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Short communication

An efficient direct method for the azo-coupling of methoxythiophenes

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Abstract

The direct azo-coupling of methoxythiophenes with diazonium salts in good/excellent yield to give previously inaccessible methoxyazothiophenes is reported. The need to prepare potentially unstable methoxy-substituted aminothiophenes is avoided. Materials may be of potential use as photosensitive media for optical data storage and as disperse dyes.

Keywords: Thiophene; Azo-coupling; Methoxythiophene

1. Introduction

Many years ago we showed that the thiophene ring in methoxythiophenes was sufficiently activated toward electrophilic attack to suffer substitution by the weak electrophile involved in the Mannich reaction [1]. We also found at that time that 2-methoxythiophene would couple with *p*-nitrobenzenediazonium chloride in excellent yield but the reaction was neither investigated further nor reported. With the advent of Blu-Ray DVD [2] and the need for photosensitive compounds to operate with blue light (405 nm) we again became interested in thiophene azo compounds since theoretical studies by Astrand et al. [3] postulate a $\pi-\pi^*$ transition for the *trans*-isomer to be centred at 415 nm.

Hence, the scope of this reaction (see Scheme 1), which negates the need to prepare methoxy-substituted aminothiophenes which we believe to be very unstable, was further explored.

2. Synthetic overview

Two procedures were used for the coupling; in the first (Method A) an aqueous solution of the diazonium chloride, prepared in the usual way, was added to the substrate dissolved in glacial acetic acid containing 4 M sodium hydroxide which served to form the necessary buffer (methoxythiophenes are susceptible to hydrolysis by strong acids) and produce a solvent mixture from which the coupling product would precipitate without much loss. The second procedure (Method B) utilized a solution of the substrate dissolved in glacial acetic acid containing anhydrous sodium acetate. The solid diazonium tetrafluoroborate was added to this with stirring and after a period of continued stirring the mixture was poured into water and the product isolated (usually by filtration). Method B had two advantages: firstly, several substrates could be investigated using the product from one preparation of diazonium tetrafluoroborate and secondly, more importantly, a lengthy period of reaction at room temperature could be used if necessary without risk of decomposition of the diazonium salt. Yields were comparable in one case where both methods were used on the same substrate (compound **2**).

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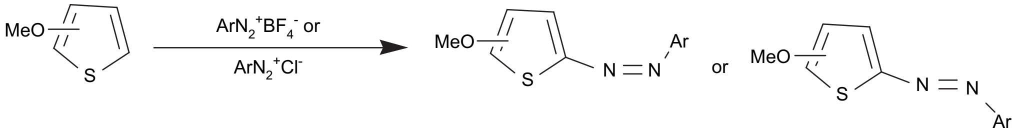


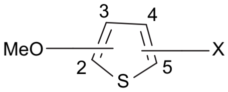
Scheme 1. Diazonium coupling of methoxythiophene.

3. Results and discussion

A series of diazonium salts of gradually decreasing activity (as suggested by the σ constants of their substituents) was employed as listed in Tables 1–3. Surprisingly it was found that even the weakly coupling *p*-anisyldiazonium chloride would react given sufficient time (the reaction mixture was left overnight instead of the usual standing period of 5–30 min [4]). 3-Methoxy- and 3,4-dimethoxy-thiophene also coupled. This result is in strong contrast to the situation with thiophene itself which fails to couple even with the very active 2,4-dinitrobenzenediazonium chloride [5] and it is also noteworthy that anisole will only react with this diazonium salt [6]. Hence the alkoxy group activates the thiophene ring towards diazo coupling in a way similar to hydroxy and amino substituents [7].

