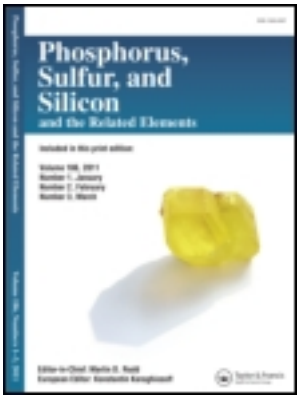

Phosphorus, Sulfur, and Silicon and the Related Elements

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MELAMINE TRISULFONIC ACID: A NEW EFFICIENT CATALYST FOR THE SYNTHESIS OF ARYLDITHIENYLMETHANES

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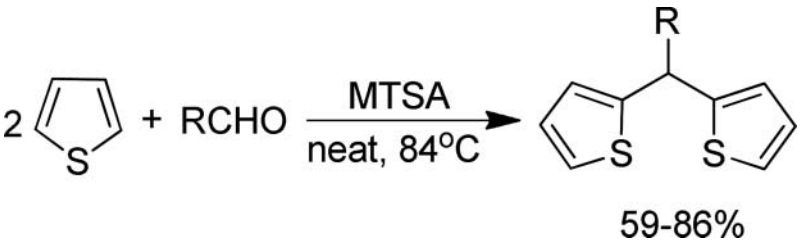
GRAPHICAL ABSTRACT



Abstract *An efficient method has been developed for the synthesis of dithienylmethanes via bisarylation of aldehydes with thiophene in the presence of melamine trisulfonic acid as a catalyst under solvent-free conditions.*

Keywords Dithienylmethanes; melamine trisulfonic acid; solvent-free; thiophene

INTRODUCTION

Dithienylmethanes are widely used as important building blocks for the synthesis of a variety of functionational porphyrins and porphyrin analogs,[1] which can be of wide interest in materials science.[2] Usually, the preparations of dithienylmethanes were carried out by the reaction of aldehydes with thiophene under catalysis of reagents such as trifluoroacetic acid,[1a] $BF_3{\cdot}Et_2O$,[1a] $TiCl_4$,[1b] and $NaHSO_4$-SiO_2.[3] However, these approaches are often hindered by the formation of by-products, high catalyst loading, long reaction time, and environmental unfriendliness. Thus, a mild, efficient, and green method using an economical, recoverable catalyst is worth exploring.

Recently, melamine trisulfonic acid (MTSA, Figure 1) has emerged as a promising solid acid catalyst for acid-catalyzed reactions, such as acetylation of alcohols, phenols, and amines,[4] oxathioacetalyzation of aldehydes,[5] methoxymethylation of alcohols,[6] and synthesis of thiocyanohydrins.[7] This catalyst is safe, easy to handle, environmentally benign,

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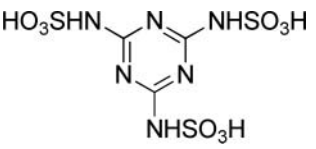
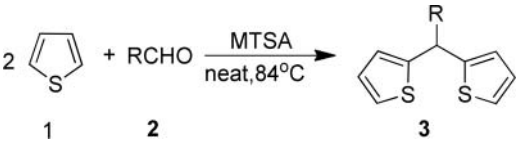


Figure 1

and presents fewer disposal problems than other catalysts. Melamine trisulfonic acid as a solid acid catalyst was prepared from the reaction of melamine with neat chlorosulfonic acid at room temperature.[4–7]

We herein report a simple and environmentally benign methodology for the synthesis of dithienylmethanes under solvent-free conditions using MTSA as the catalyst (Scheme 1).



