] Gardiner,[4] and others found that prolonged administration of estrogens increases the incidence of neoplastic lesions of the uterus, testes, pituitary, adrenals and other organs, whereas in certain instances simultaneous administration of estrogen and testosterone propionate produces no such effect. Beneficial results of

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* Harvard University Ph.D. 1942.

[1] This work was supported by funds provided by the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council. For preliminary reports see Turner, THIS JOURNAL, **69**, 726 (1947); *Science*, **106**, 248 (1947).

[2] Lathrop and Loeb, *J. Cancer Research*, **1**, 1 (1916).

[3] Lacassagne, *Compt. rend.*, **195**, 630 (1932); "Ergebnisse der Vitamin- und Hormonforschung," Vol. II, p. 258, Mellanby and Ruzicka, Academische Verlagsgesellshaft, Leipzig, 1939.

[4] Gardiner, "Recent Progress in Hormone Research," Vol. I, Pincus, Academic Press, New York, N. Y., 1947, p. 217.