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Deprotonation of thiophenes using lithium magnesates

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Abstract—Thiophene was regioselectively deprotonated at C2 on treatment with 1/3 equiv of Bu_3MgLi in THF at room temperature. The lithium arylmagnesate formed was either trapped with electrophiles or cross-coupled in a 'one-pot' procedure with aryl halides under palladium catalysis. 2-Chlorothiophene and 2-methoxythiophene were similarly deprotonated at C5 under the same reaction conditions. The enhancement of the reactivity of the base using TMEDA was evidenced using ¹H NMR spectroscopy. © 2005 Elsevier Ltd. All rights reserved.

1. Introduction

The preparation of functional heterocycles is an important synthetic goal because of the multiple applications of these molecules.¹ Deprotonation using alkyllithiums or lithium dialkylamides has been developed as one of the major tools since lithiated derivatives display a high reactivity towards many electrophilic functions.² Nevertheless, this methodology often requires low temperatures, which can be difficult to realize on an industrial scale. In addition, unlike organoboron, organotin, organozinc and organomagnesium compounds, organolithiums can hardly be involved in cross-coupling reactions.³

More recently, organomagnesium compounds have been prepared by deprotonation at higher temperatures, but the uses of such reactions have barely been explored. The pioneering work of Marxer and Siegrist in 1974 showed EtMgBr was capable of deprotonating 1-phenylpyrazole at the *ortho* position of the phenyl ring.⁴ Eaton reported in 1989 the deprotonation of both methyl benzoate and *N*,*N*-diethylbenzamide with Hauser bases (iPr₂NMgBr or TMPMgBr, TMP=2,2,6,6-tetramethylpiperidino) or magnesium diamides ((iPr₂N)₂Mg or TMP₂Mg).⁵ In 1995, Schlecker extended this methodology to the regioselective

magnesiation of pyridine derivatives;⁶ alkylmagnesium halides and dialkylmagnesiums rarely deprotonated such substrates because of easier 1,4-addition reactions.⁷ Next, Kondo and Sakamoto described the regioselective magnesiation of *N*-substituted indoles,⁸ thiophenes⁹ and thiazole⁹ using (iPr₂N)₂Mg, iPr₂NMgBr and iPr₂NMgCl. Nevertheless, because of the limited reactivity of these bases, an excess has in general to be used to ensure good yields. Pyrrole rings of numerous 1-phenyldipyrromethanes did not required protection step to be deprotonated at the position adjacent to the nitrogen atom using EtMgBr.¹⁰

Ten years after Eaton, Kondo achieved the deprotonation of methyl benzoate and other activated benzenes through the formation of an arylzincate using lithium di-t-butyl(2,2,6,6tetramethylpiperidino) zincate as a base, a methodology extended to the pyridine, quinoline, isoquinoline and ethyl thiophenecarboxylates series,¹¹ but with limited applications due to their moderate reactivity with electrophiles. The arylmagnesates usually prepared by halogen-magnesium exchange reacting with a wider range of electrophiles than arylzincates, we have been interested in deprotonation reactions using lithium magnesates. This possibility has rarely been documented. Mulvey reported in 1999, the preparation of a mixed-metal sodium-magnesium macrocyclic amide which behaves like a template for the site selective dideprotonation of benzene and toluene.¹² This process cannot be used as it is for synthetic purposes because it involves a large excess of arene (5 mmol out of the 5 mL used are consumed in the reaction). Richey observed in 2004 that treating benzene halides with

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magnesates partially results in benzyne formation.¹³ Even if the organometallic precursors have not been intercepted by electrophiles, the results show magnesates are capable of abstracting aromatic protons. Very recently, we studied the deprotonation of fluoro aromatics using lithium magnesates, the obtained arylmagnesates being either trapped with electrophiles or involved in a palladium-catalyzed crosscoupling.¹⁴

Herein, we describe the synthesis of lithium tri(2-thienyl) magnesates by deprotonation using lithium magnesates. To obtain more information on the efficiency on the process, the ¹H NMR spectra of the heterocyclic magnesium ate complexes were recorded. The reactivity of such magnesium intermediates towards electrophiles or in metalcatalyzed coupling reactions was studied.

2. Results and discussion

Lithiation of thiophene by BuLi is rapid in ethereal solvents, a result ascribed to the strong acidifying effect of the sulfur atom which compensates for an unlikely chelation of the base.¹⁵ In addition, 2-substituted thiophenes generally give exclusive lithiation at the 5-position, whatever the nature of the substituent.