Scheme 1

RESULTS AND DISCUSSION

In order to optimize the reaction conditions, we first examined the amount of catalyst and the reaction temperature. The reaction of benzaldehyde with thiophene to the corresponding 2,2′-(phenylmethylene)dithiophene was studied under solvent-free conditions in the presence of MTSA at different temperatures. The results are summarized in Table 1. As

Table 1 The amount of catalyst and the reaction temperature optimization for the synthesis of 2,2′-(phenylmethylene)dithiophene[a]

Entry	MSTA/mol%	Temp./°C	Time/min	Yield/%[b]
1	0	84	90	0
2	5	r.t.	90	41
3	5	84	40	71
4	10	r.t.	90	50
5	10	30	90	53
6	10	40	60	62
7	10	50	60	69
8	10	60	60	74
9	10	70	40	80
10	10	84	40	84
11	15	70	40	79
12	15	84	40	83
13	20	84	40	83

[a]Reaction conditions: benzaldehyde (1 mmol); thiophene (10 mmol); neat.
[b]Isolated yield.

Table 2 Synthesis of dithienylmethanes catalyzed by MTSA[a]

Entry	R	Time/min	Products[b]	Yield/%[c]	mp (L)/°C
1	C_6H_5	40	**3a**	84 (82,80,76)[d]	70–72 (73–74)[3]
2	4-Cl-C_6H_4	30	**3b**	86	53–54
3	4-Br-C_6H_4	30	**3c**	84	64–65 (62–64)[3]
4	4-F-C_6H_4	30	**3d**	86	oil
5	4-NO_2-C_6H_4	30	**3e**	85	85–86 (87–89)[3]
6	3-NO_2-C_6H_4	30	**3f**	82	70–73 (72–74)[3]
7	4-MeO-C_6H_4	50	**3g**	78	89–91 (88–90)[3]
8	4-Me-C_6H_4	60	**3h**	75	102–103
9	3-OH-C_6H_4	60	**3i**	70	oil (oil)[3]
10	4-OH-C_6H_4	60	**3j**	72	oil
11	3- MeO-4-OH-C_6H_3	90	**3k**	65	61–62 (59–61)[3]
12	4- MeO-3-OH-C_6H_3	90	**3l**	63	67–69 (66–68)[3]
13	3,4-(OCH_2O)-C_6H_3	60	**3m**	68	92–94 (94–96)[3]
14	2-Thienyl	60	**3n**	70	48–49 (50–51)[3]
15	2-furanyl	60	**3o**	72	56–57
16	4-pyridyl	60	**3p**	76	101–103
17	H	90	**3q**	60	46–47[3]
18	CH_3	90	**3r**	63	52–53
19	$(CH_3)_2CH$	90	**3s**	62	oil
20	$(CH_3)_3C$	90	**3t**	59	oil

[a]Reaction conditions: aldehyde (1 mmol); thiophene (10 mmol); MTSA (0.1 mmol); neat; 84 °C.

[b]All products except **3b**, **3d**, **3j**, **3p**, **3r**, **3o**, **3s**, **3t** were identified by comparing their physical and spectral data with those of the authentic samples (see ref. 3).

[c]Isolated yield.

[d]Yields after three times of catalyst recovery.

shown in Table 1, the reaction using 10% mmol MTSA at 84 °C temperature proceeded to highest yield.

Encouraged by the results, we investigated a number of other aldehydes to probe their behavior under the current catalytic conditions. Thus, a range of dithienylmethanes were synthesized by heating a mixture of the aldehyde, thiophene in the presence of 10 mol% MTSA at reflux temperature for 30–60 min under solvent-free conditions in 68%–86% yields. It was demonstrated that the reaction of the aldehydes with electron-withdrawing groups such as 4-chlorobenzaldehyde, 4-bromobenzaldehyde, 4-nitrobenzaldehyde, and 3-nitrobenzaldehyde went to completion in 30 min to afford the expected dithienylmethanes in good yields (entries 2–5). However, the reaction of those aldehydes with electron-donating groups such as 3-hydroxy-benzaldehyde, piperonal led to lower reaction yields and required longer time as well (entries 7–8). The results are summarized in Table 2.

