3a-Methyl-d_3-*trans*-hexahydroindan (IV).—The Clemmensen conditions described for the reduction of XXXVII were duplicated for the reduction of XLV. The attempt was equally unsuccessful.

Using the procedure described immediately above, 0.95 g. (6.0 mole) of XLV, 1.2 g. of 85% potassium hydroxide and 0.9 ml. of hydrazine hydrate (85%) in 8 ml. of diethylene glycol gave 0.48 g. (3.0 mole, 51%) of IV, b.p. 70° (21 mm.), $n^{25}D$ 1.4669, d^{25}_4 0.8923.

Anal. Calcd. for $C_{10}H_{15}D_3$: C, 85.02; H, 13.08; D/H+D, 16.7; $R^{25}D$ 43.98. Found: C, 85.33; H, 13.27; D/H+D, 15.8 ± 0.2; $R^{25}D$, 43.92.

Reduction of XXVIII to XXIX and XXX with Lithium in Anhydrous Ammonia.—In a 2-l. flask insulated with rock wool and equipped with a mercury sealed stirrer, Dry Ice condenser protected with a soda lime drying tube, dropping funnel and nitrogen inlet were placed 500 ml. of anhydrous ammonia, and 55.56 g. (0.25 mole) of XXVIII (b.p. 146–149° (1.5 mm.)) dissolved in 100 ml. of anhydrous ether. Ten and one-half grams (1.5 atoms) of lithium was added in small pieces over 0.5 hr. The usual blue color of alkali metal–ammonia solutions became evident only after an amount in excess of two equivalents of lithium had dissolved. The solution was stirred for 1 hr. after the addition of the metal, whereupon 81 g. of absolute ethanol was added dropwise over a period of 75 minutes followed by 70 g. of ammonium chloride. The ammonia was then allowed to evaporate rapidly, the residue being treated with 250 ml. of ether and 100 ml. of water. A water-cooled condenser was utilized while the mixture was cautiously acidified with dilute (2:1) hydrochloric acid. The complete operation through the acidification was carried out with stirring under a slow stream of dry nitrogen. The aqueous phase from the acidified mixture was removed and extracted three times with 100-ml. portions of ether which were combined with the original organic layer and washed once with 50 ml. of water followed by half-saturated sodium bicarbonate solution until alkaline to litmus. The ethereal solution was dried, concentrated on the steam-bath and finally distilled. The product boiling between 115–155° (0.3–1.0 mm.) was collected and weighed 31.5 g. This material was definitely composed of two substances easily separable by fractionation. However, infrared spectra showed the lower-boiling material to be mainly ketonic while the higher-boiling fraction was strongly hydroxylic and that little, if any, starting material was present. The distillate was dissolved in 70 ml. of acetic acid and added dropwise while cooling in ice to 13.8 g. of chromium(VI) oxide dissolved in 280 ml. of acetic acid containing 7 ml. of water at such a rate that the temperature did not rise above 30°. The mixture was allowed to stand at room temperature for 1 hr., then 40 ml. of ethanol was added. After standing an additional 15 minutes, the mixture was poured into 1 liter of water and extracted four times with 100-ml. portions of petroleum ether (b.p. 30–40°). The combined extracts were washed with water, half-saturated sodium bicarbonate solution until the washings were alkaline to litmus, dried and concentrated on the steam-bath. Vacuum distillation resulted in 17.7 g. (0.08 mole, 32%) of the mixture of XXIX and XXX, b.p. 120–123° (1.2 mm.).

Anal. Calcd. for $C_{18}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.75; H, 8.91.

From 1.12 g. of this product, 0.5 g. (38%) of **semicarbazone** was obtained. Two recrystallizations from 95% ethanol raised the melting point to 163–164.5° dec.

Anal. Calcd. for $C_{14}H_{23}N_3O_3$: C, 59.76; H, 8.24; N, 14.94. Found: C, 60.14; H, 8.23; N, 15.01.

BROOKLYN, NEW YORK

[CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF FORDHAM UNIVERSITY AND SETON HALL UNIVERSITY]

Heterocyclic Analogs of the Estrogenic Steroid Hormones. I. Synthesis of a Thiophene Analog of 3-Desoxyisoequilenin[1,2]

BY ROBERT J. COLLINS AND ELLIS V. BROWN[3]

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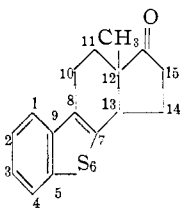
A thiophene analog of 3-desoxyisoequilenin has been prepared. The required intermediate, 4-keto-1,2,3,4-tetrahydrodibenzothiophene, was prepared both by a modification of the synthesis of Buu-Hoi and Cagniant and by a new route. Application to this material of an equilenin synthesis of Johnson gave the desired final compound. Along with the structural proof inherent in the synthesis both chemical and spectrophotometric evidence were considered. In the course of this work two new fused ring systems have been prepared for which are proposed both systematic and trivial names.