As in the above-mentioned Mannich reaction the substitution was much slower with 3,4-dimethoxythiophene than with the

Table 1
Physical characterization data for azothiophenes, **1–12**



No.	MeO	Substituent, X	(%)[i]	M.p. (°C)[j]	ε_{max}	λ_{max} (nm)[k]	Elemental analysis (%)
1	2	5-(*p*-Nitrophenylazo)[a]	94	175–176[f]	23,420	432	Fd: C, 50.21; H, 3.39, N, 15.83 Calc: C, 50.18; H, 3.46; N, 5.96
2	2	5-(*m*-Nitrophenylazo)[a]	94	148–149	23,512	407	Fd: C, 50.00; H, 3.40, N, 15.79
2	2	5-(*m*-Nitrophenylazo)[b]	98				Calc: C, 50.18; H, 3.46; N, 15.96
3	2	5-(*p*-Cyanophenylazo)[a]	99	166–168	16,451	415	Fd: C, 59.98; H, 3.67, N, 17.14 Calc: C, 59.24; H, 3.73; N, 17.27
4	2	5-(*o*-Cyanophenylazo)[b]	98	137–138	16,749	418	Fd: C, 59.21; H, 3.71, N, 17.07 Calc: C, 59.24; H, 3.73; N, 17.27
5	2	5-(*p*-Ethoxycarbonyl-phenylazo)[a]	86	105–106	28,164	412	Fd: C, 57.88; H, 4.88, N, 9.58 Calc: C, 57.92; H, 4.86; N, 9.65
6	2	5-(*p*-Chlorophenylazo)[a]	75	124–125	23,046	403	Fd: C, 52.22; H, 3.57, N, 10.88 Calc: C, 53.28; H, 3.59; N, 11.09
7	2	5-(*p*-Methoxyphenylazo)[a]	77[c]	76–77[g]	26,154	402	Fd: C, 57.96; H, 4.78, N, 11.24 Calc: C, 58.05; H, 4.87; N, 11.28
8	2	5-(3-[1,2,4-Triazolyl]azo)[a]	77[e]	165 dec[h]	19,419	395	Fd: C, 40.27; H, 3.00, N, 33.56 Calc: C, 40.38; H, 2.91; N, 33.63
9	2	5-(3-Quinolylazo)[a]	68	121–122	23451	415	Fd: C, 62.38; H, 4.04, N, 15.59 Calc: C, 62.44; H, 4.12; N, 14.33
10	4	5-(*m*-Nitrophenylazo)[b]	84	160–161	27,989	381	Fd: C, 50.14; H, 3.39, N, 15.81 Calc: C, 50.18; H, 3.46; N, 15.96
11	4	5-(*o*-Cyanophenylazo)[b]	96	119–121	19,678	391	Fd: C, 59.15; H, 3.69, N, 17.03 Calc: C, 57.24; H, 3.73; N, 17.27
12	3, 4	5-(*o*-Cyanophenylazo)[b]	89[d]	183–185[f]	22,156	381	Fd: C, 57.14; H, 4.04, N, 15.14 Calc: C, 57.13; H, 4.06; N, 15.37

[a] Method A: The methoxythiophene (5 mmol) was dissolved in glacial acetic acid (12.5 mL) to which had been added 4 M sodium hydroxide (5.5 mL). The solution was cooled in an ice bath whilst the diazonium chloride solution (prepared from the amine, 5 mmol, in 4 M HCl (5 mL) and sodium nitrite (0.35 g) in water (1.5 mL)) was gradually added. The mixture was allowed to stand for 5–30 min before the precipitate was filtered off.

[b] Method B: The methoxythiophene (5 mmol) was dissolved in glacial acetic acid (13 mL) containing anhydrous sodium acetate (0.5 g). The diazonium tetrafluoroborate (5 mmol) was gradually added with stirring. After the addition was complete the mixture was stirred for a further 1 h before being poured into water (ca. 50 mL). The resulting suspension was stirred for a further 10 min before the product was filtered off.

[c] After 24 h.

[d] After 19 h.

[e] Diazotization in 2 M H_2SO_4.

[f] Recrystallized from EtOAc.

[g] Recrystallized from aq. EtOH.

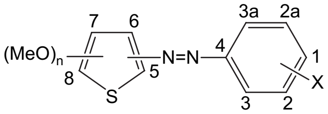
[h] From Me_2CO (Soxhlet).

[i] Crude yields reported.

[j] M.p. of pure compound.

[k] Solvent, spectroscopic grade THF.