We attempted the deprotonation of thiophenes 1-3 using lithium magnesates.¹⁶ The first experiments were conducted on thiophene (1) using 1/3 equiv of lithium tributylmagnesate (Bu₃MgLi) in THF at room temperature. Trapping the intermediate lithium magnesate with iodine or 4-anisaldehyde afforded the iodide 4a and the alcohol 4b in good yields (entries 1 and 2). Deprotonation of thiophene using BuLi being favored in the presence of TMEDA,¹⁵ the reaction was also carried out using Bu₃MgLi in the presence of 1/3 equiv of this additive, and allowed the alcohol 4c to be obtained after quenching with 3,4,5-trimethoxybenzaldehyde in 96% yield (entry 3). The reaction was next

Table 1. Deprotonation of thiophenes 1-3 and trapping with electrophiles

performed on 2-substituted thiophenes 2 and 3 to afford the 2,5-disubstituted compounds **5a–c** and **6a,b** (entries 4–8); excellent yields were again obtained adding TMEDA to the base (Table 1).

The role of TMEDA was ascertained by recording the ¹H NMR spectra of the reaction mixture obtained after the deprotonation step (Fig. 1): the hydrogen-magnesium exchange was quantitative using TMEDA whereas some substrate was detected without. The increasing reactivity may be accounted for by complexation of TMEDA to the lithium ion of the triorganomagnesate to separate the reactive magnesate ion from the intimate ion pair.

The lithium tri(2-thienyl)magnesates were next involved in cross-couplings with various aromatic halides under palladium catalysis using 1,1'-bis(diphenylphosphino)ferrocene (dppf) as ligand.^{14,18} When lithium tri(2-thienyl)magnesate was subjected to the reaction with π -deficient substrates such as 2-bromopyridine and 3-bromoquinoline to give compounds **4d**,**e**, medium to good yields were obtained: the best results were observed with the 2-bromo substrate, for which the oxidative addition step is easier, while the other reacts moderately (entries 1 and 2). Using iodobenzene and 4-bromoanisole surprisingly allowed the syntheses of the phenyl derivatives **4f**,**g** in high yields (entries 3 and 4). Similar results were obtained starting from lithium (5-chloro-2-thienyl)magnesate, affording the biaryl compounds 5d,e (entries 5 and 6), but a lower yield of 22% was noticed with methyl 4-iodobenzoate (entry 7), due to competitive reactions with the ester function. 2-Substituted 5-methoxythiophenes 6c-e were obtained from lithium (5-methoxy-2-thienyl)magnesate under the same reaction conditions (entries 8-10, Table 2).

3. Conclusion

Thiophene was regioselectively deprotonated at C2 using



Entry	Substrate	Product	Yield, (%)	
1 ^a	1 (R = H)	$4\mathbf{a} (\mathrm{El} = \mathrm{I})^{\mathrm{b}}$	90	
2 ^a	1(R=H)	4b $(El = CH(OH) - 4 - anisyl)^{c}$	60	
3 ^d	1 (R = H)	4c $(El = CH(OH) - 3, 4, 5$ -trimethoxyphenyl) ^e	96	
4 ^a	2(R=Cl)	$5a (El=I)^{b}$	68	
5 ^a	2(R=Cl)	5b $(El = CH(OH)-4-anisyl)^{c}$	78	
6 ^d	2(R=Cl)	5c $(El = CH(OH) - 3, 4, 5$ -trimethoxyphenyl) ^e	93 (79) ^f	
7 ^a	3 (R = OMe)	$6a (El=I)^b$	75	
8 ^d	3 (R = OMe)	6b (El=CH(OH)-3,4,5-trimethoxyphenyl) ^e	87	

^a The base is Bu₃MgLi (1/3 equiv).

^b The electrophile is I₂.

^c The electrophile is 4-anisaldehyde.

^d The base is Bu₃MgLi · TMEDA (1/3 equiv).

^e The electrophile is 3,4,5-trimethoxybenzaldehyde.

^f Using BuLi (1 equiv), THF, -75 °C, 2 h.¹



Figure 1. ¹H NMR spectra of lithium tri(2-thienyl) magnesates. TMEDA in THF (rt) (a) from thiophene (1); (b) from 2-chlorothiophene (2) and (c) from 2-methoxythiophene (3).