Replacement of the benzene ring in many physiologically active compounds by heterocyclic rings often has led to interesting variations in activity and sometimes to antimetabolite behavior. Applications of this approach to the estrogenic hormones have been limited to the synthetic estrogens,[4] and although several active estrogens have been produced, no effective hormonal antagonists have been obtained.

As part of a general program to prepare heterocyclic analogs of estrogenic steroid hormones, we have undertaken to prepare a 3-desoxyequilenin analog in which a thiophene ring replaces the benzene "B" ring, *cis* and *trans*-16-cyclopentano[c]-10,11,12,13,14,15-hexahydro-12-methyldibenzothiophene. The hitherto unknown cyclopentano[c]dibenzothiophene system has been tentatively assigned a numbering system which resembles that of the steroid hormones.



Of the three excellent syntheses of the equilenins which are available,[5] all beginning with a sub-

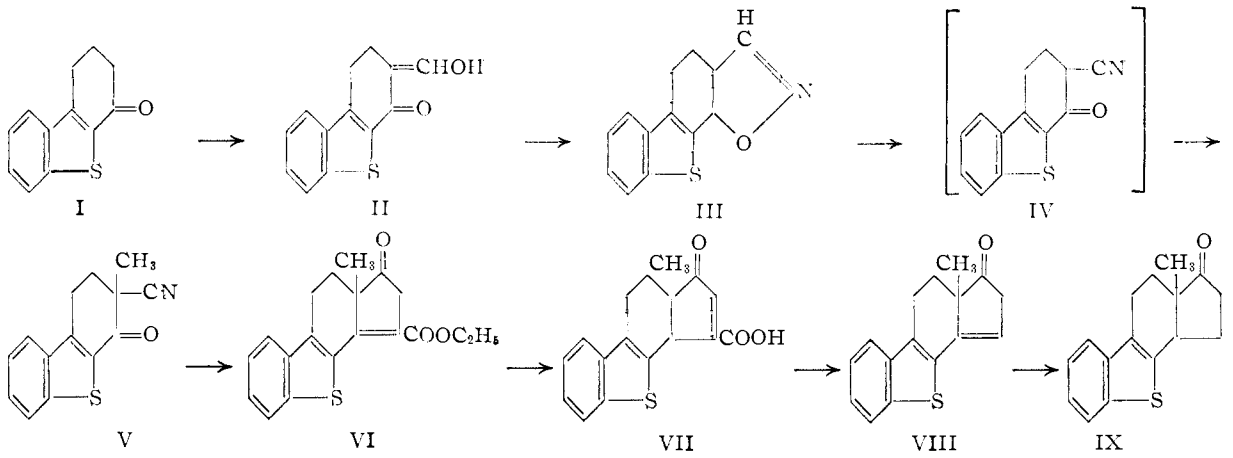
(1) Supported in part by a grant in aid from the National Cancer Institute (C-1390) of the National Institute of Health, Public Health Service.

(2) Presented at the 125th meeting of the American Chemical Society, Kansas City, March, 1954. After this paper had been submitted to the JOURNAL, an abstract of a paper presented at the 42nd Session of the Indian Science Congress, Baroda, January, 1955, came to our attention. This paper by R. B. Mitra and B. D. Tilak (*J. Sci. Ind. Research*, **14B**, 132 (1955)) reaches the same conclusions as our work except that the 154.5° melting reduction product is reported to be the thiophene analog of 3-desoxyequilenin.

(3) To whom inquiries should be addressed, Chemistry Department, Seton Hall University, South Orange, N. J.

(4) N. P. Buu-Hoi and H. Hoan, *J. Org. Chem.*, **17**, 350 (1952); W. P. Biggerstaff and O. L. Stafford, THIS JOURNAL, **74**, 419 (1952); J. Sice and M. Mednick, *ibid.*, **75**, 1628 (1953).

(5) (a) W. E. Bachmann, W. Cole and A. L. Wilds, *ibid.*, **62**, 824 (1940); (b) W. S. Johnson, J. W. Petersen and C. D. Gutsche, *ibid.*, **69**, 2924 (1947); (c) W. S. Johnson and V. L. Stromberg, *ibid.*, **72**, 505 (1950).



stituted ketotetrahydrophenanthrene, the first synthesis of Johnson[5b] was considered best suited to our requirements.

