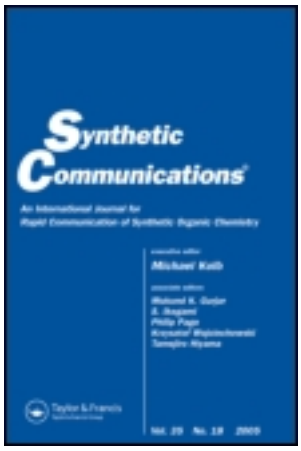

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Facile Synthesis of 2-Aroyl-3,5-diarylthiophene

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Facile Synthesis of 2-Aroyl-3,5-diarylthiophene

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ABSTRACT

2-Aroyl-3,5-diarylthiophenes were prepared in very good yields by reaction of 2,4,6-triarylpyrylium salts or 2,4,6-triarylthiopyrylium salts with an aqeous solution of sodium sulfide and iodine at room temperature.

Key Words: Ring-chain transformation; Synthesis; 2-Aroyl-3,5-diarylthiophene.

Ring-chain transformation reactions of heterocycles have been proven to be a powerful tool for the synthesis of a wide range of carbocyclic as well as heterocyclic compounds.[1] The ring transformation reactions of pyryliums and thiopyryliums have been known for a

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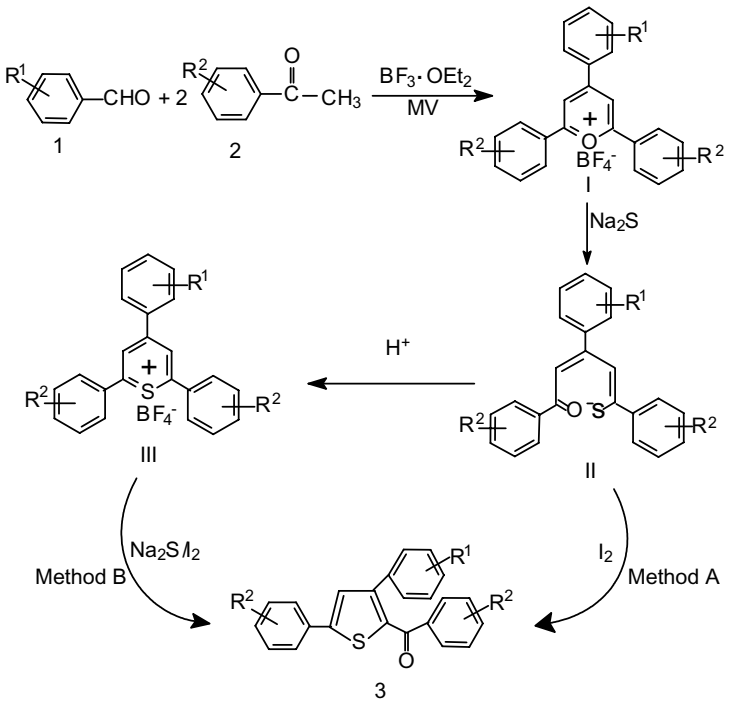
long time.[2] Many reactions about this method also have been studied.[3] The previous article by Pedersen[4,5] concerning the reaction of 2,4,6-triphenylpyrylium tetrafluoroborate with sodium sulfide and iodine that give the product of 2-benzoyl-3,5-diphenylthiophene. The mechanism of this reaction is thought to 2,4,6-triphenylpyrylium tetrafluoroborate when treated with an aqeous solution of sodium sulfide gives an intensely colored solution, possibly due to formation of the anion of **II** (Sch. 1). Upon addition of iodine, the reaction is thought to involve iodination of the anion of the pseudobase followed by intramolecular displacement of iodide ion. But the scope of this reaction was not explored.

