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Anodic thiocyanation of mono- and disubstituted aromatic compounds

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ABSTRACT

The *in situ* and environmentally friendly thiocyanation (no use of toxic oxidizing agents) electrochemical thiocyanation of aromatic compounds involving various derivatives of anisole and aniline to afford aromatic thiocyanates have been studied in organic acidic media. The initial electrochemical step involves anodic oxidation of thiocyanate anion to its radical (SCN), followed by dimerization to thiocyanogen $(SCN)_2$. The latter is polarized by the acidic solvent and attacks the aromatic nucleus of the substrate to afford the corresponding thiocyanate derivative. The sole thiocyanate products obtained in each case shows high *regio*-selectivity (no *ortho* isomer was observed) for the monosubstituted aromatics and high isomer-selectivity (no isothiocyanate isomer was detected) for both mono- and disubstituted aromatics.

1. Introduction

Aryl thiocyanates are useful precursors for agrochemicals, dyes, insecticides and drugs [1–3]. In organic synthesis, they are also used as a convenient source of ArS^- for introducing sulfur functional groups in various organic molecules [4–7]. Chemical synthesis of aryl thiocyanates can be performed via both electrophilic and radical reactions [8]. In the radical process (SCN) is produced by N-thiocyanatosuccinimide (the analog of NBS) and followed by an attack on the aromatic nucleus [9]. However, this reaction is accompanied by by-products that are difficult to remove from the reaction mixture. The electrophilic reaction involves an initial oxidation of thiocyanate anion and its recombination to the thiocyanogen dimer $(SCN)_2$. Then a polarization of the S–S bond is required in order to generate a positive charge on one of the sulfur atoms, in order to allow an electrophilic attack on the aromatic ring. Oxidation of the thiocyanate anion has been carried out by various oxidizing reagents, such as halogens [3,10], metal oxidants [11–13] and many other organic and inorganic oxidants [14–20]. The drawback is that these reactions involve the use of large amounts of the oxidizing agent or toxic metal thiocyanate.

Furthermore, the chemical thiocyanation reaction is far from being selective because usually a mixture of isomers is formed, e.g., *para* and *ortho* isomers by thiocyanation of aromatic derivatives [20], and thiocyanate and isothiocyanate isomers by addition to alkenes [3].

In comparison, the electrochemical method affords a "green" oxidizing agent – the anode. Previously we have shown [21] that under acidic conditions the anodic oxidation of thiocyanate anion to its radical favours dimerization over polymerization. In addition, the electrochemical thiocyanation of anisole affords both *regio*- and isomer-selectivities in good yields (Scheme 1).

In the present work we wish to expand the scope of the electrochemical thiocyanation reaction to other aromatic derivatives under similar conditions. Scheme 2 describes the various mono- and disubstituted aromatic substrates that have been investigated for this purpose.

2. Experimental

2.1. General

Aromatic compounds were supplied by Aldrich and Alfa and used without further purification. Analytical grade glacial acetic (supplied by Frutarom Co.) and formic 97% (supplied by Gadot Co.) acids were used without further purification. For electrochemical measurements and electrolyses, a Princeton Applied Research (PAR) Potentiostat/Galvanostat Model 173 and PAR Universal Programmer Model 175, or a computerized PAR Potentiostat/Galvanostat Model 273A, were employed. Cyclic voltammetry (CV) measurements were performed in a conventional three-electrode cell. The working electrode was a platinum disk (ca. 1 mm diameter), the reference electrode was Ag/AgCl (in 3 M NaCl), and the auxiliary electrode was a Pt cylindrical gauze or wire.