The reusability of the catalyst was tested in the synthesis of 2,2′-(phenylmethylene) dithiophene. The catalyst was recovered after each run, washed with CH_2Cl_2, dried in an oven at 100 °C for 30 min prior to use, and tested for its activity in the subsequent run and fresh catalyst was not added. The catalyst was tested for three runs and the recovery rate of catalyst was 90% in each run. It was seen that the catalyst displayed very good reusability (Table 2, entry 1). Under the same conditions, using the fresh catalyst $NaHSO_4$-SiO_2, the yield of the product 2,2′-(phenylmethylene)dithiophene was 82%, while with the recovered catalyst, the three subsequent yields were 79%, 76%, and 72%.

Table 3 MTSA-catalyzed synthesis of 2,2′-(phenylmethylene)dithiophene in comparison with other literature methods

Entry	Reaction conditions	Time/min	Yield/%	Reference
1	benzaldehyde: thiophene: MTSA = 1:10:0.1, 84 °C, neat	40	84	This work
2	benzaldehyde: thiophene: $BF_3{\cdot}Et_2O$ = 1:37:1, r.t., neat	30	62	1a
3	benzaldehyde: thiophene: CF_3COOH = 1:37:10, r.t., neat	22	60	1a
4	benzaldehyde: thiophene: $NaHSO_4$-SiO_2 = 1:37:0.5, 84 °C, neat	150	82	3

In order to assess the capability of the present method with respect to the reported methods for the preparation of dithienylmethanes from aldehydes and thiophene, the synthesis of compound **3a** was compared with the reported methods. It is clear from Table 3 that the present method has high yields, moderate reaction times, simple procedure, and uses inexpensive and environmentally benign catalysts.

CONCLUSION

In summary, we have established for the first time, a novel, eco-friendly, and simple protocol for the synthesis of dithienylmethanes using inexpensive MTSA. The short reaction procedure and reusability of the catalyst make this method one of the most efficient methods for the synthesis of this class of compounds.

EXPERIMENTAL

NMR spectra were determined on Bruker AV-400 spectrometer at room temperature using TMS as internal standard, coupling constants (J) were measured in Hz; elemental analysis was performed by a Vario-III elemental analyzer; mass spectra were taken on a Macro mass spectrometer (Waters) by electro-spray method (ES); melting points were determined on a XT-4 binocular microscope and were uncorrected; MTSA was prepared according to ref. 4; Commercially available reagents were used throughout without further purification unless otherwise stated.

General Procedure for the Synthesis of Dithienylmethanes

A mixture of aldehyde (1 mmol), thiophene (10 mmol), and MTSA (0.1 mmol) was heated at reflux for an appropriate time (TLC). After the completion of the reaction, excess thiophene was evaporated, and CH_2Cl_2 (10 mL) was added. The mixture was filtered, CH_2Cl_2 was evaporated, and the crude product was purified by silica gel column chromatography using ethyl acetate and hexane (1:10) as eluent to afford the pure product. The spectroscopic data for the new products are given below.

2,2′-((4-Chlorophenyl)Methylene)Dithiophene (3b)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40–7.18 (m, 6H), 6.97–6.60 (m, 4H), 5.79 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.2, 141.9, 132.2, 130.5, 125.9, 125.2, 123.6, 120.6, 44.1 ppm; MS (ESI): m/z 292 $[M+H]^+$; Anal. calcd for $C_{15}H_{11}ClS_2$: C 61.95, H 3.81, S 22.05%; found: C 62.06, H 3.75, S 21.98%.

2,2′-((4-Fluorophenyl)Methylene)Dithiophene (3d)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.20 (m, 6H), 6.95 (dd, 2H, $J = 3.2$, 4.8 Hz), 6.90 (d, 2H, $J = 3.2$ Hz), 5.84 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.9, 142.8, 132.6, 131.0, 126.2, 125.9, 124.9, 121.0, 42.8 ppm; MS (ESI): *m/z* 275 $[M+H]^+$; Anal. calcd for $C_{15}H_{11}FS_2$: C 65.66, H 4.04, S 23.07%; found: C 65.80, H 4.09, S 23.10%.