Table 2
^1H NMR data for the azothiophenes ($CDCl_3$, 270 MHz; 400 MHz)[a]



No.	MeO	H1	H2	H2a	H3	H3a	H5	H6	H7	H8
1	4.01	X	8.28d	8.28d	7.84d	7.84d	–	7.66d	6.41d	–
2	3.99	8.17m	7.59t	X	8.05m	8.57t	–	7.62d	6.38d	–
3	4.01	X	7.72d	7.72d	7.82d	7.82d	–	7.63d	6.40d	–
4	4.02	[a]	[a]	[a]	[a]	X	–	7.65d	6.41d	–
5	3.99	X	7.80d	7.80d	8.12d	8.12d	–	7.60d	6.36d	–
6	3.96	X	7.67d	7.68d	7.39d	7.39d	–	7.51d	6.31d	–[b]
7	3.94	X	6.95d	6.95d	7.74d	7.74d	–	7.43d	6.28d	–
8	4.05	[c]	[c]	[c]	[c]	[c]	–	7.87d	6.65d	–
9[a]	4.22	8.17m	7.58t	X	8.05m	8.54m	–	–	6.82d	7.41d
10	4.25					X	–	–	6.80d	7.42d
11[a]	3.93	[d]	[d]	[d]	[d]	[d]	–	7.63	6.31d	–
12	[e]	[f]	[f]	[f]	[f]	X	–	–	–	6.40

[a] 7.58–7.81m.

[b] CH_2: 4.39q; CH_3: 1.41t.

[c] Triazolyl 4: ca. 3.6 br; 5: 8.51; 7.30–7.80m.

[d] Quinolyl 2: 9.28d; 4: 8.34d; 5: 8.05d; 6: 7.50t; 7: 7.63t; 8: 7.83d.

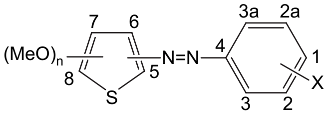
[e] 4.51 (6), 3.89 (7).

[f] 7.41–7.78m.

monomethoxy derivatives but it was possible to obtain good yields by using long reaction times (see results for compound **12**). It has been suggested [8] that the slower Mannich reaction is due to shielding of the 2- and 5-positions of the thiophene ring by the mutually repelling methoxy groups; this is supported by molecular modelling results. The azo-coupling would be expected to be similarly affected. It is noteworthy that 3,4-dimethoxyfuran couples with diazonium salts in aqueous pyridine but the reaction is totally different from the thiophene case, being an addition process [9]. Azo-coupling with 2,5-dimethoxythiophene was a much less straightforward process than was the case with the 3,4 isomer. The reaction was incomplete after 19 h (^1H nmr) using Method B with *m*-nitrobenzenediazonium tetrafluoroborate and there were several coloured products present (tlc); in view of this the process was not further investigated. The slow reaction may have been due to the lower reactivity of the thiophene β position (but note that 2,5-dimethoxythiophene undergoes the Mannich reaction normally [10]) however, the formation of a number of coloured products indicates unexpected complexity.

The azo compounds of the type described here mostly have good stability (a sample of compound **1** had an unchanged melting point after storage for 30 years) but two apparent exceptions have been noted: some material, crude m.p. 128–130 °C, made by the reaction of 3,4-dimethoxythiophene with *m*-nitrobenzenediazonium tetrafluoroborate spontaneously decomposed after 10 months. Also, the dark red compound, crude m.p. 116–119 °C, made by coupling diazotized

Table 3
^{13}C NMR data for the azothiophenes ($CDCl_3$, 67.5 MHz)