Table 2. Deprotonation of thiophenes 1-3 and cross-coupling with aromatic halides

	1) Bu ₃ MgLi (1/3 equiv)	
	THF, rt, 2 h	
R	<u> </u>	
3	2) Ar-X, reflux, 18 h	3
1-3	PdCl ₂ (dppf) 3 mol.%	4-6
	3) H ₂ O	

Entry	Substrate	Product	Ar	Yield, (%)	
1	1 (R = H)	4d ^a	2-Pyridyl	77	
2	1 (R = H)	4e ^b	3-Quinolyl	56	
3	1 (R = H)	4f ^c	Phenyl	84	
4	1 (R = H)	$4g^{d}$	4-Methoxyphenyl	92	
5	2(R=Cl)	5d ^a	2-Pyridyl	68	
6	2(R=Cl)	5e ^d	4-Methoxyphenyl	81	
7	2(R=Cl)	5f ^e	4-(Methoxycarbonyl)phenyl	22	
8	3 (R = OMe)	6c ^a	2-Pyridyl	56	
9	3 (R = OMe)	6d ^c	Phenyl	67	
10	3 (R = OMe)	6e ^e	4-(Methoxycarbonyl)phenyl	40	

^a Using 2-bromopyridine.

^b Using 3-bromoquinoline.

^c Using iodobenzene.

^d Using 4-bromoanisole.

^e Using methyl 4-iodobenzoate.

1/3 equiv of Bu₃MgLi in THF at room temperature; the thienylmagnesate generated was either intercepted with electrophiles or cross-coupled in a 'one-pot' procedure. The enhancement of the reactivity of the base using TMEDA was evidenced by recording the ¹H NMR spectra of the reaction mixtures. Similar results were observed with 2-chloro and 2-methoxythiophenes.

4. Experimental

4.1. General

Melting points were measured on a Kofler apparatus. NMR

spectra were recorded with a Bruker AM 300 spectrometer (¹H at 300 MHz and ¹³C at 75 MHz). The solvent was CDCl₃, except for the lithium magnesates for which the spectra were recorded after addition of 20% THF- d^8 (to provide a lock signal) to the reaction mixtures. IR spectra were taken on a Perkin–Elmer FT IR 205 spectrometer, and main IR absorptions are given in cm⁻¹. Elemental analyses were performed on a Carlo Erba 1106 apparatus.

Starting materials. THF was distilled from benzophenone/ Na. The water content of the solvents was estimated to be lower than 45 ppm by the modified Karl Fischer method.¹⁹ Metalation and cross-coupling reactions were carried out under dry N₂. Silica gel (Geduran Si 60, 0.063–0.200 mm) was purchased from Merck. BuLi (1.6 or 2.5 M) in hexane and PdCl₂(dppf) were supplied by Aldrich. MgBr₂ was freshly prepared in THF using a described procedure.²⁰ Petrol refers to petroleum ether (bp 40–60 °C).

Unless otherwise noted, the reaction mixture was diluted with CH_2Cl_2 (50 mL) after the reaction. The organic layer was dried over MgSO₄, the solvents were evaporated under reduced pressure, and the crude product was chromatographed on a silica gel column (eluent is given in the product description).

4.2. General procedure 1: substituted thiophenes 4a,b, 5a,b and 6a by deprotonation of thiophenes 1–3 using Bu₃MgLi and subsequent trapping with electrophiles

To a solution of $MgBr_2$ (2.0 mmol) in THF (3 mL) at -10 °C were added BuLi (6.0 mmol) and, 1 h later, the required thiophene (6.0 mmol). After 2 h at room temperature, the electrophile (6.0 mmol) was added and the mixture was stirred for 18 h at room temperature before addition of water saturated with NH₄Cl (1 mL).

4.2.1. 2-Iodothiophene (4a). The general procedure 1, starting from **1** (0.48 mL) and using a solution of I_2 (1.5 g) in THF (3 mL) (in this case, the reaction mixture was treated with Na₂S₂O₃ until bleaching), gave 90% (1.1 g) of **4a** (eluent: CH₂Cl₂) as a yellow oil. The physical and spectral data are analogous to those obtained for a commercial sample.