4-(Di(Thiophen-2-yl)Methyl)Phenol (3j)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, 2H, $J = 4.8$ Hz), 7.12 (d, 2H, $J = 8.0$ Hz), 6.92 (dd, 2H, $J = 3.2$, 5.2 Hz), 6.88 (d, 2H, $J = 3.2$ Hz), 6.70 (d, 2H, $J = 8.0$ Hz), 5.76 (s, 1H), 5.52 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 141.5, 131.2, 130.8, 128.2, 127.9, 126.8, 125.6, 52.6 ppm; MS (ESI): *m/z* 273 $[M+H]^+$; Anal. calcd for $C_{15}H_{12}OS_2$: C 66.14, H 4.44, S 23.54%; found: C 66.02, H 4.48, S 23.48%.

2-(Di(Thiophen-2-yl)Methyl)Furan (3o)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, 1H, $J = 2.0$, 5.2 Hz), 7.26 (dd, 2H, $J = 1.6$ Hz, $J = 4.8$ Hz), 7.01–6.97 (m, 4H), 6.45–6.18 (m, 2H), 5.78 (s, 1H), 5.52 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.2, 143.2, 138.5, 127.9, 127.0, 125.8, 110.8, 107.1, 50.2 ppm; MS (ESI): *m/z* 247 $[M+H]^+$; Anal. calcd for $C_{13}H_{10}OS_2$: C 63.38, H 4.09, S 26.03%; found: C 63.42, H 4.15, S 26.10%.

4-(Di(Thiophen-2-yl)Methyl)Pyridine (3p)

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, 2H, $J = 8.4$ Hz),7.50 (d, 2H, $J = 8.8$ Hz), 7.26 (d, 2H, $J = 4.2$ Hz), 6.96 (dd, 2H, $J = 3.2$, 4.8 Hz), 6.88 (d, 2H, $J = 3.2$ Hz), 5.87 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.1, 145.9, 140.2, 126.9, 126.5, 125.2, 123.8, 49.9 ppm; MS (ESI): *m/z* 258 $[M+H]^+$; Anal. calcd for $C_{14}H_{11}NS_2$: C 65.33, H 4.31, N 5.44, S 24.92%; found: C 65.28, H 4.40, N 5.44, S 25.04%.

2,2′-(Ethane-1,1-diyl)Dithiophene (3r)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, 2H, $J = 5.2$ Hz), 6.96 (dd, 2H, $J = 3.6$, 5.2 Hz), 6.89 (d, 2H, $J = 3.6$ Hz), 4.48 (d, 1H, $J = 6.8$ Hz), 1.42 (d, 3H, $J = 6.8$ Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.2, 126.9, 125.2, 123.7, 46.9, 32.9 ppm; MS (ESI): *m/z* 195 $[M+H]^+$; Anal. calcd for $C_{10}H_{10}S_2$: C 61.81, H 5.19, S 33.00%; found: C 61.82, H 5.25, S 33.12%.

2,2′-(2-Methylpropane-1,1-diyl)Dithiophene (3s)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (d, 2H, $J = 5.2$ Hz), 6.97 (dd, 2H, $J = 3.6$, 4.8 Hz), 6.92 (d, 2H, $J = 4.0$ Hz), 4.45 (m, 1H), 2.63 (d, 1H, $J = 7.2$ Hz), 1.01 (d, 6H, $J =$ 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.5, 126.4, 125.6, 122.9, 48.2, 35.5, 21.8 ppm; MS (ESI): *m/z* 223 $[M+H]^+$; Anal. calcd for $C_{12}H_{14}S_2$: C 64.81, H 6.35, S 28.84%; found: C 64.92, H 6.30, S 28.65%,

2,2′-(2,2-Dimethylpropane-1,1-diyl)Dithiophene (3t)

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, 2H, $J = 4.8$ Hz), 6.96 (dd, 2H, $J = 3.2$, 4.8 Hz), 6.90 (d, 2H, $J = 3.6$ Hz), 4.39 (s, 1H), 0.99 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.8, 126.0, 125.2, 123.4, 52.6, 35.6, 28.8 ppm; MS (ESI): m/z 237 $[M+H]^+$; Anal. calcd for $C_{13}H_{16}S_2$: C 66.05, H 6.82, S 27.13%; found: C 66.20, H 6.70, S 27.10%.

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