For controlled potential electrolysis (CPE), an H-type two-compartment cell equipped with a medium glass frit as a membrane was used. The anode compartment contained a polished

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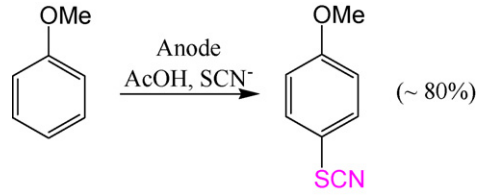
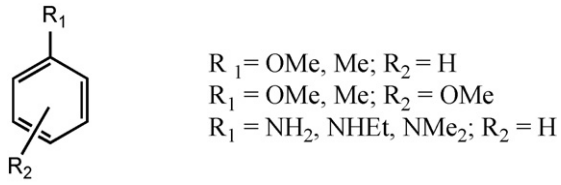


Scheme 1. Electrochemical thiocyanation of anisole as sample of substrate.



Scheme 2. Aromatic substrates.

silver wire quasi-reference electrode, immersed in electrolyte solution in a glass cylinder equipped with a fine glass frit at its end. Both compartments contained either glacial acetic acid and 0.5 M $LiClO_4$ (for entries 1, 10, 11, Table 1) or a mixture of formic and acetic acids (1:1) and 0.1 M $LiClO_4$ (for entries 2–9 and 12, Table 1) The choice of solvent-electrolyte medium depends on the optimized final outcome. Glacial acetic acid does not conduct electricity well unless a higher concentration of electrolyte was used. The aromatic substrates, and thiocyanate salt, NH_4SCN (dried at 80 °C under vacuum, for 24 h), were added to the anode compartment. A magnetic stirrer stirred the mixture during electrolysis (1–3 days) and for an additional 24 h after it stopped. Electrolysis was terminated after passing 1.5–2.2 F/mol.

CPE was conducted by controlling the potential at 1.25 V (vs. Ag wire, which corresponds to ~1.05 V vs. Ag/AgCl). This applied potential is based on the observation that the thiocyanate anion is oxidized at ~1 V (vs. Ag/AgCl) in acetic acid [21]. A platinum foil (5 cm^2) working electrode and a stainless-steel counter electrode were used. The anode compartment contained 5 mmol of aromatic substrate and 2 mmol of NH_4SCN, both dissolved in 30 ml of solvent-electrolyte solution. Initial current was typically ~5 mA in acetic acid or >20 mA in mixtures of formic/acetic acids and at the end of electrolysis it reached a value of ~1 mA. Pulsing (to 0 V for 0.5 s, every 50 s) was required during electrolysis to avoid passivation of the working electrode surface, probably due to the formation of the insulating polymer, parathiocyanogen. The reaction mixture was filtered and treated twice with 30 ml of saturated aqueous NaCl and 30 ml of CH_2Cl_2. After phase separation, the organic layer was washed with three portions of saturated $NaHCO_3$ solution, then dried over $MgSO_4$, and filtered. The solvent CH_2Cl_2 was evaporated by a rotavapor until reaching a final volume of ~1 ml. A sample of the residue was checked by glc and the yield of the product was determined by a calibration curve of an external standard consisting of 1-methoxy-4-thiocyanatobenzene [21].

Constant current electrolyses were performed in a divided H-type two-compartment cell equipped with a medium glass frit as a membrane. Both electrodes were made of Pt foils (5 cm^2) and distant from each other by 3–5 mm. The volume of the electrolyte solution (1:1 AcOH–HCOOH and 0.1 M $LiClO_4$) in each compartment was 20 ml and the ratio between substrate (5 mmol) and NH_4SCN (2 mmol) was 5:2. After passing the desired Coulombs, the solution mixture was treated as before.

2.1.1. Characterization of products

2.1.1.1. 1-Methoxy-4-thiocyanatobenzene (4-thiocyanatoanisole). Solid m.p. 40–41 °C (m.p. 43–44 °C [20]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) [21] δ: 3.83 (s, 3H, OCH_3), 6.95 (d, J = 8.9 Hz, 2H, 2-H, 6-H), 7.51(d, J = 8.9 Hz, 2H, 3-H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 55.5 (OCH_3), 111.6 (SCN), 113.9, 117.4, 132.1, 135.4 (4 different aromatic carbons); MS: m/z (%): M^+ 165 (100), 150 (75), 139 (15), 122 (50), 95 (13), 63 (18).

