Identification of (IV). The salt remaining from the hot 70% alcohol extraction was allowed to stand with 2 l. of 70% alcohol at room temperature for two and one-half days. The filtrate was combined with the filtrate from the previous step. On evaporation to dryness 58.6 g. of disodium γ-(*p*-sulfophenyl) butyrate, probably contaminated with a little sodium sulfate, was obtained. It was identified as its *p*-chlorobenzylthiuronium derivative, m.p. 150–152°.

Anal. Calcd. for $C_{15}H_{21}ClN_2O_5S_2$: C, 48.59; H, 4.76; N, 6.30; S, 14.41. Found: C, 49.18; H, 4.57; N, 6.44; S, 14.25.

A 4 g. sample of disodium γ-(*p*-sulfophenyl)butyrate was oxidized with potassium permanganate according to the procedure of Campaigne and Suter.[11] The benzylthiuronium derivative of the resulting *p*-sulfobenzoic acid, m.p. 213–214° (lit. 212–214°),[6] established the position of ring substitution.

Anal. Calcd. for $C_{15}H_{16}N_2O_5S_2$: N, 7.61. Found: N, 7.78.

Continued extractions of the residual salts with 40% alcohol yielded only sodium sulfate.

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6-Amino-2-Hexenoic Acid Lactam[1]

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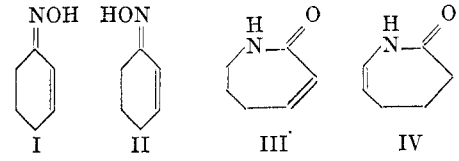
Although work has been reported concerning the Beckmann rearrangement of various substituted cyclohexenone oximes,[3,4] the rearrangement of 2-cyclohexenone oxime itself has not been reported. This rearrangement has been studied as a route to 6-amino-2-hexenoic acid lactam (III) which was of interest in connection with a projected synthesis of azepine.

2-Cyclohexenone[5] was converted to a mixture of stereoisomeric oximes by the method of Bartlett and Woods.[6] This mixture was separated into the corresponding *syn* (I) and *anti* (II) oximes melting at 97–98° and 87–88°, respectively. These melting points are in substantial agreement with those reported by Montgomery and Dougherty.[3]

A modification of the method of Horning, Stromberg, and Lloyd[4] was used in studying the Beckmann rearrangement. It was not possible to convert the *anti* oxime (II) to any isolable amount of 6-amino-5-hexenoic acid lactam (IV). The *syn* oxime (I), however, yielded 6-amino-2-hexenoic acid lactam (III) which was characterized by analysis, infrared and ultraviolet spectra, and catalytic hydrogenation to ε-caprolactam. The ultraviolet spectrum shows a shoulder in the range 235–245 mμ, ε (average) 2400, corresponding in position to the maxima reported by Montgomery and Dougherty for the lactams of 3,5,5-trimethyl- and 3-methyl-5-phenyl-6-amino-2-hexenoic acid and in position and intensity to those reported by Edwards and Singh[7] for 6-methyl and 1,6-dimethyl-5,6-dihydro-2-pyridone. These results, coupled with the known stereochemisty of the Beckmann rearrangement, confirm the assignment of the *syn* conformation to the high melting oxime.



I II III IV

EXPERIMENTAL

One hundred twenty grams of polyphosphoric acid (prepared by dissolving 65.0 g. of phosphorus pentoxide in 55 ml. of 85% phosphoric acid) was heated to 135°, the heat removed and 4.0 g. of *syn*-2-cyclohexenone oxime added with stirring. The temperature rose to 148° and after 10 min. stirring the reaction mixture was poured into 1500 ml. of an ice and water mixture. The mixture was made alkaline at 0° and adjusted to *p*H 12 by the slow addition of cold 15% sodium hydroxide. The solution was extracted exhaustively with chloroform. The extract was dried with sodium sulfate and concentrated to yield 2.3 g. of a dark brown oil. The crude product was subjected to steam distillation and the residue in the boiler decanted from a small amount of polymeric material and extracted with chloroform. The extract was dried with sodium sulfate, treated with decolorizing carbon, filtered, and concentrated to yield 1.9 g. of a light yellow oil. Distillation of this oil yielded 1.0 g. (25%) of colorless product, b.p. 60–65° at 0.5 mm; n_D^{25} 1.5238; d^{25} 1.092. The infrared spectrum shows peaks at 2.96, 6.02, and 6.20 μ. The ultraviolet spectrum shows a shoulder at 235–245 mμ and ε (average) 2400.

Anal. Calcd. for C_6H_9ON: C, 64.84; H, 8.16; N, 12.6. Found: C, 64.66; H, 8.38; N, 12.4.

Catalytic hydrogenation of the lactam at room temperature using 5% palladium-charcoal yielded ε-caprolactam as determined by infrared spectrum comparison and mixed melting point.