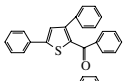
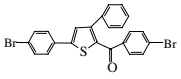
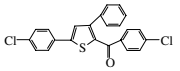
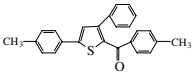
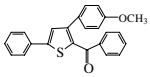
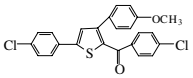
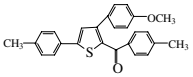
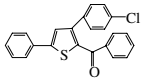
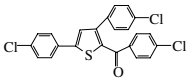
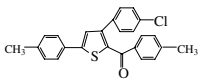
Sulfide-containing heterocyclic compounds, especially, sulfide substituted five-member heterocyclic compounds are very important in both organic synthesis and industrial fields.[6] It has been reported that 2-aroylthiophene derivatives are the materials for the preparation of 2-diaroylaminothiophene, the later is the most interesting developments in dye chemistry.[7]



Scheme 1.

Keeping in view the above facts, we have explored the scope of this reaction. We have found the reaction to be general for a variety of substitutents on the aryl rings and to proceed to give reasonable yields (65–72%) of 2-aroyl-3,5-diarylthiophene **3a–j**. The reactions are shown in Sch. 1 and the corresponding results are summarized in Table 1.

Table 1. The products of 2,4,6-triarylpyryliums or 2,4,6-triarylthiopyryliums with sodium sulfide and iodine.[d]

Entry	R^1	R^2	Product	Yield[a,c] (%)	Yield[b,c] (%)
3a	H	H		68	83
3b	H	4-Br		71	92
3c	H	4-Cl		64	89
3d	H	4-CH_3		67	85
3e	4-OCH_3	H		60	77
3f	4-OCH_3	4-Cl		68	80
3g	4-OCH_3	4-CH_3		66	78
3h	4-Cl	H		72	90
3i	4-Cl	4-Cl		75	93
3j	4-Cl	4-CH_3		69	93

[a]The yield of the product of Method A.
[b]The yield of the product of Method B.
[c]Isolated yield.
[d]All new compounds were determined by ^{1}H NMR, MS, and microanalyses.

At the same time, we have observed the same reaction sequence for a series of 2,4,6-triarylthiopyrylium salts. Thus, reaction of the salts **IIIa–j** with sodium sulfide and iodine in acetone led to the formation of the corresponding 2-aroyl-3,5-diarylthiophene **3a–j** in excellent yields (See Table 1).

Compared to the reaction of 2,4,6-triarylpyryliums with sodium sulfide and iodine, this reaction formed only desired thiophene derivatives and no other byproducts (pseudobase) were isolated.

To determine suitable reaction conditions, using the synthetic reaction of 2,4,6-triphenylthiopyrylium salt with aqeous sodium sulfide and iodine as an example, we investigated the efficiency of various solvents on the formation of 2-benzoyl-3,5-diphenylthiophene, and acetone was found to be the best solvent. Other solvents were also studied and their efficiency are in the order: acetone $\approx$ trichloromethane > benzene > dichloromethane > ethanol > DMF. Specially, when DMF is used as solvent in this reaction, the yield of compound **3a** is considerably poor. In addition, we have investigated the effect of different substitutents for this reaction, and found that the presence of either very strong electron groups or electron withdrawers represents apparent limitations of this method. For example, in our hands, 2,4,6-*tris*(4-nitrophenyl)- and 2,4,6-*tris*-(4-cyanophenyl)pyrylium tetrafluoroborate were unstable, and could not be used in this process, and 2,4,6-*tris*(4-*N*,*N*-dimethylaminophenyl)pyrylium tetrafluoroborate is formed only in very low yields.

In summary, we suggest that the present reaction is a convenient synthetic method of preparing 2-aroyl-3,5-diarylthiophenes.

EXPERIMENTAL

Melting points were determined with an Electrothermal Micromelting point apparatus and are uncorrected. ^{1}H NMR data were recorded on an FT-80 spectrometer with $CDCl_3$ as solvent and TMS as internal reference. Mass spectra were obtained on a Nippon Shimadzu QP-100 GC-MS spectrometer. Elemental analysis was performed on a Carlo-Erba 1106 Elemental Analysis Instrument.

