viscous tar. The sudden occurrence of this decomposition indicates the potential hazard involved in carrying the distillation too far.[13]

The first fraction (35.5 g.) was redistilled through a short Vigreux column, and 30.1 g. of IV was collected at 52–56° (0.25–0.3 mm.), yield 29.6%. A center cut (15.8 g.) boiled at 52–53° (0.25 mm.), n^{25}D 1.4413. This product was analyzed.

Another portion of redistilled γ-nitrocaproaldehyde (1.51 g.) was treated with 2.03 g. of 2,4-dinitrophenylhydrazine in 160 ml. of boiling 95% ethanol containing 1 ml. of concentrated hydrochloric acid. The resulting derivative weighed 3.14 g. (93% yield) and melted at 101.5–102.5°. An analytical sample melted at 101.5–102° (crystallized from ethanol).

4-Amino-1-hexanol (VII).—Compound IV (14.5 g., 0.1 mole) was dissolved in 100 ml. of absolute ethanol and 0.7 g. of Adams platinum oxide catalyst was added. After approximately two moles of hydrogen had been consumed an additional 0.6 g. of catalyst was added and the hydrogenation was resumed. Approximately 3.8 moles of hydrogen was consumed after a total of 48 hours. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo*. The crude product yielded 6.3 g. of distillate at 61–63° (0.27 mm.) and 2.2 g. at 63–65° (0.27 mm.). The combined fractions represent a yield of 73%. The first fraction was analyzed.

Anal. Calcd. for $C_6H_{15}ON$: C, 61.5; H, 12.9; N, 11.93. Found: C, 61.96; H, 12.69; N, 12.04.

The reaction of the reduced product with 3,5-dinitrobenzoyl chloride yielded the bis-3,5-dinitrobenzoyl derivative of VII melting at 193–194° after recrystallization from an ethanol–ethyl acetate solvent mixture.

Anal. Calcd. for $C_{20}H_{19}O_{11}N_5$: C, 47.5; H, 3.8; N, 13.9. Found: C, 47.88; H, 3.76; N, 13.99.

Periodate Treatment of 4-Amino-1-hexanol (VII).—4-Amino-1-hexanol (0.1646 g.) was treated with 40 ml. of 0.44 *M* periodic acid solution at room temperature. Aliquot samples taken after one-half hour and three-fourths hour showed no periodate uptake in the reaction mixture.

α-Ethylpyrrolidine (VIII). A.—Product IV (13.8 g.) was dissolved in 60 ml. of absolute ethanol and 4.0 g. of a moist paste of Raney nickel was added. The hydrogenation was carried out at an initial pressure of 700 p.s.i. at 125–130° over a period of four hours. The catalyst was removed by filtration and the filtrate was acidified with hydrochloric acid and concentrated *in vacuo*. The residual sirupy material was dissolved in 200 ml. of water and made alkaline with 4.8 g. of NaOH. The mixture was steam distilled and one liter of distillate was collected containing a small quantity of insoluble oil. The distillate was acidified and concentrated *in vacuo* to a thin sirup. This sirup was treated with 50 ml. of 40% KOH solution and the oil which separated was taken up in ether (100 ml.). The ether layer was dried over anhydrous sodium sulfate. After removal of the ether through a Vigreux column the α-ethylpyrrolidine distilled at 121–128° (740 mm.), n^{15}D 1.4425; given[9] for pure α-ethylpyrrolidine, n^{15}D 1.4442, weight 0.75 g., 8% yield. Some higher boiling material was obtained at 200–225° (740 mm.). This product was not characterized.

Crude α-ethylpyrrolidine was reacted with *p*-toluenesulfonyl chloride in aqueous sodium hydroxide. The product separated in the alkaline media, as would be expected of a secondary amine derivative. After two recrystallizations from 80% ethanol it melted at 76.5–77.5° (corrected); given[9] for the *p*-toluenesulfonyl derivative of α-ethylpyrrolidine, m.p. 76.9°.

Anal. Calcd. for $C_{13}H_{19}O_2SN$: C, 61.63; H, 7.56. Found: C, 62.03; H, 7.45.

B.—Compound VII (4.79 g.) was refluxed for 16 hours with 30 ml. of 48% hydrobromic acid. The light brown hydrolyzate was concentrated *in vacuo* to a thin paste. This paste was dissolved in 500 ml. of water and made alkaline with 10 g. of sodium hydroxide. The mixture was steam distilled and then processed further as described under Method A.

α-Ethylpyrrolidine, VIII (1.78 g., 44%), was collected at 121–126° (736 mm.), n^{15}D 1.4427. VIII was again converted to the *p*-toluenesulfonate (m.p. 75.5–76.5°) and also to the phenylthiourea derivative, m.p. 87–87.6°.

