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Synthesis of 2,5-Diaroylthiophene

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Abstract

The treatment of 1,6-hexanediones [1,6-diphenyl-1,6-hexanedione **1a**, 1,6-bis(p-methylphenyl)-1,6-hexanedione **1b**, 1,6-bis(p-chlorophenyl)-1,6-hexanedione **1c**, 1,6-bis(p-methoxyphenyl)-1,6-hexanedione **1d**, and 1,6-bis(2-thienyl)-1,6-hexanedione **1e**] with the excess of thionyl chloride in the presence of the catalytic amount of pyridine produced the corresponding 2,5-diaroylthiophenes **2a-2e** in only 28-47% yield.

Many reactions of carboxylic acids with thionyl chloride have been reported. However, little work have been done on the reaction aliphatic and aromatic ketones¹⁻⁴). Thionyl chloride, in the presence of catalytic amount of pyridine react abnormally with aliphatic ketones. It has been clearly shown by Krubsack *et al*¹⁾ that the treatment of methylketones with excess thionyl chloride in the presence of the catalytic amount of pyridine at room temperature yielded 3-thietanone, presumably though α -chloro- α -chlorosulfonyl derivatives. Another example is the conversion of aromatic ketone to 3,4-dibenzoylthiophenes⁴⁾. The thiophene formation involved 2 key steps, olefin formation and cyclic sulfonylation. However, there has been no report on the use of diaroylketones. We were interested in these simple synthetic methods using thionyl chloride and have examined the reaction of diaroylbutanes with thionyl chloride. In the present paper we give the discussion about the synthesis of 2,5-diaroylthiophenes by mean of one-step reaction of diaroylbutane with thionyl chloride.

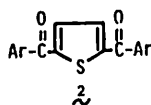
Results and Discussion

The 1,4-diaroylbutanes (**1a-1e**) were prepared by Friedel-Crafts reaction of the corresponding aromatic compounds with adipyl chloride. The results obtained are shown in Table 2. When 1,6-diphenyl-1,6-hexanedione **1a** was dissolved in 10 molar equivalent of thionyl chloride in the present of pyridine at room temperature, spontaneous evolution of hydrogen chloride and sulfur dioxide were observed. After five hours, the excess thionyl chloride was evaporated at room temperature and products were purified on silica gel column eluted with benzene to give an inseparable mixture and 2,5-dibenzoylthiophene **2a** in 33 and 45% yield, respectively. Similarly, 1,6-bis(p-methylphenyl)-1,6-hexanedione **1b** gave 2,5-bis(p-methylbenzoyl)-thiophene **2b** in 37% yield. 1,6-bis(p-chlorophenyl)- **1c**, 1,6-bis(p-methoxyphenyl)- **1d** and 1,6-bis(2-thienyl)-1,6-hexanedione **1e** furnished 2,5-diaroylthiophene **2c**, **2d** and **2e** in 47, 28 and 32% yield, respectively. No attempt was made to maximize the yields of these products. The structure of **2a-2e** were determined by spectroscopic data and elemental analysis. Unfortunately, the mechanisms of the formation of thiophene in the reaction of diaroylbutane with thionyl chloride are still not clear. However, a tentative reaction pathway of the

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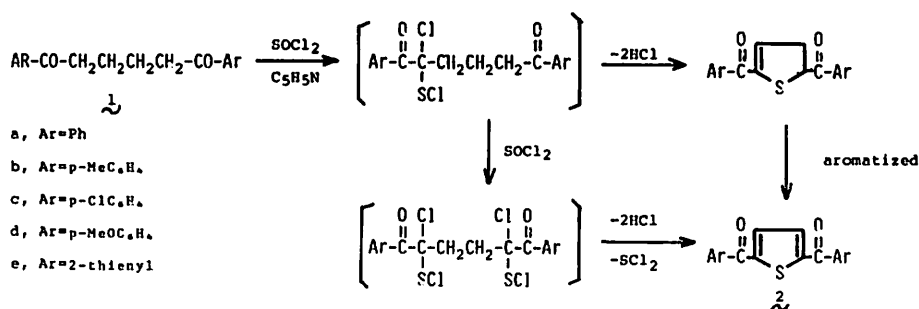
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Table 1. 2,5-diaroylthiophenes