No.	MeO	Data
1	60.2	C1(X):147.4; C2,C2a,C3,C3a:122.7,124.7; C4:155.9; C5:146.7; C6:136.1; C7:106.7; C8:173.95
2	60.1	C1:123.3; C2:129.75; C2a(X):149.0; C3:128.65; C3a:116.4; C4:152.85; C5:146.3; C6:135.2; C7:106.15; C8:173.0
3	60.15	C1(X):112.1; C2,2a:122.8; C3,3a:133.1; C4:154.5; C5:146.65; C6:135.4; C7:106.4; C8:173.4
4	60.4	C1,C2:133.5,133.1; C2a:129.0; C3:117.35; C3a(X):117.1; C4:153.4; C5:146.8; C6:135.75; C7:106.95; C8:174.2; CN:111.3
5	60.0	C1(X):130.7; C2,2a: 122.1; C3,3a: 130.5; C4: 154.9; C5: 147.0; C6: 134.2; C7: 105.9; C8: 172.4; CO: 166.2; CH_2: 61.1; CH_3: 14.3
6	59.9	C1(X): 135.25; C2,2a: 129.2; C3,3a: 123.5; C4: 150.6; C5: 146.8; C6: 133.0; C7: 105.4; C8: 171.5
7	59.7	C1(X): 160.95; C2,2a: 114.1; C3,3a: 124.0; C4: 146.7; C5: 147.3; C6: 130.5; C7: 104.6; C8: 169.8; PhOMe: 55.4
8	60.6	C5: 145.5; C6: 136.6; C7: 107.0; C8: 172.1; triazoyl CH; 145.5; triazoyl quaternary C: 172.1
9	60.1	C1: 123.4; C2: 129.7; C2a(X): 148.9; C3: 128.4; C3a: 116.7; C4: 153.1;C5: 138.0; C6: 159.9; C7: 118.2; C8: 130.75;
10	60.2	C1,C2: 133.5, 133.1; C2a: 129.1; C3: 118.2; C3a(X): 117.0; C4: 153.6;C5: 138.85; C6: 160.4; C7: 117.8; C8: 131.85; CN: 111.0
11[a]	60.1	C5:147.2;C6:134.1;C7:106.0;C8:172.4; quinolyl: 127.4;128.1;128..3;129.1; 129.5;130.2;144.8;146.2;148.3
12[a]	57.3(6) 62.7(7)	C1,C2: 137.69, 133.81; C2a: 129.3; C3: 118.3; C3a(X): 117.0; C4: 153.2; C5: 137.6; C6,C7: 148.1, 149.6; C8: 101.9

[a] 100 MHz.

2-aminothiazole with 2-methoxythiophene, appeared to partially decompose on attempted crystallization.

4. Summary

In summary, the methodology developed, either Method A or Method B, leads to the formation of some previously inaccessible methoxy-substituted azothiophenes. The need to prepare potentially unstable methoxy-substituted aminothiophenes is avoided.

References

[1] Barker JM, Huddleston PR, Wood ML. Synth Commun 1975;5:59.

[2] For a full account of Blu-Ray technology see <http://www.blu-ray.com/info/> Mustroph H, Stollenwerk M, Bressau V. Angew Chem Int Ed 2006;45:2016.

[3] Astrand P-O, Sommer-Larsen P, Hvilsted S, Ramanujam PS, Bak KL, Sauer SPA. Chem Phys Lett 2000;325:115.

[4] Result originally obtained by Mr. S. Armstrong, a final year student in this Division. It is only possible to use the long standing period because of the relatively high stability of *p*-anisyldiazonium chloride in aqueous solution; see Snow CC. Ind Eng Chem 1932;24:1420.

[5] Bartle MG, Gore ST, Mackie RK, Tedder JM. J Chem Soc Perkin Trans 1 1976:1636;
Gore ST, Mackie RK, Tedder JM. J Chem Soc Perkin Trans 1 1976:1639. Note that 2,5-dimethylthiophene reacts at both the ring and the side-chain with this salt.

[6] Meyer KH, Irschick A, Schlösser H. Ber 1914;47:1741.

[7] For some recent examples see Hurd CD, Kreuz KL. J Am Chem Soc 1950;72:5543;
Norris RK. In: Gronowitz S, editor. Thiophene and its derivatives, Part 2. New York, London: John Wiley; 1986. p. 631;
Hallas G, Choi J-H. Dyes Pigments 1999;40:119;
Hallas G, Choi J-H. Dyes Pigments 1999;42:249.

[8] Barker JM. Private communication.

[9] Iten PX, Eugster CH. Helv Chim Acta 1978;61:1033.

[10] Barker JM, Huddleston PR, Shutler SW. J Chem Soc Perkin Trans 1 1975:2483.