2.1.1.2. 1-Methyl-4-thiocyanatobenzene (4-thiocyanotoluene). Solid (m.p. 40–41 °C [22]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 2.50 (s, 3H, CH_3), 7.05–7.23 (m, 4H, ring protons); MS: m/z (%): M^+ 149 (100), 116 (75), 91 (90), 65 (18).

2.1.1.3. 1,3-Dimethoxy-4-thiocyanatobenzene. Oil [18]; IR: a sharp peak of thiocyanate group at 2153 cm^{-1}, 3013, 2938, 2838, 1595, 1481, 1306, 1205, 1166, 1071; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 3.77 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 6.46 (s, 1H, 2-H), 6.48 (d × d, J = 8.2, 2.5 Hz, 1H, 6-H), 7.38 (d, J = 8.2 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 55.6 (OCH_3), 56.1 (OCH_3), 111.3 (SCN), 97.8, 101.1, 104.5, 107.9, 132.1, 135.3 (6 aromatic carbons); MS: m/z (%): M^+ 195 (100), 180 (45), 152 (25), 95 (10), 69 (12).

2.1.1.4. 1,2-Dimethoxy-4-thiocyanatobenzene. Solid m.p. 48–50 °C (m.p. 49–50 °C [23]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}, 3007, 2933, 2830, 1600, 1502, 1453, 1238, 1170; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 3.90–3.92 (s + s, 6H, OCH_3), 6.88 (d, J = 8.4 Hz 1H, 6-H), 7.05 (d, J = 2.2 Hz, 1H, 3-H), 7.15 (d × d, J = 8.4, 2.2 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 55.9 (OCH_3), 56.0 (OCH_3), 111.3 (SCN), 111.9, 113.7, 114.3, 125.1, 149.9, 150.7 (6 aromatic carbons); MS: m/z (%): M^+ 195 (100), 180 (45), 152 (15), 125 (12), 94 (30).

2.1.1.5. 1,4-Dimethoxy-2-thiocyanatobenzene. Solid m.p. 67–69 °C (m.p. 68–69 °C [23]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}, 3002, 2935, 2830, 1600, 1502, 1450, 1240, 1166, 1037; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 3.80 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.87–6.88 (m, 2H, 2-H, 6-H), 7.12 (d, J = 1 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 55.0 (OCH_3), 55.8 (OCH_3), 110.3 (SCN), 111.6, 113.0, 113.9, 114.7, 149.4, 153.3 (6 aromatic carbons); MS: m/z (%): M^+ 195 (80), 180 (100), 152 (25), 107 (10), 79 (12).

2.1.1.6. 1-Methoxy-3-methyl-4-thiocyanatobenzene. Solid m.p. 41–42 °C; IR: a sharp peak of thiocyanate group at 2153 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 2.51 (s, 3H, CH_3), 3.81 (s, 3H, OCH_3), 6.78 (d × d, J = 8.6, 2.8 Hz, 1H, 6-H), 6.86 (d, J = 2.8 Hz, 1H, 2-H), 7.54 (d, J = 8.6 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 21.1 (CH_3), 55.4 (OCH_3), 111.4 (SCN), 114.6, 115.4, 118.6, 134.0, 137.3, 142.8 (6 aromatic carbons); MS: m/z (%): M^+ 179 (100), 164 (50), 136 (20), 109 (18), 77 (17).