Compd No.	Ar	Yield (%)	Mp (°C)	IR(KBr, cm ⁻¹) and MS m/z(rel. intensity)	NMR(CDCl ₃) δ ppm	Found (Calcd), % C H
2a	Ph	45	117-118 (114.5-115) ^a	IR 1626, 1594cm ⁻¹ MS 292(41.8, M ⁺), 215(57.9), 187(15.4), 103(100)	7.60 (2H, s), 7.40-8.0(10H, m)	73.78 4.10 (73.94) (4.14)
2b	p-MeC ₆ H ₄	37	142-143 (143.5-144) ^a	IR 1637, 1562cm ⁻¹ MS 320(19.8, M ⁺), 229(18.1), 201(8.8), 119(100)	2.44(6H, s), 7.61(2H, s), 7.20-7.90(8H, m)	74.69 4.88 (74.99) (5.03)
2c	p-ClC ₆ H ₄	47	249-250 (244-245) ^a	IR 1625, 1583cm ⁻¹ MS 364,362,360(23.5, M ⁺), 251,249(44.1), 223,221(8.9), 141,139 (100)	7.64(2H, s), 7.40-7.90(8H, m)	59.76 2.52 (59.86) (2.79)
2d	p-MeOC ₆ H ₄	28	192-193 (192.5-193) ^a	IR 1624, 1597cm ⁻¹ MS 352(29.2, M ⁺), 245(8.1), 217(5.1), 135(100)	3.87(6H, s), 7.63(2H, s),	67.91 4.60 (68.18) (4.58)
2e	2-thienyl	32	182-183 (182.5-183) ^a	IR 1613, 1595cm ⁻¹ MS 304(31.9, M ⁺), 221(18.3), 193(4.6), 111(100)	7.10-7.30(3H, m) 7.70-8.0(5H, m)	55.20 2.57 (55.27) (2.65)

a) Ref. J. Heterocyclic Chem., 16, 1147(1979).



Scheme 1

formation of thiophene might be proposed as the following Scheme 1.

For the preparation of 2,5-diacylthiophenes, several methods have been reported⁵⁻⁹). In the direct Friedel-Crafts diacylation of thiophene, the substitution pattern may not always be the expected 2,5-substitution but rather 2,4-substitution, due to the fact that 4-position is the least deactivated by the acyl group in the 2-position. Recently, Miyahara reported on the synthesis of 2,5-diaroylthiophenes by a Hinsberg reaction from glyoxal and the disulfides prepared from halomethyl ketones and sodium sulfide¹⁰). In our opinion, because of the satisfactory yield and mild conditions employed, the present procedure provides a convenient one-step synthesis of 2,5-diaroylthiophenes from readily available nonthiophenic precursors.

Experimental

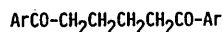
Melting points were determined with a Yanagimoto micromelting point apparatus Model MP-S3

and are uncorrected. The elemental analyses were performed on a Yanaco CHN corder MT2. Infrared spectra were measured using potassium bromide pellets by a JASCO A302 spectrophotometer. The nuclear magnetic resonance spectra were taken by a Hitachi R-24 spectrometer, using tetramethylsilane as the internal reference. Mass spectra were measured with a Hitachi RMU-6L mass spectrometer at 70 eV.

Thionyl chloride (Kanto Chemical Co., INC.) was distilled, the fraction boiling over the range 76-80° was used.

Preparation of Diaroylbutanes 1a-1e: Diaroylbutane **1a**, **1b**, **1c**, **1d** and **1e** were prepared by Friedel-Crafts reaction of the corresponding aromatic compounds with adipyl chloride, according to the literature¹¹⁾ with slight modification. The results are shown in Table 2.

Table 2. 1,4-diaroylbutanes



Compd No.	Ar	Yield (%)	Mp (°C)	Formula	Found (Calcd), %		IR, cm ⁻¹ , in KBr CO
					C	H	
1a	Ph	82	106-107	C ₁₈ H ₁₈ O ₂	81.53 (81.17)	6.81 (6.81)	1676
1b	p-MeC ₆ H ₄	75	133-134	C ₂₀ H ₂₂ O ₂	81.63 (81.60)	7.45 (7.53)	1669
1c	p-ClC ₆ H ₄	63	175-176	C ₁₈ H ₁₄ O ₂ Cl ₂	64.15 (64.48)	4.70 (4.81)	1676
1d	p-MeOC ₆ H ₄	78	148-149	C ₂₀ H ₂₂ O ₄	73.57 (73.60)	6.56 (6.79)	1669
1e	2-thienyl	41	127-128	C ₁₄ H ₁₀ O ₂ S ₂	60.51 (60.43)	5.21 (5.07)	1657

Reaction of thionyl chloride with diaroylbutanes 1: A typical procedure is shown in the case of 1,6-diphenyl-1,6-hexanedione **1a**. To a mixture of **1a** (2.66 g, 10 mmol) and 0.1 ml (1 mmol) of pyridine was added 12 g (0.1 mol) of thionyl chloride at room temperature. Spontaneous evolution of hydrogen chloride and sulfur dioxide was observed. After five hours, the excess thionyl chloride was evaporated and the mixture was chromatographed on silica gel (80 g). The column was eluted with benzene to furnish 30 fractions (10 ml each). Fraction 1-5 were inseparable mixture. Recrystallization of fraction 6-12 from ethanol afforded 0.5 g (45%) of **2a** as colorless needles: IR (cm⁻¹, KBr) 1626 (C=O), 1594 (C=C); NMR (CDCl₃) δ 7.60 (2H, s, thiophene ring protons), 7.4-8.0 (10H, m, ArH); Mass m/z (rel. intensity) 292 (M⁺, 41.8), 215 (M⁺-Ph, 57.9), 187 (M⁺-PhCO, 15.4), 105 (PhCO⁺, 100).

Found: C, 73.73; H, 4.10. Calcd for C₁₈H₁₈O₂S: C, 73.94; H, 4.14. Similarly, the other diaroylthiophenes were prepared and the results are summarized in Table 1.

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