[CONTRIBUTION FROM THE RESEARCH AND DEVELOPMENT LABORATORIES, UNIVERSAL OIL PRODUCTS COMPANY]

Reaction of 1,3-Butadiene and of Isoprene with Thiophene

BY HERMAN PINES, BRUNO KVETINSKAS, J. A. VESELY AND EDMOND BACLAWSKI

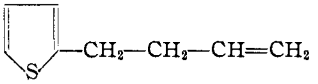
Butenyl- and pentenylthiophene were formed when thiophene was contacted with 1,3-butadiene and with isoprene, respectively, in the presence of 85% aqueous phosphoric acid. The butenylthiophenes were composed of 2-(3-butenyl)-thiophene and of 2-(2-butenyl)-thiophene. The pentenylthiophene consisted of 2-(3-methyl-2-butenyl)-thiophene. The alkenylthiophenes produced were hydrogenated to the corresponding alkylthiophenes in the presence of palladium deposited on alumina.

The reaction of conjugated diolefins with thiophenes has heretofore not been reported in the literature. The study of this reaction was of special interest as a possible method for synthesizing alkenylthiophenes. It was found that butenyl- and pentenylthiophene were formed when thiophene was contacted with 1,3-butadiene and with isoprene, respectively, in the presence of 85% aqueous phosphoric acid. The reaction with butadiene proceeded under pressure and at 120°, while isoprene reacted at room temperature and at atmospheric pressure.

The butenylthiophenes, produced from the condensation of 1,3-butadiene with thiophene, were separated by distillation into two fractions boiling at (a) 182° and at (b) 190°.

The fractions a and b yielded on hydrogenation products having identical boiling points, refractive indices and infrared spectra. The products were identified as 2-*n*-butylthiophene by comparison with a known sample synthesized by Clemmensen reduction of 2-butyrylthiophene. The infrared spectra of the products and of the synthetic 2-*n*-butylthiophene were identical.[1] Comparison of chloromercury derivatives further confirmed the identity of the hydrogenated products as 2-*n*-butylthiophene.

Possible structures for the original reaction products are 2-(3-butenyl)-thiophene (I), 2-(2-butenyl)-thiophene (II) and 2-(1-butenyl)-thiophene (III).



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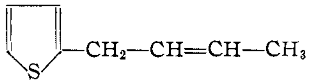

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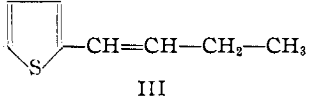


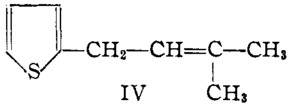
III

The positions of the double bond in fractions a and b were determined by use of well established spectroscopic correlations. Intense bands at 910 and 970 cm.$^{-1}$ in the infrared spectrum of fraction a indicated that the principal component contained a vinyl group, —CH=CH$_2$.[2] Therefore, the principal component of fraction a must be 2-(3-butenyl)-thiophene (I).

The infrared spectrum of fraction a also had a moderate intensity band at 960 cm.$^{-1}$. A strong band at this position is well known to indicate the presence of a symmetrical disubstituted olefinic linkage, RCH=CHR′. Therefore, the presence of a lesser amount of either the compounds (II) or (III) must be considered. Structure (III), in which the side chain olefinic linkage is conjugated with the thiophene ring, was ruled out by ultraviolet spectroscopic analysis.[3]

Fraction b was shown to have an infrared absorption band at 960 cm.$^{-1}$, but no absorption at 890 or 910 and 970 cm.$^{-1}$, indicating that the olefin was exclusively of the RCH=CHR′ type. An ultraviolet analysis again showed no conjugation (absorptivity equal to 54 l./g. cm. at 2340 Å.). Therefore, the structure of fraction b is 2-(2-butenyl)-thiophene (II).

Isoprene on reaction with thiophene formed predominantly 2-(3-methyl-2-butenyl)-thiophene (IV). On hydrogenation compound (IV) yielded



IV

2-isoamylthiophene, which according to infrared analysis and solid chloromercury derivative was identical to 2-isoamylthiophene prepared from 2-(3-methylbutyryl)-thiophene by means of a Wolff–Kishner reduction. Infrared analysis showed that the hydrogenated pentenylthiophene did not contain any *t*-amylthiophene.