The required intermediate, 4-keto-1,2,3,4-tetrahydrodibenzothiophene has been prepared[6] by a succinoylation of thianaphthene, reduction of the resulting ketoacid and cyclization of the acid to the ketone. However, in our hands neither of the Friedel–Craft succinoylations[6] gave the reported yields of β-(3-thianaphthoyl)-propionic acid and, because this product was formed along with the 2-isomer, separations were required which on a large scale became tedious. As an alternate route, 3-bromothianaphthene (prepared by the method of Komppa[7] in 97% yields) was converted to the Grignard reagent which, when reacting with succinic anhydride, furnished the keto acid in 66% yield. This acid was reduced by a modification of the Clemmensen reduction of Buu-Hoi and Cagniant[6a] to a 91% yield of γ-thianaphthylbutyric acid. This in turn was cyclized to the ketone, through the acid chloride, by a modification of the Friedel–Crafts method of Cagniant and Cagniant[6b] in 95% yield. The butyric acid also could be cyclized directly to the ketone in 90% yields by a short treatment with commercial polyphosphoric acid. The ketone I could thus be obtained in an over-all yield of 57% from thianaphthene.

Treatment of I with ethyl formate and sodium methylate gave a 97% yield of 3-hydroxymethylene-4-keto-1,2,3,4-tetrahydrodibenzothiophene (III). When crude II, as obtained from the reaction mixture, was treated with hydroxylamine hydrochloride, an 88% yield of 9,10-dihydrodibenzothiopheno-3,4-(d)-isoxazole (III), a representative of a new ring system, was obtained. The isoxazole was cleaved to 4-keto-3-cyano-1,2,3,4-tetrahydrodibenzothiophene (IV) by the action of sodium methylate and this ketonitrile reacted *in situ* as the 3-sodio derivative to produce 4-keto-3-methyl-3-cyano-1,2,3,4-tetrahydrodibenzothiophene (V) in 77% over-all yield from the isoxazole.

Stobbe condensation of V with diethyl succinate in the presence of potassium *t*-butylate furnished an 81% yield of ethyl 13,14-dehydro-16-cyclopentano[c]-12-methyl-10,11,12,13,14,15-hexahydrodibenzothiophene-14-carboxylate (VI) referred to in this paper as ethyl 3-desoxy-13,14-dehydrothiaquilenin-14-carboxylate.

Hydrolysis of the dehydro-ester VI with barium hydroxide gave 75% of the 3-desoxy-14,15-dehydrothiaquilenincarboxylic acid (VII). In alkaline solution the acid was oxidized rapidly with the formation of a deep purple solution, and for this reason the hydrolysis was conducted under nitrogen with the rigid exclusion of air.

Decarboxylation of the acid VII with pyridine and hydrochloric acid produced a 91% yield of crude material melting at 163–168° with some previous softening. Recrystallization from petroleum ether (90–100°) furnished a 61% yield of a compound melting 173–174.3°, found to be 3-desoxy-13,14-dehydrothiaquilenin (VIII). The 14,15-dehydro compound, if present in the mother liquor, could not be isolated.

The 13,14-dehydro compound VIII purified by vacuum sublimation was hydrogenated at room temperature and atmospheric pressure over 10% palladium-on-charcoal to give a 95% yield of pink crystals. The product, m.p. 90.0–91.5°, after recrystallization from methanol, was believed to be the *cis* compound IX. Attempts to obtain the *trans* form from this reaction were unsuccessful.

Hydrogenations of VIII over 30% Pd/C resulted in more rapid hydrogen absorption and gave 20% of the *cis* compound and 10% of a material, m.p. 131.0–142.5°, which could not be further purified.

Reduction of VIII over 30% Pd/C in the presence of a trace of hydrochloric acid, to favor formation of the *trans* product, gave 37.5% of IX and 20% of a crude material, m.p. 143.0–147.5°. Repeated recrystallization of the latter compound raised the melting point to 154.0–154.5°. This product was shown to be polymorphic with the dehydro-compound VIII.

Structural Proofs

Ultraviolet Spectroscopy.—Assignment of the double bond in the Stobbe condensation ester VI at the 13,14-position was based on the intense ultraviolet absorption at 320 mμ (Fig. 1) which was believed to be characteristic of such a thianaphthyl-2-acrylic acid system. This belief was substantiated when a model compound, methyl thia-

(6) (a) N. P. Buu-Hoi and P. Cagniant, *Ber.*, **76B**, 1269 (1943); (b) P. Cagniant and M. Cagniant, *Bull. soc. chim.*, 336 (1952).

(7) G. Komppa, *J. prakt. Chem.*, **122**, 319 (1929).