2,4,6-Triarylpyrylium salts **Ia–j** and 2,4,6-triarylpyrylium salts **IIIa–j** were prepared according to literature procedures.[8]

Typical Produce for Preparation of 2-Benzoyl-3,5-diphenylthiophene

Method A. 2,4,6-Triphenylpyrylium tetrafluoroborate (0.5 g, 1.26 mmol) was suspended in acetone (15 mL) and an aqeous solution of sodium sulfide (0.6 g, 2.0 mmol) was added. The mixture was stirred for 0.5 h. Iodine (1.0 g, 3.89 mmol) was then added, and stirring was continued until the mixture turned into pale-yellow. After addition of chloroform, excess iodine was removed by extraction with dilute sodium thiosulfate. The organic phase was separated and dried over sodium sulfate. After evaporation of the chloroform, the crude product was purified by column chromatography on silica gel (petroleum/ethyl acetate 10:1) to give **3a** (68%). M.p. 109–110 (Lit.[4] 103–104). ^{1}H NMR ($CDCl_3$): δ 7.74–7.62 (t, 4H, $J = 6.2$ Hz), 7.50–7.33 (m, 5H, $J = 6.8$ Hz), 7.31–7.14 (m, 7H, $J = 4.9$ Hz). MS (*m*/*e*, %): 340 (M^+, 100), 263 (52), 234 (28), 105 (26), 77 (78). Anal. calcd. for $C_{23}H_{16}OS$: C, 81.14; H, 4.74; S, 9.42. Found: C, 81.16; H, 4.72; S, 9.38.

Method B. A mixture of 2,4,6-triphenylthiopyrylium tetrafluoroborate (0.2 g, 0.5 mmol) in acetone (10 mL) and sodium sulfide nonahydrate (0.2 g, 1.0 mmol) in water (5 mL) was stirred for 5 min. Iodine (0.4 g, 1.5 mmol) was then added and stirring was continued for 2 min. The pale-yellow mixture was poured into a solution of $Na_2S_2O_3$ (4 mmol) in water (10 mL) and the aqeous phase was extracted with $CHCl_3$. The organic phase was washed with water, dried with anhydrous Na_2SO_4, and evaporated in vacuo. The crude product was purified by simple crystallization (hexane/benzene) to give **3a** (83%).

3b. M.p. 188–189°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.55–7.39 (m, 6H, $J = 5.3$ Hz), 7.29–7.17 (m, 8H, $J = 3.0$ Hz). MS (*m*/*e*, %): 497 ($M + 1$, 87), 343 (33), 234 (57), 185 (60), 155 (100), 103 (51), 89 (83), 75 (88). Anal. calcd. for $C_{23}H_{14}OSBr_2$: C, 55.45; H, 2.83; S, 6.44. Found: C, 55.58; H, 2.86; S, 6.41.

3c. M.p. 181.5–182°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.65–7.51 (m, 4H, $J = 7.0$ Hz), 7.44–7.36 (m, 3H, $J = 5.3$ Hz), 7.26–7.11 (m, 7H, $J = 4.3$ Hz). MS (*m*/*e*, %): 408 (M^+, 62), 297 (22), 139 (48), 111 (100), 89 (48), 75 (66). Anal. calcd. for $C_{23}H_{14}OSCl_2$: C, 76.40; H, 3.45; S, 7.83. Found: C, 67.45; H, 3.32; S, 7.79.

3d. M.p. 157–158°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.62–7.56 (m, 4H, $J = 6.0$ Hz), 7.40 (s, 1H), 7.31–7.16 (m, 7H, $J = 4.3$ Hz), 7.02–6.98 (d, 2H, $J = 4.0$ Hz), 2.40–2.30 (d, 6H, $J = 3.3$ Hz). MS (*m*/*e*, %): 368 (M^+, 100), 277 (25), 249 (9), 119 (12), 91 (27), 77 (19),

65 (10). Anal. calcd. for $C_{25}H_{20}OS$: C, 81.49; H, 5.47; S, 8.70. Found: C, 81.64; H, 5.35; S, 8.64.

