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PREPARATION OF 3,4-DIBENZOYLTHIOPHENES FROM ALKYL PHENYL KETONES UNDER THE ACTION OF THIONYL CHLORIDE

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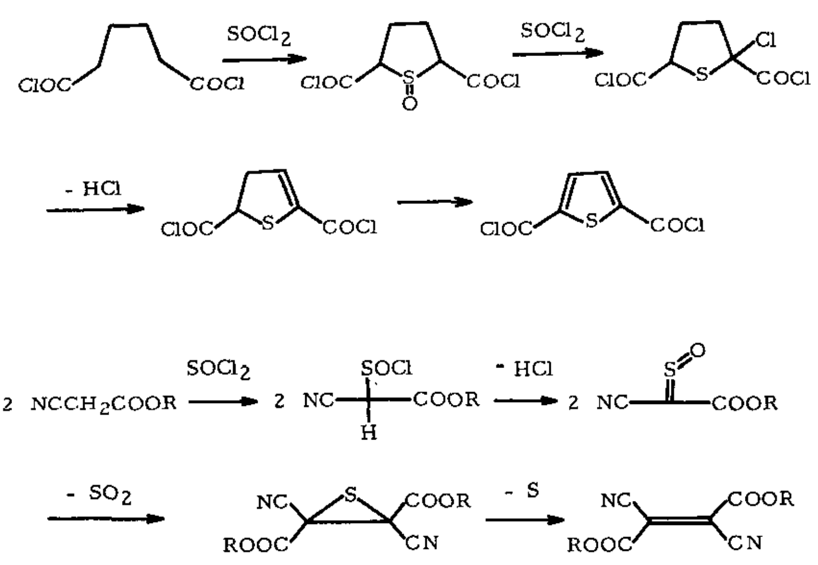
Abstract – Preparation of 3,4-dibenzoylthiophenes from alkyl phenyl ketones such as propiophenone by treatment with a slightly excess thionyl chloride is described. This reaction involves two key steps: (a) olefin-formation and (b) cyclic sulfinylation.

During our investigation of the reaction of thionyl chloride with various active methylene compounds,[1] we found that propiophenone give 3,4-dibenzoylthiophene (IIIa) upon treatment with 1.0-2.0 molar equivalent of the reagent. Adipic and related carboxylic acids were shown to give thiophene derivatives upon treatment with thionyl chloride in the presence of pyridine.[2] The formation of thiophenes is considered to proceed the following sequential steps: cyclic sulfinyla-

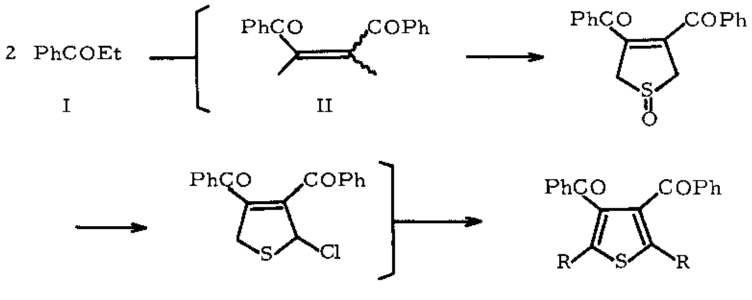
Scheme I



tion,[3] Pummerer rearrangement, dehydrochlorination, and aromatization as illustrated in Scheme I. Meanwhile, English workers[4] reported a convenient olefin synthesis from active methylene compounds such as cyanoacetates by treatment with a slightly excess of thionyl chloride. This reaction can also be rationalized in terms of the initial sulfinylation followed by dehydrochlorination[5] and dimerization[6] of the resulting sulfine to form thiiranes as illustrated similarly in Scheme I. This paper describes our new method to synthesize thiophenes from several alkyl phenyl ketones, involving a combination of the two reaction sequences mentioned above.