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Catalytic Reduction of 2-Acylthiophenes

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The removal of sulfur from the thiophene nucleus attached to aromatic compounds has been reported to proceed satisfactorily when the parent substance

TABLE I

PHYSICAL CONSTANTS OF REDUCTION PRODUCTS

Starting Material	Products	Found B.p., °C.	n_D^{15}	d_4^{20}	Literature[a] Values B.P., °C.	n_D^{15}	d_4^{20}
2-Benzylthiophene[5]	1-phenylpentane	200–203	1.4886	.861	205.0	1.4883	.858
2-Acetothienone[6]	*n*-hexane	68–69	1.3752		68.72	1.3750	.659
2-Propiothienone[7]	2-methylhexane	90–92	1.3845	.677	90.10	1.3849	.679
2-Butyrothienone[7]	*n*-octane	125–127	1.3980		125.6	1.3976	.703
2-Benzothienone[8]	1-phenylpentane	204–205	1.4888	.863	205.0	1.4883	.858
	1-phenyl-1-pentene[b]	202–203	1.5154	.874	202	1.5158	.878
2-Octadecanothienone[9]	docosane[9]	45.1° (m.p.)	1.4406		45.7° (m.p.)	1.4400	

(a) M.P. Doss, *Physical Constants of the Principal Hydrocarbons*, The Texas Company, New York, N. Y., 3rd edition, 1942.
(b) This product was obtained when the reaction was stopped after approximately one-half as much hydrogen had been absorbed as when the reaction was allowed to go to completion.

is refluxed with Raney nickel.[1,2] The product of each reaction was an aromatic ring attached to a saturated aliphatic residue. Thus, it seemed that this reduction might be applied to various substituted thiophenes in order to produce hydrocarbons of specific structure that might be difficult to obtain by other means.

However, when the reaction was attempted with various 2-alkylthiophenes very little of the expected hydrocarbons could be isolated. 2-Benzylthiophene did give a 25% yield of 1-phenylpentane by this route.

Since the 2-acylthiophenes are more readily prepared in a pure state than are the 2-alkylthiophenes, it seemed advisable to use these 2-thienyl ketones as starting materials for the study. At this time we secured a Tungsten-Nickel Sulfide Catalyst from Shell Oil Company which was similar to one previously used to hydrogenate and desulfurize 2-alkylthiophenes.[3] Subsequently, the reductions of various 2-acylthiophenes with the Tungsten-Nickel catalyst were carried out in this laboratory in an effort to develop a satisfactory method of synthesizing pure hydrocarbons.

While this work was in progress, Campaigne and Diedrich[4] reported the reduction of 2-acylthiophenes with a cobalt polysulfide catalyst to the corresponding thiophenes (thiocyclopentanes).

In the course of our work we reduced 2-benzo-, 2-aceto-, 2-propano-, 2-butyro-, and 2-octadecanothienone. The principal product from all but one of these reductions was a hydrocarbon with the same number of carbon atoms and without rearrangement of the carbon skeleton. However, in the case of the 2-propiothienone, the product was a rearranged one, namely, 2-methylhexane. Appleby and his coworkers[3] noted that isomeric hydrocarbons were obtained when they reduced 2-*tert*-butylthiophene.

The reduction of 2-benzothienone proved to be a very interesting reaction insomuch as a variety of products was obtained, depending upon the conditions of the reaction. Complete reduction of this ketone gave a 46% yield of *n*-amylbenzene. However, when only a partial reduction was carried out, other reduction products were obtained, 2-benzylthiophene and 1-phenyl-1-pentene. We were unable to isolate any of the corresponding alcohol from this reaction, or to obtain a positive alcohol test from the reaction mixture. Although we could not isolate any tetrahydrothiophene derivatives, the reaction mass had a characteristic thiophane odor. Some unreacted ketone was recovered. The 1-phenyl-1-pentene was identified by index of refraction, boiling point, and oxidation to benzoic acid. Our work did not preclude the presence of isomeric 1-phenylpentenes although benzoic acid was obtained in nearly quantitative yield.

The reduction of 2-octadecanoylthiophene gave an excellent yield of docosane. A mass spectrogram of this material showed less than 0.1% of combined tertiary carbon and carbon-to-carbon double bond. This showed that no rearrangement occurred even with this very long chain ketone.

EXPERIMENTAL

Ketones. The ketones were prepared by the action of phosphorus pentoxide and carboxylic acid on thiophene in an inert solvent. The ketones were carefully fractionated before use and their physical data corresponded to those given in the literature.

Reductions. A 1-l., high-pressure, high temperature bomb was charged with the ketone and Tungsten-Nickel sulfide catalyst in a 2-1 weight ratio. Hydrogen was introduced under a pressure of 1500 p.s.i. The bomb was heated to 300°

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and shaken at constant temperature until no further drop in hydrogen pressure was noted.