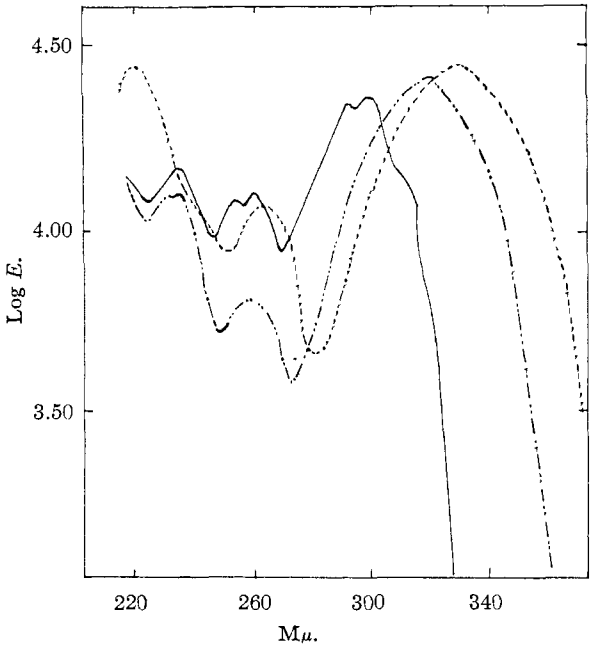
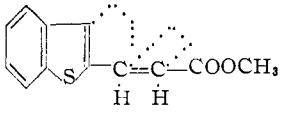


Fig. 1.—Ethyl-3-desoxy-13,14-dehydrothiaquilenin-14-carboxylate, (VI) - - - -; methy-β-(2-thianaphthyl)-acrylate (X) —··—··; 3-desoxy-13,14-dehydrothiaquilenin, (VIII) ———.

naphthyl-2-acrylate, was prepared and was found to have an equally intense absorption at 320 mμ.



X

Hydrolysis of the dehydro-ester (VI) gave the acid VII which was completely lacking in strong absorption above 275 mμ (Fig. 2), suggesting that the ethylenic bond had shifted to the 14,15-position. An α,β-unsaturated ketone of this type with a β-carboxy substituent has been estimated to absorb below 220 mμ. Further evidence of the position of the ethylenic bond in VII is the remarkable resemblance (Fig. 2) of its absorption curve to that of the reduced compound IX.

The ethylenic bond in VIII, the compound produced by decarboxylation of the acid VII, was assigned the 13,14-dehydro position because of the intense absorption at 298 mμ. The spectrum of the compound resembled that of ester VI and the model acrylic ester, except that the maximum had shifted probably due to the bathochromic influence of the ester groups. Analogous bond migrations have been shown to occur in the equilenin and 3-desoxyequilenin series[5b] and in the 3-desoxy-6-methoxyequilenin series.[8]

Infrared Spectra.—The correlation of infrared absorptions with specific structural features in steroids has been investigated extensively by Jones and associates.[9] Based on this background, structural assignments have been made for the

(8) R. Hirschmann and W. S. Johnson, THIS JOURNAL, **73**, 326 (1951).

(9) R. N. Jones and H. Herlin, *J. Org. Chem.*, **19**, 1252 (1954).

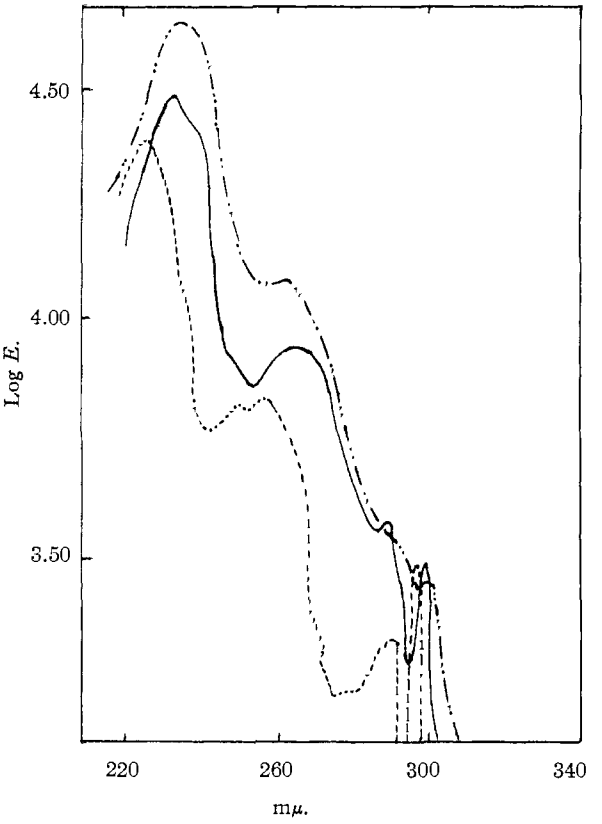


Fig. 2.—3-Desoxy-14,15-dehydrothiaquilenin-14-carboxylic acid (VII) — · · —; 3-desoxyequilenin thiophene analog (IX), ———; thianaphthene - - - -

bands exhibited by the dehydrocompound VIII and the desoxyisoequilenin analog IX (Table I). These assignments are compatible with the ethylenic bond positions determined from the ultraviolet spectra.