3e. M.p. 90°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.73–7.62 (m, 4H, $J = 7.3$ Hz), 7.47–7.12 (m, 10H, $J = 7.0$ Hz), 6.72–6.67 (d, 1H), 3.74 (s, 3H). MS (*m*/*e*, %): 370 (M^+, 100), 339 (4), 293 (31), 265 (91), 105 (17), 77 (35). Anal. calcd. for $C_{24}H_{18}O_2S$: C, 77.81; H, 4.89; S, 8.66. Found: C, 77.90; H, 4.95; S, 8.63.

3f: M.p. 146–147°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.65–7.53 (m, 6H, $J = 4.0$ Hz), 7.26 (s, 1H), 7.19–7.12 (m, 4H, $J = 3.5$ Hz), 6.73–6.69 (d, 2H, $J = 4.0$ Hz), 3.76 (s, 3H). MS (*m*/*e*, %): 438 (M^+, 100), 407 (5); 327 (23), 139 (29), 111 (36), 81 (5). Anal. calcd. for $C_{24}H_{16}O_2SCl_2$: C, 65.61; H, 3.67; S,7.30. Found: C, 65.61; H, 3.60; S, 7.24.

3g. M.p. 156–157°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.61–7.57 (d, 4H, $J = 4.0$ Hz), 7.36–7.20 (m, 5H, $J = 6.4$ Hz), 7.04–6.95 (d, 2H), 6.74–6.70 (d, 2H, $J = 4.0$ Hz), 3.75 (s, 3H); 2.39–2.31 (d, 6H, $J = 8.0$ Hz). MS (*m*/*e*, %): 398 (M^+, 100), 383 (10), 307 (21), 119 (16), 91 (30). Anal. calcd. for $C_{26}H_{22}O_2S$: C, 78.36; H, 5.56; S, 8.05. Found: C, 78.34; H, 5.50; S, 8.02.

3h. M.p. 108–109°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.73–7.63 (m, 4H, $J = 5.0$ Hz), 7.50–7.36 (m, 5H, $J = 5.6$ Hz), 7.27–7.12 (m, 6H, $J = 5.0$ Hz). MS (*m*/*e*, %): 374 (M^+, 31), 297 (16), 111 (10), 105 (33), 77 (100). Anal. calcd. for $C_{23}H_{15}OSCl$: C, 73.69; H, 4.03; S, 8.55. Found: C, 73.58; H, 4.01; S, 8.49.

3i. M.p. 190–191°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.64–7.56 (m, 2H, $J = 8.0$ Hz), 7.44–7.36 (m, 2H, $J = 8.0$ Hz), 7.26–7.19 (m, 9H, $J = 4.7$ Hz). MS (*m*/*e*, %): 443 (M + 1, 100), 331 (38), 139 (47), 111 (60), 81 (10), 75 (26). Anal. calcd. for $C_{23}H_{13}OSCl_3$: C, 62.25; H, 2.95; S, 7.23. Found: C, 62.58; H, 2.98; S, 7.18.

3j. M.p. 155–157°C (hexane/benzene). ^{1}H NMR ($CDCl_3$): δ 7.60–7.56 (d, 4H, $J = 8.0$ Hz), 7.35 (s, 1H), 7.26–7.14 (m, 6H, $J = 4.0$ Hz), 7.07–7.03 (d, 2H, $J = 4.0$ Hz), 2.40–2.34 (d, 6H, $J = 6.0$ Hz). MS (*m*/*e*, %): 402 (M^+, 51), 387 (3), 367 (2), 311 (16), 119 (50), 91 (100), 65 (52). Anal. calcd. for $C_{25}H_{19}OSCl$: C, 74.52; H, 4.75; S, 7.96. Found: C, 74.41; H, 4.91; S, 7.93.

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