Anal. Calcd. for $C_{13}H_{18}N_2S$: C, 66.62; H, 7.74; N, 11.96. Found: C, 66.93; H, 7.68; N, 12.69.

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[13] A similar decomposition was observed by Fort and McLean, see reference 5.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF FORDHAM UNIVERSITY]

The Willgerodt Reaction in the Heterocyclic Series. III. Temperature Studies with Thienyl Ketones

BY JOSEPH A. BLANCHETTE AND ELLIS V. BROWN

2-Thienyl methyl ketone has been found to undergo the Willgerodt reaction with the yield dependent on the operation temperature. Temperature studies with 2-thienyl methyl ketone, 2,5-dimethyl-3-thienyl methyl ketone and 3,4-dimethyl-2-thienyl methyl ketone have shown that the yields of the corresponding amides decrease sharply above 160°. When these amides were subjected to the conditions of the Willgerodt reaction at a temperature of 190° only small amounts could be recovered. Lengthening of the aliphatic chain of 2-thienyl ketones was accompanied by a decrease in the yield of amide. A comparison of the yields obtained from the thiophene compounds investigated is included.

In previous reports[1] we have shown that α-vinyl, α-acetonyl- and α-(1-hydroxyethyl)-thiophenes yielded the respective amides by the Willgerodt reaction in yields of 20–35%. 5-Alkyl-2-thienyl methyl ketone and 2,3-dimethyl-5-thienyl methyl ketone gave 40–55% yields of the corresponding amides by the Willgerodt reaction. However, the compounds which contained an alkyl group in the β-position ortho to the α-carbonyl group were converted to the respective amides in yields of only 25–35%. When both α-positions contained alkyl substituents yields of 70–90% were obtained with these 3-thienyl methyl ketones while 3-thienyl methyl ketone itself gave the lowest yield, 5–13%. Earlier in this study, a series of experiments with 2-acetothienone was carried out but no amides could be isolated from the reaction mixtures. This observation has also been reported by several investigators[2,3,4] who used the morpholine and sulfur modification of the Willgerodt reaction. This failure of 2-thienyl methyl ketone to react while other α-monosubstituted thiophenes were converted to the corresponding amides required a reasonable explanation. Any assumption that

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[1] J. A. Blanchette and E. V. Brown, THIS JOURNAL, **73**, 2779 (1951); **72**, 3414 (1950).

[2] E. Schwenk and D. Papa, *J. Org. Chem.*, **11**, 798 (1946).

[3] Buu-Hoi and Nguyen-Hoan, *Rec. trav. chim.*, **68**, 5 (1949).

[4] B. H. Ford, G. C. Prescott and D. R. Colingsworth, THIS JOURNAL, **72**, 2109 (1950).

the unsubstituted character is responsible for the unique results obtained with 2-thienyl methyl ketone is no longer valid, yet some peculiarity of this particular molecule seemed to prevent its conversion to the amide by the Willgerodt reaction. In an attempt to interpret these seemingly anomalous results, we have reinvestigated the Willgerodt reaction with 2-thienyl methyl ketones using the conditions that we have found successful for other compounds of the thiophene series and also investigated the reaction over a wide range of temperature.

2-Thienyl methyl ketone was converted to 2-thienylacetamide in yields of 53% with ammonium polysulfide and 43% with ammonium hydroxide and sulfur at a temperature of 140°. Our earlier experiments were conducted at higher temperatures to yield black resinous reaction mixtures from which no amide could be isolated. The lower temperatures yielded cleaner reaction mixtures from which the amide was readily isolated. As this manuscript was being prepared, a paper by Dann and Distler[5] appeared which reported the conversion of 2-thienyl methyl ketone to 2-thienylacetamide by the Willgerodt reaction. These authors modified the time and temperature of reaction and combined the ammonium polysulfide, ammonium hydroxide and sulfur reagents. We have found that temperature is the critical factor.

In order to study the effect of temperature on yield, experiments were carried out with 2-thienyl methyl ketone, 2,5-dimethyl-3-thienyl methyl ketone, and 3,4-dimethyl-2-thienyl methyl ketone at various temperatures. These results are shown in Table I. In general, a maximum yield was obtained at 140–150° with a sharp decrease above 160°. In an attempt to determine whether the usual product of the Willgerodt reaction was stable when the reaction was run at higher temperatures, 2-thienylacetamide was introduced along with ammonium polysulfide into a Carius tube and heated to 190° for 12 hr. No amide was recovered after this treatment. Similar treatment of 2,5-dimethyl-3-thienylacetamide and 3,4-dimethyl-2-thienylacetamide permitted an amide recovery of 45 and 16%, respectively.