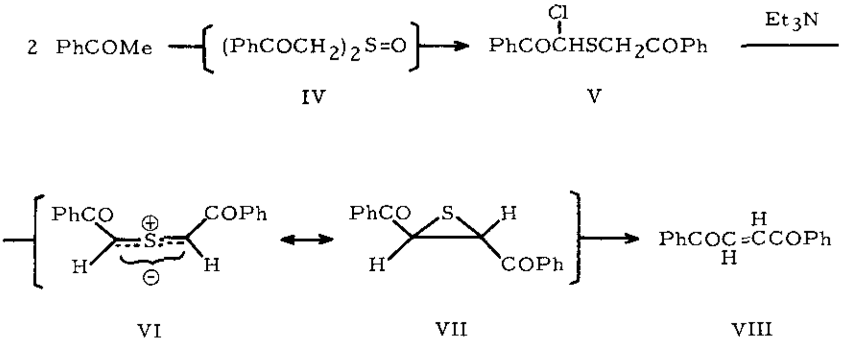
Experimental details of the reaction with propiophenone are as follows. To a mixture of pyridine (0.01 ml) and propiophenone (2.0 g) in a 50 ml round bottomed flask was added thionyl chloride (1.43 ml; 1.3 m. eq.). The mixture was heated in a silicone bath at 80°C. After 2 min, vigorous evolution of HCl and SO_2 gases ceases and gentle evolution was observed for about 3 hr at the same temp. The resulting mixture was dissolved in 3 ml of a 1 : 1 mixture of *n*-hexane and benzene and purified by column chromatography using 10 g of silica gel (100 mesh) and a 10% EtOAc—*n*-hexane mixture as the solvent system. The eluate containing thiophene (IIIa) was evaporated to dryness and recrystallization from an EtOAc—*n*-hexane mixture gave 720 mg (34%) of plates: mp 115-115.5°C; IR (KBr) 3104, 3046, 1626; ^{1}H-NMR ($CDCl_3$) 7.38-7.65 (m, 6H), 7.64 (s, 2H), 7.85 (d,d, 4H, J = 7.2 and 2.5 Hz); ^{13}C-NMR ($CDCl_3$) 187.8 (C=O), 148.5 (SCH=), 137.3, 132.8, 128.6 (Ph), 133.6 ($SC{=}\underline{C}$): (chemical shifts were confirmed by off resonance technique); MS 292 (M, 73%), 215 (M-Ph, 61%), 187 (M-PhCO, 16%), 105 (PhCO, 100%), 77 (Ph, 63%).

Scheme II



IIIa, R = H
b, R = Me

Scheme III



Obviously the olefin (II) as an intermediate is conceivable. However, the olefin formation via the sulfine is still umbiguous, since the reaction of acetophenone with 1.04 molar equivalents of thionyl chloride under the mild conditions at room temperature gave the α-chlorosulfide (V) in 35% yield: mp 65-68°C; IR (KBr) 1690; ^{1}H-NMR ($CDCl_3$) 4.27 and 4.34 (ABq, J = 16 Hz, 2H), 6.56 (s, 1H), 7.35-7.70 (m, 6H), 7.85-8.08 (m, 4H); MS 304 (M, 1.3%); which then afforded trans dibenzoyl ethylene (VIII) upon treatment with triethylamine: mp 111-111.5°C. The α-chlorosulfide (V) is considered to be formed via the sulfoxide (IV) and its Pummerer rearrangement. Dehydrochlorination of V to give thiocarbonyl S-ylide (VI), canonical structure of thiirane (VII), has been well anticipated.[7] In the case of propiophenone, this sequence could be quite important. Thus the olefin (II) should be a key intermediate of the thiophene synthesis.

The later stage of the reaction may proceed through the following reaction sequence: cyclic sulfinylation, Pummerer rearrangement, and dehydrochlorination as shown in Scheme II.

To extend the scope of the reaction we examined the reaction with phenyl propyl ketone. In this case, we obtained 2,5-dimethyl-3,4-dibenzoylthiophene (III b): colorless oil; IR (neat) 3050, 1639; ^{1}H-NMR (CCl_4) 2.37 (s, 6H), 7.22-7.50 (m, 6H), 7.75 (d,d, J = 8.0 and 2.5 Hz, 4H); MS 320 (M, 100%); in only 7% yield after isolation by HPLC using 20 g of spherically shaped 5 μ-silica gel and 4% EtOAc in n-hexane as the solvent system.

As compared to the known reactions of an excess thionyl chloride to give the sulfenyl chlorides by treatment with alkyl phenyl ketones,[1,8] the first stage of this thiophene synthesis proceeded very fast. However, in order to increase the yields of thiophene derivatives, the reaction of dialkyl olefins with thionyl chloride is currently under investigation and will be a subject of our future publication.

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