The absorption of the keto group in VIII at 1748 cm.$^{-1}$ supported the assignment of the double bond at the 13,14-position, β-γ to the ketone. The predicted value for such a ketone would be 1752–1754 cm.$^{-1}$ while a ring "D" ketone with an α,β-double bond should absorb at 1716 cm.$^{-1}$. In the hydrogenation product IX (m.p. 91.5°) carbonyl stretching occurred at 1736 cm.$^{-1}$, in the normal range for steroids having a saturated ring "D."

Identity of the 154.5° Reduction Product.—The ketone, m.p. 154.5°, obtained by acid hydrogenation of VIII showed an ultraviolet spectrum resembling that of VIII particularly in the twinned absorption maxima at 291 mμ (log E 4.2) arising from a conjugated double bond. The infrared absorption spectrum resembled that of VIII in major details, including carbonyl absorption at 1749 cm.$^{-1}$, when crystalline material in KBr pills was examined. The spectra of VIII and the 154.5° ketone became identical when carbon tetrachloride solutions were examined. Although the two forms had different melting points, a mixed melting point caused no depression.

The foregoing evidence indicated that the 154.5° ketone was a polymorphic modification of the unchanged starting material VIII.

Experimental

4-Keto-1,2,3,4-tetrahydrodibenzothiophene (I).—β-(3-Thianaphthoyl)-propionic acid[6a] was prepared in 66% yield from 3-bromothianaphthene,[7] magnesium and succinic anhydride in anisole at 0°, reduced by the Clemmensen method to γ-(3-thianaphthyl)-butyric acid[6b] in 91% yield and cyclized to the ketone[6b] in 90% yield by the Friedel–Crafts process ($SnCl_4$) or with commercial polyphosphoric acid at 70–80°.

3-Hydroxymethylene-4-keto-1,2,3,4-tetrahydrodibenzothiophene (II).—Ethyl formate, 8.4 g. (0.113 mole) and 6.1 g. (0.113 mole) of commercial sodium methylate were dissolved in 132 ml. of dry benzene and the system flushed with dry nitrogen while connected to a mercury trap. To this solution was added with swirling a solution of 10.3 g. (0.051 mole) of compound I in 161 ml. of dry benzene. This was allowed to stand at room temperature for 5 hr. with occasional swirling (nitrogen passed in the first hour, mercury trap connected through the entire period.)

At the end of 5 hr. the greenish yellow precipitate was hydrolyzed by the addition of 300 ml. of ice-water. After complete solution of the solid, the organic layer was separated and washed with two 60-ml. portions of 5% sodium hydroxide which were combined with the original 300 ml. of alkaline solution and the whole washed twice with ether. The alkaline solution was then slowly acidified with 6 *N* hydrochloric acid with stirring and ice cooling. The yellow crystalline powder was filtered, washed well with water and air-dried. The yield was 11.4 g. (97.2%), m.p. 109.5–110.5°, with slight previous softening. Recrystallization from cyclohexane gave yellow rhombic crystals, m.p. 114.5–116.5°.

Anal. Calcd. for $C_{13}H_{10}SO_2$: C, 67.83; H, 4.35. Found: C, 68.18; H, 4.15.

When the compound was crystallized from ethanol–water, a polymorphic modification resulted, a reddish-brown brittle mass of crystals, m.p. 126.0–128.5°. Recrystallization of this material from cyclohexane again produced the form, m.p. 114.5–116.5°. Both forms gave an olive-green color with alcoholic ferric chloride.

9,10-Dihydrodibenzothiopheno-3,4,(d)-isoxazole (III).—The hydroxymethylene ketone (II), 14.3 g. (0.062 mole), m.p. 109.5–110.5°, and 6.6 g. of dry hydroxylamine hydrochloride were dissolved in 350 ml. of glacial acetic acid. The flask was then introduced into an oil-bath preheated to 170° and maintained at this temperature. Within 5 minutes the mixture refluxed with much foaming and was then kept at reflux for 10 minutes. While still hot, 150 ml. of boiling water was added to the mixture with swirling and the whole then allowed to cool. Precipitation of the lustrous tan platelets began immediately. The mixture was cooled at 5° for 24 hr. and then the product filtered, washed with a little cold 25% acetic acid, then with a little cold water, sucked dry and air dried. The yield was 12.4 g. (87.8%), m.p. 140.5–142.5°. This material was of sufficient purity for the next step.

Anal. Calcd. for $C_{13}H_9NSO$: C, 68.69; H, 3.96; N, 6.16. Found: C, 68.70; H, 4.21; N, 6.36.

The material was prepared for analysis by several recrystallizations from ethanol and melted at 140.5–142.5°.