4.2.2. α-(4-Methoxyphenyl)-2-thiophenemethanol (4b).²¹ The general procedure 1, starting from 1 (0.48 mL) and using 4-anisaldehyde (0.73 mL), gave 60% (0.79 g) of 4b (eluent: CH₂Cl₂/AcOEt 90:10) as a yellow oil: ¹H NMR δ 7.36 (d, 2H, J = 6.8 Hz), 7.25 (dd, 1H, J = 3.8, 1.1 Hz), 6.91 (m, 4H), 5.97 (s, 1H), 3.80 (s, 3H), 2.61 (s, 1H); ¹³C NMR δ 159.3 (q), 148.9 (q), 134.6 (q), 127.8 (t, 2C), 126.7 (t), 125.2 (t), 124.8 (t), 114.1 (t, 2C), 72.0 (t), 55.4 (p); IR (KBr) ν ; 3429, 2836, 1610, 1511, 1248, 1174, 1033, 834, 704, 579. Anal. Calcd for C₁₂H₁₂O₂S (220.29): C, 65.43; H, 5.49; S, 14.56. Found: C, 65.81; H, 5.87; S, 14.26.

4.2.3. 2-Chloro-5-iodothiophene (**5a**).²² The general procedure 1, starting from **2** (0.55 mL) and using a solution of I₂ (1.5 g) in THF (3 mL) (in this case, the reaction mixture was treated with Na₂S₂O₃ until bleaching), gave 68% (1.0 g) of **5a** (eluent: petrol) as a yellow oil: ¹H NMR δ 7.06 (d, 1H, J=3.8 Hz), 6.61 (d, 1H, J=4.1 Hz); ¹³C NMR δ 137.6 (t), 134.6 (q), 129.1 (t), 71.6 (q); IR (KBr) ν ; 3094, 2923, 1515, 1408, 1204, 1062, 1003, 934, 785, 466. Anal. Calcd for C₄H₂CIIS (241.24): C, 19.65; H, 0.82; S, 13.12. Found: C, 20.02; H, 0.85; S, 13.21.

4.2.4. 5-Chloro-α-(4-methoxyphenyl)-2-thiophenemethanol (5b). The general procedure 1, starting from **2** (0.55 mL) and using 4-anisaldehyde (0.73 mL), gave 78% (1.2 g) of **5b** (eluent: cyclohexane/AcOEt 70:30) as a yellow oil: ¹H NMR δ 7.25 (d, 2H, J=8.3 Hz), 6.83 (d, 2H, J= 8.3 Hz), 6.60 (d, 1H, J=3.8 Hz), 6.45 (d, 1H, J=3.8 Hz), 5.75 (d, 1H, J=3.8 Hz), 2.44 (d, 1H, J=3.8 Hz), 3.72 (s, 3H); ¹³C NMR δ 159.3 (q), 147.1 (q), 134.6 (q), 129.6 (q), 127.5 (t, 2C), 125.5 (t), 123.7 (t), 113.8 (t, 2C), 71.9 (t), 55.2 (p); IR (KBr) ν ; 3001, 2956, 2932, 2906, 2835, 1610, 1511, 1451, 1249, 1173, 1033, 996, 837, 801. Anal. Calcd for C₁₂H₁₁ClO₂S (254.73): C, 56.58; H, 4.35; S, 12.59. Found: C, 56.69; H, 4.38; S, 12.29.

4.2.5. 2-Iodo-5-methoxythiophene (**6a**). The general procedure 1, starting from **3** (0.60 mL) and using a solution of I₂ (1.5 g) in THF (3 mL), gave 75% (1.1 g) of **6a** (eluent: petrol) as a yellow oil: ¹³C NMR δ 169.9 (q), 134.4 (t), 105.7 (t), 60.3 (p), 57.2 (q); IR (KBr) ν ; 3009, 2960, 2934, 2822, 1547, 1466, 1421, 1234, 1199, 1058, 995, 932, 762, 573. The other analyses are in accordance with those of the literature.²³

4.3. General procedure 2: substituted thiophenes 4c, 5c and 6b by deprotonation of thiophenes 1–3 using Bu₃MgLi.TMEDA and subsequent trapping with electrophiles

To a solution of MgBr₂ (2.0 mmol) in THF (3 mL) at -10 °C were added BuLi (6.0 mmol) and, 1 h later, TMEDA (0.30 mL, 2 mmol). After stirring for 1 h at -10 °C, the required thiophene (6.0 mmol) was introduced. After 2 h at room temperature, 3,4,5-trimethoxybenzalde-hyde (1.2 g, 6.0 mmol) was added and the mixture was stirred for 18 h at room temperature before addition of water saturated with NH₄Cl (1 mL).