2.1.1.7. 1-Methoxy-2-methyl-4-thiocyanatobenzene. Oil (yellowish [23]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 2.22 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.84 (d, J = 8.5 Hz, 1H, 6-H), 7.36 (d, J = 2.5 Hz, 1H, 3-H), 7.38 (d × d, J = 8.6, 2.5 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 16.1 (CH_3), 55.5 (OCH_3), 111.2 (SCN), 111.4, 112.9, 129.6, 131.2, 134.1, 159.4 (6s, ring carbons); MS: m/z (%): M^+ 179 (100), 164 (80), 148 (15), 109 (15), 78 (20).

2.1.1.8. 1-Methoxy-4-methyl-2-thiocyanatobenzene. Oil (yellowish [23]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 2.32 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 6.82 (d, J = 8.2 Hz, 1H, 6-H), 7.14 (d × d, J = 8.2, 2.0 Hz, 1H, 3-H), 7.36 (d, J = 2.0 Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 18.8 (CH_3), 55.5 (OCH_3), 113.2 (SCN), 111.3, 113.6, 129.0, 133.5, 136.1, 148.5 (6

Table 1
Electrochemical thiocyanation of substituted anisole, toluene and aniline derivatives under CPE conditions[a].

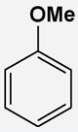
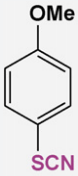
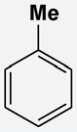
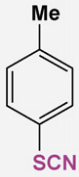
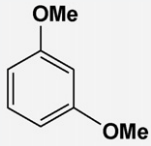
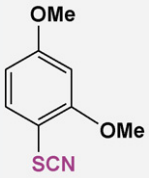
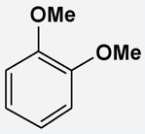
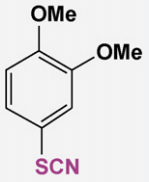
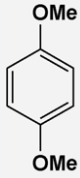
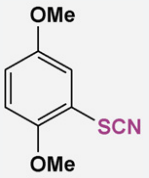
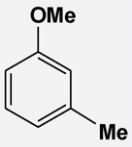
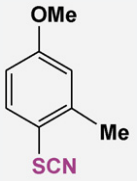
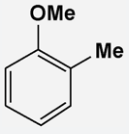
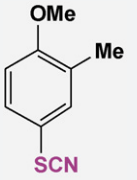
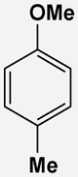
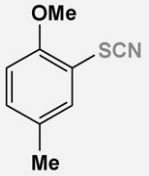
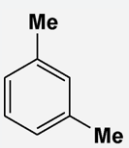
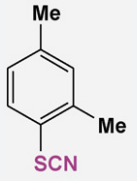
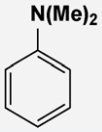
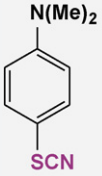
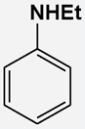
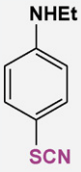
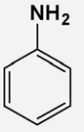
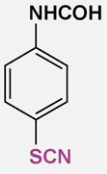
Entry	Substrate[b]	E_p(ox)/V[c]	Product	Yield (%)
1		1.95		80%[d]
2		2.24		15%[e]
3		1.55		74%
4		1.49		66%
5		1.35 ($E_{1/2}$, quasi-reversible)		12%[e]
6		1.74		38%
7		1.79		60%
8		1.60		10%[e]
9		2.15		13%[e]

Table 1 (*Continued*)

Entry	Substrate[b]	E_p(ox)/V[c]	Product	Yield (%)
10		0.80 ($E_{1/2}$)		42%
11		0.83 ($E_{1/2}$)		15%[f]
12		1.36[g]		15%[f]

[a] The oxidation peak potential of thiocyanate anion is ~1 V (vs. Ag/AgCl). All substrates in entries 1–9 have peak potentials in the range of 1.35–2.2 V (vs. Ag/AgCl), well above the oxidation potential of the thiocyanate anion. As to entries 10–12, see Section 3. The proper experimental conditions for each entry are described in Section 2. The initial current was typically ~5 mA in acetic acid and >20 mA in mixtures of acetic/formic acids.