The infrared spectrum of the unhydrogenated reaction product did not have bands of appreciable intensity of 890, 910 and 970, or 960 cm.$^{-1}$. Therefore, the respective olefin types RR′C=CH$_2$, RCH=CH$_2$ or RCH=CHR′ which these bands represent, could not be present in any appreciable amounts. The ultraviolet absorption spectra showed that the alkenyl double bond is not in conjugation with the thiophene ring. Had conjugation been present an increase in specific extinction coefficient would have been noticed when compared to 2-isopentylthiophene. The

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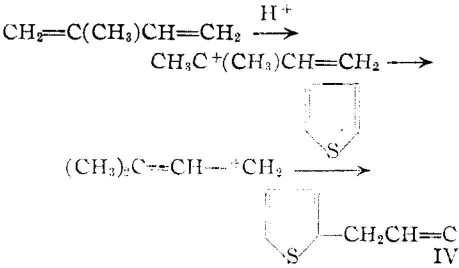
[1] Examination of the spectra of the hydrogenated products at the characteristic absorption wave lengths for 2-*s*-, 2-iso- and 2-*t*-butylthiophenes indicated the absence of significant amounts of these compounds.

[2] These bands, which always occur in olefinic hydrocarbons containing a vinyl group, are due to C–H bending vibrations (N. Sheppard and G. Sutherland, *Proc. Roy. Soc.* (*London*), **A196**, 195 (1949)). They appear to be relatively unaffected by conjugation (*e.g.*, styrene, A. P. I. Project 44 spectrogram 170) and are also present in the spectrum of 2-vinylthiophene (A. P. I. Project 44 spectrogram 800). The possible interference effect of bands due to the substituted thiophene ring structure was ruled out by the observation that 2-*n*-butylthiophene has no major bands in this region.

[3] The absorptivity of fraction a had a maximum of 54 l./g. cm. at 2340 Å., indicating no conjugation (*e.g.*, 2-methylthiophene, K = 76 l./g. cm. at 2340 Å.). It is well known that conjugation would shift the λ to higher wave lengths and increase the absorptivity.

pentenylation of thiophene is accompanied most probably by an allylic rearrangement



While the infrared data appear to establish the structure of Compound IV ozonolysis and oxidation experiments gave results of an anomalous nature. Ozonolysis yielded acetone, 2-thiophenecarboxylic acid, and 2-thiophenealdehyde.[4] Oxidation with 5% aqueous potassium permanganate yielded acetone and 2-thiophenecarboxylic acid. It is probable that if 2-thiopheneacetic acid was produced during the latter oxidation it underwent further oxidation to 2-thiophenecarboxylic acid. The behavior of 2-thiopheneacetic acid is probably similar to that of phenylacetic acid which even on mild oxidation forms benzoic acid.

Experimental Part

I. **Reaction of Butadiene with Thiophene.**—Seventy-six grams (0.9 mole) of thiophene, 17 g. (0.3 mole) of 1,3-butadiene and 15 ml. of 85% phosphoric acid were heated at 100–120° for 4 hours in an 850-ml. rotating autoclave provided with a glass liner. After the autoclave was cooled the organic material was separated from the acid layer, washed with water and with 10% aqueous sodium hydroxide, dried over potassium carbonate and distilled on a column of about seven-plate efficiency. The following fractions were separated: (1) thiophene 47 g., (2) butenylthiophene b.p. 72–76° at 16.5 mm., 28 g., (3) dithienylbutane, b.p. 109–110° at 1.5 mm., 3 g., $n^{20}\text{D}$ 1.5834, $d^{20}{}_4$ 1.1213; $MR\text{D}$ obsd. 56.7, $MR\text{D}$ calcd., 65.3; (4) higher boiling compounds, 10 g.

Anal. Calcd. for $C_{12}H_{14}S_2$: C, 64.86; H, 6.48; S, 28.83. Found: C, 65.03; H, 6.41; S, 28.60.

The fraction corresponding to butenylthiophene was redistilled on a column of 50-plate efficiency at a reflux ratio of 10 to 1. The following constant boiling products were separated: **a**, b.p. 99.5° at 48 mm. (182° at 760 mm.[5]), 40%, $n^{20}\text{D}$ 1.5251, $d^{20}{}_4$ 0.9906; $MR\text{D}$ obsd. 42.7, $MR\text{D}$ calcd. 41.8.[6]

Anal. Calcd. for $C_8H_{10}S$: C, 69.57; H, 7.25; S, 23.19. Found: C, 70.14; H, 7.59; S, 23.06.

b, b.p. 97° at 39 mm. (190° at 760 mm.), 35%, $n^{20}\text{D}$ 1.5280, $d^{20}{}_4$ 0.9928; $MR\text{D}$ obsd. 42.8, $MR\text{D}$ calcd. 41.8.