TABLE I

EFFECT OF TEMPERATURE ON YIELD

2-Thienyl methyl ketone			3,4-Dimethyl-2-thienyl methyl ketone		2,5-Dimethyl-3-thienyl methyl ketone	
Temp., °C.	Yield, % A[a]	Yield, % B	Temp., °C.	Yield, % A	Temp., °C.	Yield, % A
100	7	21				
120	27	30	130	14	130	27
140	53	43	150	32	150	80
150	47	45	160	30	160	95
160	43	11	170	28	170	53
180	1–2	1	190	1	190	19

[a] See experimental for details of Methods A and B.

2-Thienyl ethyl ketone and 2-thienyl propyl ketone were also converted to the corresponding amides, but with the expected decrease in yield that has been found to accompany an increase in the aliphatic chain.[6,7] The expected acids were obtained by hydrolysis with aqueous potassium hydroxide and are listed with the yields of the amides in Table II.

TABLE II

2-THIENYL ALKANOIC AMIDES AND ACIDS BY WILLGERODT REACTION

2-Thienyl ketones	Amide	M.p., °C.	Yield, % A	Yield, % B	Acid	M.p., °C.
Methyl	2-Acetamide	148[a]	43	53	2-Acetic	62–63[a]
Ethyl	2-Propionamide	99–100[b]	25	42	2-Propionic	44–45[b]
Propyl	2-Butyramide	83–84[c]	18	37	2-Butyric	Oil[d]

[a] These compounds are described by Ford, Prescott and Colingsworth, THIS JOURNAL, **72**, 2109 (1950); Cagniant, *Bull. soc. chim.*, 847 (1949); Crowe and Nord, *J. Org. Chem.*, **15**, 81 (1950). [b] These compounds are described by Barger and Easson, *J. Chem. Soc.*, 2100 (1938). [c] *Anal.* Calcd. for $C_8H_{11}NOS$: N, 8.28. Found: N, 8.31. [d] See experimental part.

Experimental

Preparation of 2-Thienyl Ketones.—2-Thienyl methyl ketone, 2-thienyl ethyl ketone and 2-thienyl propyl ketone were prepared from thiophene and the appropriate acid chlorides by the method of Johnson and May.[8]

Willgerodt Reaction.—2-Thienyl methyl ketone (10 g.), 25 g. of sulfur, 25 ml. of concentrated ammonium hydroxide 30 ml. of dioxane were sealed in a Carius tube and heated for 12 hours at 140° (Method A). 2-Thienyl methyl ketone (5 g.), 25 g. of yellow ammonium polysulfide, 3.5 g. of sulfur and 30–35 ml. of dioxane were sealed in a Carius tube and heated for 12 hours at 140° (Method B). The contents were evaporated to dryness and the residue extracted with 100–150 ml. of boiling water. The aqueous extracts were treated twice with norit and concentrated to one-half the original volume. After chilling for some time in an ice-bath the crude amide was removed by filtration and crystallized from water. The reaction mixture from Method A was usually much darker than that from Method B.

The other ketones were converted to the amides and isolated in the same manner. 2-Thienylpropionamide was crystallized efficiently from benzene-petroleum ether.

The acids were obtained by hydrolysis of the amides with 20% aqueous potassium hydroxide in the usual manner. 2-Thienylbutyric acid has been prepared by Fieser and Kennelly[9] who report m.p. as 13.5–15° and the b.p. as 130–134° at 1.5 mm. For further characterization, the oil obtained by hydrolysis of 2-thienylbutyramide was converted to the *p*-bromophenacyl ester with *p*-bromophenacyl bromide and crystallized from 95% alcohol, m.p. 51.5–52.5°.

Anal. Calcd. for $C_{16}H_{15}BrO_3S$: C, 52.32; H, 4.09. Found: C, 52.50; H, 4.03.

Temperature Studies.—These experiments were carried out in the manner previously described for 2-thienyl methyl ketone with temperature as the variable. In the experiments where the effect of temperature on the amide was studied, 5 g. of the corresponding amide was substituted for the thienyl ketone in the Carius tube.

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(5) O. Dann and H. Distler, *Ber.*, **84**, 423 (1951).

(6) C. W. Willgerodt and F. H. Merck, *J. prakt. Chem.*, [2] **80**, 192 (1909).

(7) D. F. DeTar and M. Carmack, THIS JOURNAL, **68**, 2025 (1946).

(8) J. R. Johnson and C. E. May, "Organic Syntheses," Coll. Vol. II, Wiley and Sons, Inc., New York, N. Y., 1944, p. 8.

(9) Fieser and Kennelly, THIS JOURNAL, **57**, 1611 (1935).