4.3.1. α-(3,4,5-Trimethoxyphenyl)-2-thiophenemethanol (4c). The general procedure 2, starting from 1 (0.48 mL), gave 96% (1.6 g) of 4c (eluent: cyclohexane/AcOEt 70:30): mp 90–92 °C; ¹H NMR δ 7.25 (d, 1H, J=4.9 Hz), 6.94 (t, 1H, J=4.2 Hz), 6.89 (d, 1H, J=3.0 Hz), 6.66 (s, 2H), 5.96 (d, 1H, J=2.3 Hz), 3.82 (s, 9H), 2.74 (d, 1H, J=3.4 Hz); ¹³C NMR δ 153.1 (q, 2C), 147.8 (q), 138.8 (q), 137.3 (q), 126.5 (t), 125.4 (t), 124.8 (t), 103.1 (t, 2C), 72.3 (t), 60.7 (p), 56.0 (p, 2C); IR (KBr) ν ; 3495, 3377, 3005, 2940, 2833, 1597, 1508, 1464, 1421, 1332, 1234, 1126, 1065, 1007, 741, 719, 699. Anal. Calcd for C₁₄H₁₆O₄S (280.35): C, 59.98; H, 5.75; S, 11.44. Found: C, 59.89; H, 5.82; S, 11.28.

4.3.2. 5-Chloro-α-(**3**,**4**,**5**-trimethoxyphenyl)-2-thiophenemethanol (5c). The general procedure 2, starting from **2** (0.55 mL), gave 93% (1.8 g) of **5**c (eluent: cyclohexane/AcOEt 70:30): mp 94–95 °C; ¹H NMR δ 6.70 (d, 1H, J= 3.8 Hz), 6.59 (m, 3H), 3.80 (s, 9H), 5.77 (s, 1H), 3.38 (br s, 1H); ¹³C NMR δ 153.1 (q, 2C), 146.7 (q), 138.3 (q), 137.2 (q), 129.7 (q), 125.5 (t), 123.9 (t), 103.0 (t, 2C), 72.3 (t), 60.7 (p), 55.9 (p, 2C); IR (KBr) ν ; 3307, 3219, 2934, 2834, 1596, 1509, 1466, 1418, 1330, 1238, 1132, 1059, 993, 750. Anal. Calcd for C₁₄H₁₅ClO₄S (314.79): C, 53.42; H, 4.80; S, 10.19. Found: C, 53.59; H, 4.94; S, 10.03.

4.3.3. 5-Methoxy-α-(3,4,5-trimethoxyphenyl)-2-thiophenemethanol (6b). The general procedure 2, starting from **3** (0.60 mL), gave 87% (1.6 g) of **6b** (eluent: cyclohexane/AcOEt 70:30): mp 80–82 °C; ¹H NMR δ 6.67 (s, 2H), 6.51 (d, 1H, J=3.8 Hz), 6.01 (d, 1H, J=3.8 Hz), 5.81 (d, 1H, J=3.0 Hz), 3.85 (s, 12H), 2.43 (d, 1H, J=3.8 Hz); ¹³C NMR δ 166.8 (q), 153.2 (q, 2C), 138.4 (q), 137.3 (q), 133.5 (q), 122.8 (t), 103.1 (t, 2C), 102.8 (t), 72.8 (t), 60.8 (p), 60.2 (p), 56.1 (p, 2C); IR (KBr) ν ; 3362, 2936, 2835, 1595, 1558, 1509, 1462, 1422, 1329, 1238, 1209,

1129, 1036, 1005, 757. Anal. Calcd for $C_{15}H_{18}O_5S$ (310.37): C, 58.05; H, 5.85; S, 10.33. Found: C, 58.26; H, 5.55; S, 10.19.

4.4. General procedure 3: substituted thiophenes 4d–g, 5d–f and 6c–e by deprotonation of thiophenes 1–3 using Bu₃MgLi and subsequent cross-coupling with aromatic halides

To a solution of MgBr₂ (2.0 mmol) in THF (3 mL) at -10 °C were added BuLi (6.0 mmol) and, 1 h later, the required thiophene (6.0 mmol). After 2 h at room temperature, the mixture thus obtained was added dropwise to a solution of the aromatic halide (6.0 mmol) and PdCl₂(dppf) (49 mg, 60 µmol), and the mixture was heated at reflux for 18 h before addition of water saturated with NH₄Cl (1 mL).