Anal. Calcd. for $C_8H_{10}S$: C, 69.57; H, 7.25; S, 23.19. Found: C, 69.07; H, 7.18; S, 23.50.

Hydrogenation of a.—Six grams was heated at 80–100° for 6 hours under 100 atmospheres initial hydrogen pressure in the presence of 2.5 g. of a palladium–alumina (0.5% Pd) catalyst. The hydrogenation was carried out in a 130-ml. rotating autoclave. About 1 mole of hydrogen was absorbed per mole of butenylthiophene charged. The butylthiophene obtained distilled at 175–178°, $n^{20}\text{D}$ 1.5015.

Chloromercury Derivative.—The chloromercury derivative of the above butylthiophene was prepared according to the method described previously.[7] After crystallizing from absolute ethanol the derivative melted at 141–142°, and did not depress the mixed melting point of the chloromercury derivative of known 2-*n*-butylthiophene.

Hydrogenation of b.—Results and products obtained were similar to those described for a.

II. **Synthesis of 2-*n*-Butylthiophene. 2-Butyrylthiophene.**—It was prepared according to the method of Hartough and Kosak[8] using 31.6 g. of *n*-butyric anhydride, 50.4 g. of thiophene and 5 g. of boron fluoride ethyl etherate. The 2-butyrylthiophene distilled at 97° at 5 mm., $n^{20}\text{D}$ 1.5440; yield was 11 g. or 40%. The semicarbazone derivative of the 2-butyrylthiophene, after recrystallizing from 30% ethanol, melted at 173.5–174°; this corresponds to the reported melting point.[9]

2-*n*-Butylthiophene.—It was obtained by the reduction of 9 g. of the above ketone with amalgamated zinc and hydrochloric acid. The crude 2-butylthiophene was redistilled from sodium; b.p. 97° at 18 mm., $n^{20}\text{D}$ 1.5004; yield 3.5 g. or 40%.

2-*n*-Butyl-5-thiophenemercurichloride Derivative.—After crystallization from absolute alcohol it melted at 143–144°.

Anal. Calcd. for $C_8H_{11}SHgCl$: C, 25.59; H, 2.93; S, 8.53. Found: C, 25.83; H, 3.01; S, 8.29.

III. **Reaction of Isoprene with Thiophene.**—The apparatus used was a two-liter three-neck flask fitted with a mercury sealed stirrer, a dropping funnel and a reflux condenser. Two hundred ml. of 85% phosphoric acid and 504 g. of thiophene were stirred in the flask while a mixture of 504 g. of thiophene and 272 g. of isoprene was added dropwise over a period of 1 hour; stirring was continued for 5 hours at 27–37°. The acid layer increased in volume by 34 ml. The organic material was washed, dried, and distilled on a 7-plate column. The following fractions were obtained from the distillation of 1196 g. of material: (1) thiophene 723 g., (2) pentenylthiophene 345 g., b.p. 79–81° at 10 mm., (3) 60 g., b.p. 100–140° at 3.0 mm., $n^{20}\text{D}$ 1.5292; (4) higher boiling compounds, 54 g.

The pentenylthiophenes were redistilled on a 50-plate column and at a reflux ratio of about 10:1. Ninety per cent. distilled at 79° at 9.7 mm. (205° at 760 mm.), $n^{20}\text{D}$ 1.5251, $d^{20}{}_4$ 0.9819.

Anal. Calcd. for $C_9H_{12}S$: C, 71.05; H. 7.89; S, 21.05; $MR\text{D}$, 47.16. Found: C, 70.91; H, 8.05; S, 21.36; $MR\text{D}$, 47.12.

Oxidation with Potassium Permanganate.—Pentenylthiophene (15.2 g.) and 150 ml. of water were stirred in a 1-liter 3-neck flask which was immersed in an ice-bath. A solution of 31.6 g. of potassium permanganate dissolved in 400 ml. of water was added over a period of 4 hours; the rate of addition was such that the temperature did not exceed 5°. The product was filtered to remove the manganese dioxide. The filter cake was washed twice with hot water. The filtrates were combined and distilled. The first 15 ml. of product which distilled over was saturated with potassium carbonate which produced the separation of acetone, b.p. 56°, the semicarbazone of which melted at 183–183.2°.

