

lized from boiling alcohol, or a mixture of benzene and alcohol. The semicarbazone of 5-bromo-2-acetylthiophene was the most difficult to recrystallize.

Preparation of the Thiophenecarboxylic Acids.—The procedure followed was a modification of that given for the preparation of 2-naphthoic acid from 2-acetylnaphthalene in *Organic Syntheses*.⁴

The sodium hypochlorite solution was freshly prepared for each experiment, heated on a steam-bath to 55°, and the corresponding acetylthiophene introduced slowly over a period of thirty to sixty minutes. In the case of 2-acetylthiophene and the three isomeric methylacetylthiophenes, cooling was necessary to maintain the reaction mixture below 75°. With the other acetylthiophenes it was necessary to apply heat until the reaction was complete.

Attempts to use a more concentrated sodium hypochlorite solution in general were unsuccessful since the reactions were sluggish and the products were obtained in lower yields and in a lower state of purity.

The acids were purified by recrystallization from water or from benzene. It was found advantageous to recrystallize the higher alkyl thiophenecarboxylic acids from petroleum ether to effect final purification.

(4) "Organic Syntheses," Coll. Vol. II, 428 (1943).

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Summary

Eleven acetylthiophenes, three of which are described for the first time, are listed with some of their physical properties.

The semicarbazones of each of the acetylthiophenes have been prepared and characterized.

Each of the acetylthiophenes was subject to oxidation with sodium hypochlorite solution and converted to the corresponding thiophenecarboxylic acid with the single exception of 2,5-*t*-butyl-3-acetylthiophene. This compound appeared to be a hindered ketone and oxidation seemed to take place at the sulfur atom rather than at the ketone group. Four new acids have been prepared and characterized for the first time.

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Acylation Studies in the Thiophene and Furan Series. VI. Direct Acylation with Carboxylic Acids and Phosphorus Pentoxide

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The authors reported previously that iodine thiophene with acid anhydrides and acyl halides. and hydriodic acids,² zinc chloride,³ naturally It has now been found that acylation of thio-

TABLE I

ACYLATION OF THIOPHENE AND FURAN

	Yield, %	°C. B. p.	Mm.	M. p., °C.	n_D^{20}	Formula
2-Acetylthiophene ^a	44	87	7	10–11	1.5666	
2-(2-Ethylbutanoyl)-thiophene	65	91–93	2		1.5390 ^b	C ₁₀ H ₁₄ OS
2-(2-Ethylhexanoyl)-thiophene	65	116–117	4		1.5176	C ₁₂ H ₁₈ OS
2-Decanoylthiophene	42	179–180	8		1.5083	C ₁₄ H ₂₂ OS
2,5-Didecanoylthiophene ^a	23	230–250	8	109–109.5 ^c		C ₂₄ H ₄₀ OS
2-(Δ 9,10-Octadecenyl)-thiophene	55	250–255	2			C ₂₂ H ₃₆ OS
Dimer of 2-(Δ 9,10-octadecenyl)-thiophene ^{d,e}	42					C ₄₄ H ₇₂ O ₂ S ₂
2-Benzoylthiophene	66	160–163	6	56.5–57 ^{d,h}		
2-Thenoylthiophene	52	189–190	10	88–89 ^{d,i}		
2-Acetylfuran	7	47–48	3	30–32 ^{d,j}		
2-Decanoylfuran	18	150–154	4			
2-Benzoylfuran ^k	40	142–145	2	43.5–44 ^d		

occurring clays of the montmorillonite type and synthetic silica-metal oxide gels,⁴ and strong oxyacids of fluorine, phosphorus and sulfur⁵ were efficient catalysts for the acylation of furan and

phene and furan with organic acids may be effected in one operation by means of phosphorus pentoxide.⁶ This method is particularly adaptable to the preparation of the higher aliphatic and aromatic ketones since the halides and anhydrides

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(2) Hartough and Kosak, *THIS JOURNAL*, **68**, 2639 (1946).

(3) Hartough and Kosak, *ibid.*, **69**, 1012 (1947).

(4) Hartough, Kosak and Sardella, *ibid.*, **69**, 1014 (1947).

(5) Hartough and Kosak, *ibid.*, **69**, 3093 (1947).

(6) Steinkopf, *Ann.*, **413**, 346 (1917), and Steinkopf and Schubert, *Ann.*, **424**, 1 (1921), reported that catalytic amounts of phosphorus pentoxide caused acylation of thiophene with acid anhydrides and acyl halides. The yields were of the order of 50%.

of the appropriate acids are often expensive and difficult to obtain in the pure state. In the case of thiophene, the yield of ketone increased with the increase in the molecular weight of the acid, ranging from 45% with acetic acid to 97% with oleic acid. The product in the latter case consisted of a mixture of the normal product and a dimer; see Table I. The low yield with acetic acid appeared to be due to the formation of decomposition products resulting from the rapidity of its reaction with phosphorus pentoxide. An attempt to prepare 2-thiophenealdehyde from thiophene and formic acid was unsuccessful. The yields of acylated furans were much lower, ranging from 7 to 40% with acetic and benzoic acids, respectively.