4-Keto-3-cyano-3-methyl-1,2,3,4-tetrahydrodibenzothiophene (V).—A solution of 7.6 g. (0.033 mole) of the isoxazole III was dissolved in 28 ml. of dry benzene and this solution added to a solution of 2.43 g. of sodium methoxide in 46 ml. of absolute methanol. After standing at room temperature for 30 minutes with occasional swirling, the mixture was refluxed for 10 minutes and then cooled. Methyl iodide (4.9 ml.) was added, the solution shaken and allowed to stand for 1 hr. An additional 3.2 ml. of methyl iodide was added, and after standing for 2 hr. at room temperature, the mixture was refluxed for 4 hr. After cooling, the mixture was evaporated almost to dryness under diminished pressure, the residue taken up in benzene and extracted with five 100-ml. portions of 0.5% KOH and then with two 50-ml. water portions.

The benzene solution containing the methylated ketonitrile was dried, treated hot with Norite, filtered and the benzene evaporated under reduced pressure. The tan crystalline residue was recrystallized from 15 parts of methanol yielding a first crop of tan plates 5.23 g. (65.0%), m.p. 108.5–110.5°. Reduction of the volume of the mother liquor gave an additional 0.95 g. (11.9%), m.p. 104.0–107.0°. Therefore the total yield of the methylated ketonitrile V was 76.9%. Repeated recrystallization from 15 parts methanol raised the melting point to 112.0–114.0° (hexagonal plates).

Anal. Calcd. for $C_{14}H_{11}SNO$: C, 69.69; H, 4.56; N, 5.81. Found: C, 69.66; H, 4.60; N, 5.25.

When the methylated compound V was recrystallized from more concentrated solution, such as 10 parts of methanol or less, it crystallized in a polymorphic modification as small platelets, m.p. 85–100°. This form, when allowed to stand under the mother liquor, reverted to the higher melting hexagonal plates in from 12 hr. to 7 days.

Ethyl 3-Desoxy-13,14-dehydrothiaquilenin-14-carboxylate (VI).—A 500-ml. three-necked flask with ground glass joints was fitted with a Hershberg wire stirrer and a special seal which could function under reduced pressure. It was also fitted with a reflux condenser, to the top of which was connected a 2-way stopcock connected in turn to a source of nitrogen and vacuum. The apparatus was flame dried and charged with 1.4 g. (0.036 mole) of potassium metal and 60 ml. of dry *t*-butyl alcohol. The flask was evacuated and filled with nitrogen and then refluxed gently until all the potassium had dissolved (about 3 hr.). After cooling, nitrogen was added to equalize the pressure. The flask was then quickly charged with 4.0 g. (0.0166 mole) of the methyl ketonitrile V and 13.2 ml. of diethyl succinate (0.085 mole). The system was then evacuated until the solvent began to boil, filled with nitrogen and allowed to stir at room temperature for 7 hr. After 30 minutes the solid methyl ketonitrile had dissolved to form a deep red solution and after an additional hour an orange precipitate appeared.

After an elapsed time of 7 hr. the mixture was slowly acidified with 35 ml. of dilute (1:1) hydrochloric acid. During the acidification the orange precipitate dissolved and a yellow precipitate appeared with evolution of carbon dioxide. Most of the alcohol was then removed at reduced pressure, the residue taken up in a mixture of benzene and ether, washed well with water, twice with 5% HCl, then three times with 5% KOH, then again with water and the organic solution dried over sodium sulfate.

Evaporation of the solvent under reduced pressure deposited 4.38 g. (81.0%) of the dehydro keto-ester VI as orange needles, m.p. 150.5–154.5° with some previous softening. Several recrystallizations from 40 parts of cyclohexane gave the compound as yellow micro-needles, m.p. 154.0–155.5°.

Anal. Calcd. for $C_{19}H_{18}SO_3$: C, 69.91; H, 5.53; S, 9.84. Found: C, 69.89; H, 5.56; S, 9.89.

In attempts to recrystallize the ester from methanol, decomposition occurred and the ester could be recovered only to the extent of 60–70%. Evaporation of these mother liquors to dryness yielded a red oil with a fruity odor which was not further identified.

The acid and water washings and residues from the above reaction were combined and an aliquot tested for nitrogen by a modified Dumas method. It was found that about 86% of the theoretical amount of possible nitrogen released in the reaction was present.

3-Desoxy-14,15-dehydrothiaquilenin-14-carboxylic Acid (VII).—The keto-ester VI (4.0 g., 0.0123 mole) was refluxed with vigorous stirring for 90 minutes under an atmosphere of nitrogen with 4.0 g. of barium hydroxide in 47 ml. of water and 61 ml. of ethanol. While still hot most of the alcohol was evaporated under vacuum and the mixture slowly acidified with 525 ml. of dilute (1:2) hydrochloric acid. The suspension was heated on the steam-bath with stirring for 90 minutes. The yellow powder was then filtered, washed well with water and air dried. Recrystallization from benzene gave 2.80 g. (73.7%) of the acid VII as tan needles, m.p. 213.9–219.0° decomposed when introduced at 200°.