The volume of the main product was reduced to about 150 ml. by distilling at reduced pressure. After extracting with ether it was acidified with hydrochloric acid; the acid obtained melted at 128° after resublimation and its neutral equivalent was found to be 128.8. This corresponded to 2-thiophenecarboxylic acid, which is reported to melt at 129°.

Ozonolysis.—Eleven grams of the fraction corresponding to pentenylthiophene dissolved in 100 ml. of carbon tetrachloride was subjected to a stream of ozonized air. The approximate ratio of ozone to product used was 0.9 mole to

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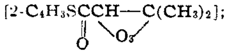
[4] *It has been observed recently by Ipatieff, Huntsman and Pines* (unpublished work) that alkaline hydrogen peroxide does not completely decompose the ozonide of hydrocarbons. Part of the decomposition occurs during the steam distillation as evidenced by the evolution of oxygen. In this particular case it is very probable that part of the ozonide is oxidized by hydrogen peroxide to give the keto ozonide  $[2\text{-}C_4H_3S\underset{\underset{O}{\|}}{C}CH\text{—}C(CH_3)_2]$ (O_3 bridging CH and C); the latter on steam distillation may decompose to 2-thiophenealdehyde, acetone and carbon dioxide. Part of the aldehyde might have undergone oxidation by hydrogen peroxide to form 2-thiophenecarboxylic acid. Additional work is contemplated in order to determine whether the above expressed hypothesis is correct.

[5] Temperature conversion taken from "Vapor Pressure–Temperature Nomograph," by S. B. Lippincott and M. M. Lyman, *Ind. Eng. Chem.*, **38**, 322 (1946).

[6] The value 7.00 was used for the atomic refraction of sulfur, reference 11.

[7] W. Steinkopf, *Ann.*, **424**, 23 (1920).

[8] H. D. Hartough and A. I. Kosak, THIS JOURNAL, **70**, 867 (1948).

[9] W. Steinkopf and I. Schubart, *Ann.*, **424**, 1 (1921).

1.0 mole. The ozonide was decomposed with 20 ml. of solution consisting of equal volumes of 30% hydrogen peroxide and 10% sodium carbonate; these were heated for 3 hours at 60°. Acetone (0.4 g.) b.p. 55–57°, semicarbazone, m.p. 183°, 2-thiophenealdehyde (3.3 g.) and 2-thiophenecarboxylic acid, 1.6 g., were isolated from the reaction product.

The liquid corresponding to 2-thiophenealdehyde boiled at 69° at 8 mm. The phenylhydrazone of the aldehyde melted at 135–136° after recrystallizing once from ethanol; the melting point of the phenylhydrazone was in agreement with the phenylhydrazone of 2-thiophenealdehyde reported in the literature.[10]

The isolated acid, after sublimation, had a neutral equivalent of 128.8 and melted at 129°, corresponding to 2-thiophenecarboxylic acid.[11]

Hydrogenation.—Ten grams of the pentenylthiophene was hydrogenated in the presence of 3 g. of palladized alumina (0.5% palladium) under conditions described for the hydrogenation of butenylthiophene. The pentylthiophene obtained distilled at 42–44° at 2 mm., $n^{20}D$ 1.5011.

The chloromercury derivative of the pentenylthiophene after crystallization from absolute ethanol melted at 168°. It showed no depression in melting point when mixed with a known sample of 2-isopentyl-5-chloromercurithiophene.

Anal. Calcd. for $C_9H_{13}SHgCl$: S, 8.23. Found: S, 8.37.

IV. Synthesis of 2-Isopentylthiophene. 2-Isovalerylthiophene.—The synthesis was made according to the method of Hartough and Kosak[12] using 200 ml. of thiophene, 42.6 g. of phosphorus pentoxide and 30.6 g. of isovaleric acid. Thirty-four grams (67% yield) of 2-isovalerylthiophene boiling at 77–79° at 2.0 mm., $n^{20}D$ 1.5329, was obtained. The semicarbazone melted at 165–166°.

Anal. Calcd. for $C_{10}H_{15}N_3SO$: N, 18.67. Found: 18.63.

2-Isopentylthiophene.—2-Isovalerylthiophene (12 g.) was reduced by a modified Wolff–Kishner reduction.[13] The 2-isopentylthiophene (3 g.) was distilled from sodium. It boiled at 65–66° at 8.5 mm., $n^{20}D$ 1.4981, yield 25%. Its 2-isopentyl-5-thiophenemercurichloride melted at 168°, reported,[6] 171.5–172°, after recrystallization from absolute ethanol.