4.4.1. 2-(2-Thienyl) pyridine (4d). The general procedure 3, starting from **1** (0.48 mL) and using 2-bromopyridine (0.58 mL), gave 77% (0.74 g) of **4d** (eluent: CH_2Cl_2) as a white solid. The physical and spectral data are analogous to those obtained for a commercial sample.

4.4.2. 3-(2-Thienyl) quinoline (4e). The general procedure 3, starting from **1** (0.48 mL) and using 3-bromoquinoline (0.83 mL), gave 56% (0.71 g) of **4e** (eluent: CH_2Cl_2/Et_2O 80:20) as a yellow solid. The physical and spectral data are in accordance with those of the literature.^{18b,24}

4.4.3. 2-Phenylthiophene (4f). The general procedure 3, starting from **1** (0.48 mL) and using iodobenzene (0.67 mL), gave 84% (0.81 g) of **4f** (eluent: petrol/CH₂Cl₂ 80:20) as a white solid: mp 94 °C. The physical and spectral data are analogous to those obtained for a commercial sample.

4.4.4. 2-(4-Methoxyphenyl) thiophene (4g). The general procedure 3, starting from **1** (0.48 mL) and using 4-bromoanisole (0.75 mL), gave 92% (1.1 g) of **4g** (eluent: petrol/CH₂Cl₂ 60:40) as a white solid: mp 102 °C (lit.²⁵ 106–107 °C); IR (KBr) ν ; 3099, 3072, 2961, 2930, 2835, 1604, 1500, 1293, 1274, 1261, 1104, 1031, 822, 810, 698. The other analyses were found identical to those previously described.²⁵

4.4.5. 2-(5-Chloro-2-thienyl) pyridine (5d). The general procedure 3, starting from 2 (0.55 mL) and using 2-bromopyridine (0.58 mL), gave 68% (0.80 g) of 5d (eluent: CH₂Cl₂): mp 69–70 °C (lit.²⁶ 69–70 °C); ¹H NMR δ 8.53 (d, 1H, *J*=4.9 Hz), 7.68 (td, 1H, *J*=7.9, 1.5 Hz), 7.58 (d, 1H, *J*=7.1 Hz), 7.33 (d, 1H, *J*=3.8 Hz), 7.15 (ddd, 1H, *J*=7.1, 4.9, 1.1 Hz), 6.92 (d, 1H, *J*=3.8 Hz); ¹³C NMR δ 150.8 (q), 148.7 (t), 143.0 (q), 135.9 (t), 131.4 (q), 126.7 (t), 122.9 (t), 121.5 (t), 117.2 (t). Anal. Calcd for C₉H₉ClNS (195.67): C, 55.25; H, 3.09; N, 7.16; S, 16.39. Found: C, 55.16; H, 3.03; N, 7.07; S, 16.33. The other analyses were found identical to those previously described.²⁶

4.4.6. 2-Chloro-5-(4-methoxyphenyl) thiophene (5e).²⁷ The general procedure 3, starting from **2** (0.55 mL) and using 4-bromoanisole (0.75 mL), gave 81% (1.1 g) of **5e** (eluent: petrol/CH₂Cl₂ 60:40): mp 100 °C; ¹H NMR δ 7.40 (d, 2H, *J*=8.6 Hz), 6.91 (d, 1H, *J*=4.1 Hz), 6.87 (d, 2H, *J*=8.7 Hz), 6.82 (d, 1H, *J*=3.8 Hz), 3.74 (s, 3H); ¹³C NMR

δ 159.3 (q), 142.8 (q), 127.8 (q), 126.8 (t), 126.7 (t, 2C), 126.4 (q), 121.0 (t), 114.3 (t, 2C), 55.2 (p); IR (KBr) ν; 2956, 2836, 1603, 1505, 1438, 1288, 1257, 1180, 1031, 827, 793. Anal. Calcd for C₁₁H₉ClOS (224.71): C, 58.80; H, 4.04; S, 14.27. Found: C, 58.53; H, 4.11; S, 14.48.