Anal. Calcd. for $C_{17}H_{14}SO_3$: C, 68.43; H, 4.69. Found: C, 68.10; H, 4.39.

In alkaline solutions the acid was sensitive to oxygen and rapidly decomposed to give a deep purple solution. For this reason it was necessary to conduct the entire reaction with the careful exclusion of air.

3-Desoxy-13,14-dehydrothiaquilenin (VIII).—A solution of 0.5 g. (0.0017 mole) of the acid VII was dissolved in 3.8 ml. of dry pyridine and to this solution was added dropwise with cooling and shaking 7.5 ml. of concentrated hydrochloric acid. The suspension was then refluxed for 1 hr. under nitrogen. At the end of this time evolution of CO_2 had ceased, and the product had crystallized from the hot solution as fine yellow needles. The solution was cooled and

diluted with water and extracted with ether–benzene. The organic solution was washed successively with dilute hydrochloric acid, water, sodium bicarbonate solution and then with water. The solution was then dried and evaporation of the organic solution with the exclusion of air gave 0.390 g. (91.3%) of the crude decarboxylation product as fine pink needles, m.p. 163.0–168° with previous softening from the introduction at 140°. Recrystallization from 40 parts of petroleum ether (90–100°) gave 0.26 g. (66.7% recovery) (60.9% yield) as orange needles, m.p. 173.0–174.3° with previous softening from 168° (introduced at 160°). After vacuum sublimation this material melted at 174–175.5° (introduced at 160°).

Anal. Calcd. for $C_{16}H_{14}SO$: C, 75.56; H, 5.51; S, 12.63. Found: C, 75.68, 75.40; H, 5.46, 5.48; S, 12.60.

Reduction with 10% Pd/C.—In 25 ml. of dry pure ethyl acetate, 0.2 g. (0.0008 mole) of the dehydro-ketone (m.p. 174–175.5° after sublimation) was hydrogenated over 0.10 g. 10% palladium-on-charcoal catalyst. The required amount of hydrogen was absorbed in 6 hr. The catalyst was filtered, the solvent evaporated under vacuum and the residual oil triturated for 24 hr. at 0° with 5 ml. of acetone. Evaporation of the decanted and filtered acetone solution and recrystallization of the solid residue from 4 ml. of methanol gave 0.140 g. (70%) of IX, m.p. 88.5–92.0°, as pink crystals. Concentration of the mother liquor furnished another 0.051 g. (25.0%), m.p. 87.0–89.0°. The total yield was therefore 95.0%. Repeated recrystallization from methanol gave IX, the desoxyisothiaquilenin, m.p. 90.0–91.5°, as slightly pink crystals.

Anal. Calcd. for $C_{16}H_{16}SO$: C, 74.79; H, 6.25; S, 12.53. Found: C, 75.21, 74.25; H, 6.12, 6.28; S, 13.28.

Hydrogenation of VIII with 30% Pd/C. (Neutral Conditions.)—In 25 ml. of dry pure ethyl acetate, 0.200 g. (0.0008 mole) was hydrogenated in the presence of 0.100 g. of 30% palladium–charcoal catalyst. The required amount of hydrogen was absorbed in 3 hr. Evaporation of the filtered solution gave an oil which was triturated with 5 ml. of methanol and furnished 0.040 g. (20.0%) of pink crystals, m.p. 87.5–91.5°. Two recrystallizations from methanol raised the melting point to 90.0–91.5°. Mixed melting point showed this compound to be identical with that obtained by reduction with 10% Pd/C.

A second crop of crystals (0.020 g.) from the original mother liquor melted at 131–142.5°, with previous softening, and the material continued to melt over a wide range even after several recrystallizations from methanol. The mother liquor from which the second crop was obtained furnished only an intractable oil on evaporation.

It is of note that hydrogen take-up did not cease after the amount required for one double bond was absorbed but became even more rapid at this point. When reduction was allowed to go to completion hydrogen take-up ceased at an amount corresponding to about 1.5 double-bonds and only intractable oils were obtained.

Reduction with 30% Pd/C. (Acid Conditions.)—When a 0.200-g. sample of dehydro-compound was hydrogenated with 0.100 g. of 30% palladium–charcoal catalyst with addition of a trace of concd. hydrochloric acid (about 0.0006 mole), the calculated amount of hydrogen was adsorbed in 3 hr. The filtered solution was evaporated and the residual partly crystalline oil triturated with 5 ml. of acetone at 0° for 24 hr. Evaporation of the filtered acetone solution yielded a crystalline residue which on recrystallization from 4 ml. of methanol gave 0.040 g. of pink crystals (20.0%), m.p. 143–147.5°. Several recrystallizations of this material from methanol raised the melting point to 154–155.5°. In spite of the low purity of this compound as shown by analysis, previously detailed evidence indicates that it is another form of the starting material VIII.