The ketones obtained from 2-ethylbutanoic and 2-ethylhexanoic acids are sterically hindered and form oximes and semicarbazones with difficulty. The 2,4-dinitrophenylhydrazones could not be obtained.

Phosphorus trichloride, thionyl chloride and sulfonyl chloride failed to promote acylation of thiophene and furan under conditions that gave good yields of acylated heterocyclics with phosphorus pentoxide.

Experimental

General Acylation Procedure. A. **Thiophene.**—Phosphorus pentoxide, 142 g. (one mole), was weighed directly into 500 to 1000 ml. of benzene containing 1.1 to 1.5 moles of thiophene. Acetic acid, one mole, was slowly added to the well-stirred mixture through a dropping funnel. External cooling is essential with acetic acid

is not noticeable and the acid is added in one portion. The reaction mixture is refluxed for four to six hours and then cooled. The benzene layer was decanted from the sludge, washed with 10% sodium hydroxide and the ketones distilled *in vacuo*. All crystalline ketones were distilled in suitable apparatus and recrystallized once from dilute alcohol before melting points were taken.

Since the thiophene is not recoverable when blended with benzene, 500 ml. of thiophene may be used instead of the benzene diluent. This method allows complete recovery of the thiophene and gives similar yields of the ketone.

B. Furan.—The phosphorus pentoxide was weighed into benzene and the acid added to the slurry as described above. This mixture was refluxed for one hour, cooled to 20°, and 80 g. of furan added. This mixture was stirred further at ambient temperatures for four to six hours and then completed as described above under A.

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Summary

A new method is presented for producing acylated thiophenes and furans directly from the carboxylic acids and the heterocyclic compound in the presence of phosphorus pentoxide. The method is particularly useful with the higher aliphatic acids and the yields approach the theoretical with oleic acid.

The following new compounds have been prepared and characterized: 2-(2-ethylbutanoyl)-thiophene, 2-(2-ethylhexanoyl)-thiophene, 2-decanoylthiophene, 2,5-didecanoylthiophene, 2-($\Delta^{9,10}$ -octadecenoyl)-thiophene and its dimer, and 2-decanoylfuran.

TABLE I (Continued)

Calcd.	Sulfur, % Found	Derivative	M. p., °C.	Formula	Nitrogen, % Calcd.	Found
17.58	17.50	Oxime	112–113			
15.24	14.86	Oxime ^l	78–79	C ₁₀ H ₁₅ NOS	7.11	7.84
13.4	13.7	Oxime ^l	53–55	C ₁₂ H ₁₉ NOS	6.22	6.10
		Oxime ^l	Oil			
		Semicarbazone	110–110.5	C ₁₆ H ₂₆ N ₃ OS	14.27	14.33
8.3	8.7	2,4-Dinitrophenylhydrazone	119.5–120.5	C ₂₀ H ₂₆ N ₄ O ₄ S	13.39	13.40
9.2	9.3	2,4-Dinitrophenylhydrazone ^m	68–68.5	C ₂₈ H ₄₀ N ₄ O ₄ S	11.00	10.95
9.2	9.1					
		Oxime	102–103.5			
		2,4-Dinitrophenylhydrazone	219–220	C ₁₂ H ₁₀ N ₄ O ₅	19.31	19.14
		2,4-Dinitrophenylhydrazone	90.5–91.5	C ₃₀ H ₂₆ N ₄ O ₅	13.96	13.93
		Oxime ^l	138–139			

^a Physical constants compare favorably with those of Johnson, *THIS JOURNAL*, **69**, 150 (1947). ^b Refractive index, n_D^{20} , was 1.5268. ^c Recrystallized twice from absolute alcohol. ^d Recrystallized once from dilute alcohol before taking melting point. ^e Obtained in the same preparation along with the 2-decanoylthiophene; cotton-like crystals. ^f Obtained as still residue from distillation of monomer. ^g Calcd.: iodine no., 44. Found: iodine no., 37. ^h Mixed melting point with an authentic sample, ref. 3, showed no depression. ⁱ Steinkopf and Hempel, *Ann.*, **495**, 162 (1932), report 88°. ^j Mixed melting point with an authentic sample, ref. 2, showed no depression. ^k Asahina and Murayama, *Arch. Pharm.*, **252**, 435 (1914), list properties as a liquid, b. p. 282–284°, n_D^{20} 1.4798; m. p. of oxime, 138°; m. p. of semicarbazone, 182°. ^l Prepared by the pyridine method, Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1945, p. 167. ^m Red wax-like crystals.

but with higher acids such as decanoic the heat of reaction

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