4.4.7. Methyl 4-(5-chloro-2-thienyl) benzoate (5f). The general procedure 3, starting from **2** (0.55 mL) and using methyl 4-iodobenzoate (1.6 g), gave 22% (0.33 g) of **5f** (eluent: petrol/CH₂Cl₂ 70:30): mp 146–148 °C; ¹H NMR δ 8.03 (d, 2H, *J*=8.3 Hz), 7.56 (d, 2H, *J*=8.3 Hz), 7.19 (d, 1H, *J*=4.1 Hz), 6.93 (d, 1H, *J*=3.8 Hz), 3.93 (s, 3H); ¹³C NMR δ 167.0 (q), 141.9 (q), 138.2 (q), 131.2 (q), 130.8 (t, 2C), 129.5 (q), 127.8 (t), 125.4 (t, 2C), 124.1 (t), 52.6 (p); IR (KBr) ν ; 3014, 2958, 1725, 1603, 1436, 1291, 1277, 1187, 1112, 1007, 850, 801, 765, 695. Anal. Calcd for C₁₂H₉CIO₂S (252.72): C, 57.03; H, 3.59; S, 12.69. Found: C, 56.95; H, 3.41; S, 12.63.

4.4.8. 2-(5-Methoxy-2-thienyl) pyridine (6c). The general procedure 3, starting from 3 (0.60 mL) and using 2-bromopyridine (0.58 mL), gave 56% (0.64 g) of 6c (eluent: petrol/ CH₂Cl₂ 70:30): mp <50 °C (lit.²⁸ 42–43.5 °C); ¹³C NMR δ 168.0 (q), 152.3 (q), 148.7 (t), 135.8 (t), 130.1 (q), 122.4 (t), 120.4 (t), 116.8 (t), 104.3 (t), 59.4 (p); IR (KBr) ν ; 3072, 3007, 2965, 2936, 2873, 2827, 1589, 1556, 1494, 1461, 1427, 1299, 1278, 1237, 1209, 1151, 1091, 1067, 1043, 997, 961, 766, 744, 728, 620. The other analyses are in accordance with those of the literature.²⁸

4.4.9. 2-Methoxy-5-phenylthiophene (6d). The general procedure 3, starting from **3** (0.60 mL) and using iodobenzene (0.67 mL), gave 67% (0.76 g) of **6d** (eluent: petrol/ CH₂Cl₂ 80:20) as a pale blue oil: ¹H NMR δ 7.48 (d, 2H, *J* = 7.2 Hz), 7.33 (t, 2H, *J*=7.5 Hz), 7.21 (t, 1H, *J*=7.3 Hz), 6.18 (d, 1H, *J*=3.8 Hz), 6.18 (d, 1H, *J*=3.8 Hz), 6.18 (d, 1H, *J*=3.8 Hz), 3.92 (s, 3H); ¹³C NMR δ 165.8 (q), 134.5 (q), 129.9 (q), 128.7 (t, 2C), 126.4 (t), 124.6 (t, 2C), 120.4 (t), 104.5 (t), 59.8 (p); IR (KBr) *v*; 3023, 2939, 2827, 1555, 1508, 1480, 1446, 1428, 1269, 1231, 1204, 1059, 1000, 752, 690. Anal. Calcd for C₁₁H₁₀OS (190.26): C, 69.44; H, 5.30; S, 16.85. Found: C, 69.23; H, 5.47; S, 16.81.

4.4.10. Methyl 4-(5-methoxy-2-thienyl) benzoate (6e). The general procedure 3, starting from **3** (0.60 mL) and using methyl 4-iodobenzoate (1.6 g), gave 40% (0.60 g) of **6e** (eluent: petrol/CH₂Cl₂ 50:50): mp 126–127 °C; ¹H NMR δ 7.99 (d, 2H, J=8.3 Hz), 7.52 (d, 2H, J=7.9 Hz), 7.10 (d, 1H, J=3.8 Hz), 6.22 (d, 1H, J=4.1 Hz), 3.94 (s, 3H), 3.91 (s, 3H); ¹³C NMR δ 167.3 (q), 166.8 (q), 139.0 (q), 130.1 (t, 2C), 128.6 (q), 127.6 (q), 124.1 (t, 2C), 122.5 (t), 105.0 (t), 60.2 (p), 52.0 (p); IR (KBr) ν ; 3084, 2942, 2831, 1709, 1604, 1511, 1482, 1430, 1411, 1291, 1212, 1180, 1111, 1065, 1014, 988, 848, 762, 696. Anal. Calcd for C₁₃H₁₂O₃S (248.30): C, 62.88; H, 4.87; S, 12.91. Found: C, 62.59; H, 4.83; S, 12.81.

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