Anal. Calcd. for $C_{16}H_{14}SO$: C, 75.76; H, 5.51. Found: C, 73.90; H, 5.65.

Concentration of the mother liquor (to about 1 ml.) yielded 0.075 g. (37.5%) of pink crystals, m.p. 87–91°, IX, which on repeated recrystallization from methanol melted at 90–91.5°.

β-(2-Thianaphthyl)-acrylic Acid.—A mixture of 20.0 g. (0.12 mole) of thianaphthene aldehyde (prepared by the method of Shirley and Danzig[10]), 60.0 ml. of pyridine, 2.4 ml. of piperidine and 31.0 g. of malonic acid was heated on the steam-bath for 2 hr. and refluxed for 5 minutes. The mixture was cooled, poured into an excess of water and acidified with cooling. A 96.4% yield (24.2 g.) of crude material was obtained which when recrystallized from 25 parts of 95% ethanol (Norite) gave as a first crop 17.9 g. (71.3%), m.p. 235–237° dec. Reduction of the volume of the mother liquor gave a second crop of 2.6 g. (10.4%), m.p. 234–237° dec.

Total yield was therefore 81.7%. Repeated recrystallization from ethanol gave material melting at 236–237°.

Anal. Calcd. for $C_{11}H_8SO_2$: C, 64.05; H, 3.88. Found: C, 63.72; H, 3.96.

Methyl β-(2-Thianaphthyl)-acrylate (X).—A solution of 10.2 g. (0.05 mole) of thianaphthylacrylic acid in 400 ml. of dry dioxane was added dropwise with stirring to a solution of 8.4 g. (0.2 mole) of diazomethane in 300 ml. of dry ether. After standing for 4 hr. at room temperature the solvents were evaporated in a current of air, the residue dissolved in ether–benzene and extracted with 5% bicarbonate solution. The organic solution was dried over sodium carbonate, the solvents evaporated and the crystalline residue recrystallized from petroleum ether to yield 9.9 g. (91.1%) of the methyl ester as fine needles, m.p. 123–125°. Repeated recrystallization from pet. ether raised the melting point to 124.5–125.5°.

Anal. Calcd. for $C_{12}H_{10}SO_2$: C, 66.02; H, 4.49; S, 14.72. Found: C, 66.20; H, 4.53; S, 14.79.

Ultraviolet Spectra.—The determinations were performed in absolute alcohol solution with a Beckman ultraviolet spectrophotometer. The principal absorption maxima are recorded below.

3-Desoxy-13,14-dehydrothiaquilenin (VIII): max. 235.5 mμ (log E 4.18), 255.0 (4.09), 261.5 (4.10), 292 (4.35), (4.37).

Ethyl 5-desoxy-13,14-dehydrothiaquilenin-14-carboxylate (VI): max. 222.0 mμ (log E 4.45), 263.0 (4.07), 328.5 (4.45).

3-Desoxy-14,15-dehydrothiaquilenin-14-carboxylic acid (VIII): max. 234.0 mμ (log E 4.64), 261.0 (4.09), 299.5 (3.45).

3-Desoxyisothiaquilenin (IX): max. 233.0 mμ (log E 4.47), 264.0 (3.95), 290.0 (3.56), 300.0 (3.47).

Reduction compound (m.p. 154.0–155.5°): max. 234.0 mμ (log E 4.42), 256.5 (4.08), 263.0 (4.10), 291.0 (4.20), 300.0 (4.22).

Methyl β-(2-thianaphthyl)-acrylate (X): max. 233.0 mμ (log E 4.11), 258.0 (3.82), 319.5 (4.42).

Infrared Spectra.—The compounds were pressed into KBr pills and examined with a Perkin–Elmer infrared spectrophotometer. The principal maxima are recorded below.

3-Desoxy-13-14-dehydrothiaquilenin (VIII): 3075, 2935, 2865, 1736, 1635, 1461, 1448, 1436, 1400, 1378 cm.$^{-1}$.

3-Desoxyisothiaquilenin (IX): 3077, 2970, 2910, 1748, 1468, 1441 1408, 1380 cm.$^{-1}$.

Reduction compound (m.p. 154.0–155.5°): 3075, 2950, 2900, 1749, 1463, 1451, 1439, 1404, 1308 cm.$^{-1}$.

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(10) D. A. Shirley and M. J. Danzig, THIS JOURNAL, **74**, 2935 (1952).