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[10] A. Hantzsch, *Ber.*, **22**, 2827 (1889).

[11] C. Paal and J. Tafel, *ibid.*, **18**, 456 (1885).

[12] H. D. Hartough and A. I. Kosak, THIS JOURNAL, **69**, 3098 (1947).

[13] W. J. King and F. F. Nord, *J. Org. Chem.*, **14**, 638 (1949).

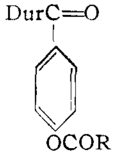
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Replacement of Nuclear Acyloxyl Groups by the Action of a Grignard Reagent

BY REYNOLD C. FUSON AND WILLIAM D. EMMONS[1]

Acetic, benzoic, mesitoic and benzenesulfonic esters of duryl *p*-hydroxyphenyl ketone react with *t*-butylmagnesium chloride to yield *p*-*t*-butylphenyl duryl ketone.

The discovery that certain Grignard reagents are capable of displacing the cyano group in *p*-cyanophenyl duryl ketone[2] suggested that other groups which could be detached as stable ions might behave in a similar manner. The mesitoxy radical seemed particularly attractive since its carbonyl group is known to be resistant to attack. Moreover, by coördination with the magnesium atom of the Grignard reagent it could conceivably serve to facilitate attack of the nucleus by making the essential step intramolecular.



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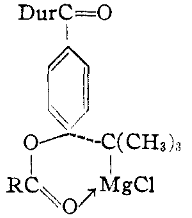

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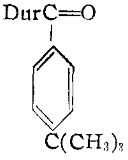

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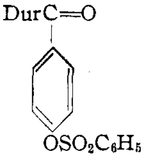

IV

Experiments with duryl *p*-mesitoxyphenyl ketone (I, R = Mes) and *t*-butylmagnesium chloride bear out this speculation. *p*-*t*-Butylphenyl duryl ketone (III) is produced in a 74% yield, and 65% of the mesitoxy moiety is accounted for as mesitoic acid. The hypothetical coördination complex is represented by II (R = Mes). Further study showed, however, that the displacement could be effected with unhindered acyloxy groups. The acetoxy (I, R = CH_3) and benzoxy (II, R = C_6H_5) derivatives were converted to *p*-*t*-butylphenyl duryl ketone (III) in yields of 70 and 43%, respectively. In the experiment with the benzoxy compound benzoic acid was isolated in a 25% yield.

It is of especial interest that the same type of change can be effected with sulfonic esters. The benzenesulfonate (IV) derived from duryl *p*-hydroxyphenyl ketone yields the *p*-*t*-butyl ketone (III) in 17% yield when treated with the *t*-butyl reagent.

The duryl *p*-hydroxyphenyl ketone, from which all the esters were derived, is readily obtained by treatment of *p*-anisyl duryl ketone with a mixture of hydrobromic and acetic acids. A much better method is the Friedel–Crafts condensation of *p*-acetoxybenzoyl chloride and durene. During the reaction the acetate group is hydrolyzed and the product, obtained in 76% yield, is duryl *p*-hydroxyphenyl ketone. The cleavage of the ester group is not surprising since *p*-acetoxyphenyl duryl ketone is a vinylog of an acid anhydride.

Experimental

Duryl *p*-Hydroxyphenyl Ketone.—To a solution of 90.0 g. of *p*-acetoxybenzoyl chloride, 61.7 g. of durene and 300 ml. of carbon disulfide was added over a 30-minute period 122.1 g. of aluminum chloride. The solution was stirred and heated under reflux for 90 minutes and poured into a mixture of ice and dilute hydrochloric acid. The carbon disulfide was distilled and the residue steam distilled to remove impurities. The residual oil crystallized when cooled and was recrystallized from benzene (Darco); m.p. 202.0–202.5°; yield 88 g. (76%).

Anal.[3] Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.28; H, 7.39.

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[1] Rohm and Haas Fellow 1949–1950; Socony-Vacuum Oil Company Fellow 1950–1951; present address, Rohm and Haas Company, Huntsville, Alabama.

[2] R. C. Fuson, W. D. Emmons and R. Tull, *J. Org. Chem.*, **16**, 648 (1951).

[3] The microanalyses were performed by Miss Emily Davis and Miss Rachel Kopel.