The reaction mass was filtered to remove the catalyst and the liquid product was carefully fractionated or recrystallized. (See Table I for the data.) The fractionizations were carried out with a 10-plate, glass helices-packed column. A Corad head was used with the column.

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Analogs of 4-(*p*-Dimethylaminostyryl)-quinoline[1]

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The anti-tumor activity of 4-(*p*-dimethylaminostyryl)quinoline(I)[2-5] and 1-(*p*-dimethylaminostyryl)naphthalene[6] encouraged us to synthesize several analogous compounds in which a nitrogen atom occupies the place of one of the carbons in the ethylene bridge. *N*-(*p*-Dimethylaminophenyl)quinoline-4-aldimine did not produce regression or significant inhibition of the growth of Lymphoma 8 tumors in rats, either when the compound was mixed in the diet or administered by subcutaneous injection of a solution in vegetable oil, although identical concentrations of I brought about prompt regression of similar tumors.[7] The following new compounds have not yet been tested against tumors.

EXPERIMENTAL

N-(*p*-Dimethylaminophenyl)naphthalene-1-aldimine. A mixture of 22 g. of *p*-aminodimethylaniline and 24.8 g. α-naphthaldehyde was heated 5 hr. at 135°. The product was recrystallized from ethyl acetate, from isohexane, and four times from isopropyl ether to yield 7.4 g. (17%) dark yellow crystals, m.p. 77–79°.

Anal.[8] Calcd. for $C_{19}H_{18}N_2$: C, 83.20; H, 6.57. Found: C, 83.08, 82.82; H, 6.57, 6.76.

N-(*p*-Dimethylaminophenyl)pyridine-4-aldimine. A mixture of 8.6 g. of pyridine-4-aldehyde and 10.9 g. of *p*-dimethylaminoaniline was heated 45 min. at 105°. The dirty green crystals were recrystallized twice from isopropyl ether to give 8.5 g. (47%) of light yellow crystals, m.p. 195°.

(1) The research was aided by a grant from the American Cancer Society.

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(7) We are indebted to Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Mr. Aubrey L. Bates for testing the compounds at the Wistar Institute of Anatomy and Biology, with the aid of a grant from the National Cancer Institute.

(8) Analyses by Drs. G. Weiler and F. B. Strauss, Oxford, England.

Anal. Calcd. for $C_{14}H_{15}N_3$: C, 74.68; H, 6.71. Found: C, 74.75; 74.75; H, 6.79, 6.59.

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4-[4-(*p*-Dimethylaminophenyl)-1,3-butadienyl]quinoline[1]

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The activity of 4-(*p*-dimethylaminostyryl)quinoline[2,3] and 4-(*p*-dimethylaminostyryl)quinoline methiodide[4] in causing regression of Lymphoma 8[5] tumors in rats encouraged the authors to synthesize the corresponding compounds in which the ethylene bridge is replaced by a butadiene bridge. The antitumor activity of the compounds has been investigated at the Wistar Institute of Anatomy and Biology through the cooperation of Dr. Margaret Reed Lewis, Dr. Boland Hughes, and Aubrey L. Bates, with the assitance of a grant from the National Cancer Institute. 4-[4-(*p*-Dimethylaminophenyl)-1,3-butadienyl]quinoline did not seem exceptionally toxic but had little or no effect on Lymphoma 8 when fed at a concentration of 0.03% in the diet. The methiodide, however, seemed more toxic than 4-(*p*-dimethylaminostyryl)quinoline methiodide.

EXPERIMENTAL

4-[4-(p-Dimethylaminophenyl)-1,3-butadienyl]quinoline. A mixture of 10.3 g. (0.059 mole) of *p*-dimethylaminocinnamaldehyde,[6] 8.5 g. (0.059 mole) of lepidine, and 2.1 g. (0.03 mole) of anhydrous zinc chloride was heated 8 hr. at 120°. The resulting tar was washed thoroughly with concentrated ammonium hydroxide and crystallized from ethanol. The 7 g. of crude product was recrystallized twice from ethyl acetate to obtain 1.3 g. of brown crystals, 7%, m.p. 165–166°.

Anal.[7] Calcd. for $C_{21}H_{20}N_2$: C, 83.95; H, 6.77. Found: C, 83.74, 83.82; H, 6.59, 6.51.

4-[4-(p-Dimethylaminophenyl)-1,3-butadienyl]quinoline methiodide. A mixture of 15 g. (0.080 mole) of *p*-dimethylamino cinnamaldehyde and 22.5 g. (0.079 mole) of lepidine methiodide was poured into 500 ml. of boiling acetic an-

(1) This project was aided by a grant from the American Cancer Society.

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