[b] No thiocyanation products were detected when the substrate contains a deactivating substituent such as, Cl, NHCOMe or NO_2.

[c] Oxidation peak potentials (vs. Ag/AgCl) were measured by CV in solutions of acetic–formic acids (1:1)–0.1 M $LiClO_4$ on a glassy carbon working electrode; scan rate: 50 mV/s.

[d] This result is taken from Ref. [21].

[e] The rest is mostly unreacted starting material.

[f] A formylation reaction occurred at the amino group converting the substrate to its formamide derivative, prior to thiocyanation.

[g] This relatively high value is attributed to the oxidation of the formamide derivative, PhNHCHO.

aromatic carbons); MS: *m*/*z* (%): M^+ 179 (100), 164 (30), 151 (55), 136 (15), 109 (15), 78 (35).

2.1.1.9. 1,3-Dimethyl-4-thiocyanatobenzene. Oil (b.p. 133–134 °C at 12 Torr [24]); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 400 MHz) δ: 2.33 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 7.06 (d, J = 8 Hz, 1H, 6-H), 7.11 (s, 1H, 2-H), 7.49 (d, J = 8, Hz, 1H, 5-H); ^{13}C NMR (in $CDCl_3$, 400 MHz) δ: 20.3 (CH_3), 23.5 (CH_3), 110.7 (SCN), 128.3, 129.0, 132.1, 132.6, 139.6, 140.7 (6 aromatic carbons); MS: *m*/*z* (%): M^+ 163 (100), 135 (90), 121 (15), 103 (20), 91 (20), 77 (25).

2.1.1.10. N,N-dimethyl-4-thiocyanatoaniline. Solid m.p. 70–72 °C (m.p. 72–74 °C [25]); IR: a sharp peak of thiocyanate group at 2147 cm^{-1}, 3452.5, 3010, 2942.5, 1615, 1510, 1367.5, 1112.5; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 3.02 (s, 6H, $N(CH_3)_2$), 6.68 (d, J = 9 Hz, 2H, 2-H, 6-H), 7.43 (d, J = 9 Hz, 2H, 3-H, 5-H); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 40.1 ($N(CH_3)_2$), 112.6 (SCN), 111.5, 114.6, 132.8, 136.1 (4 aromatic carbons); MS: *m*/*z* (%): M^+ 178 (100), 161 (15), 152 (20), 145 (35), 136 (13), 119 (13).

2.1.1.11. N-ethyl-4-thiocyanatoaniline. Solid m.p. 53–54 °C (m.p. 52–44 °C [26] IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 1.27 (t, J = 7.1 Hz, 3H, NCH_2CH_3), 3.16 (q, J = 7.2 Hz, 2H, NCH_2CH_3), 3.91 (s (broad), 1H, HN), 6.57 (d, J = 8.8 Hz, 2H, 2-H, 6-H), 7.43 (d, J = 9 Hz, 2H, 3-H, 5-H; ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 14.4 (NCH_2CH_3), 37.9 (NCH_2CH_3), 112.4 (SCN), 106.5, 113.4, 134.6, 150.0 (4 aromatic carbons); MS: *m*/*z* (%): M^+ 178 (45), 163 (100), 152 (10), 138 (10), 105 (15), 63 (10).

2.1.1.12. N-(4-thiocyanatophenyl)formamide. Oil (yellowish); IR: a sharp peak of thiocyanate group at 2155 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 6.74 (m), 7.16 (m), 7.36 (m), 7.54 (m), 7.64 (m) (ring H for the two forms), 8.4 (m), 8.7 (m) (for the two forms NHCHO); ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 111.9 (SCN), 113.7, 114.4, 114.5, 114.7, 120.0, 120.9, 120.1, 168.3, 169.1 (aromatic carbons, for the two forms); MS: *m*/*z* (%): M^+ 178 (100), 150 (30), 118 (40), 106 (10), 80 (12).

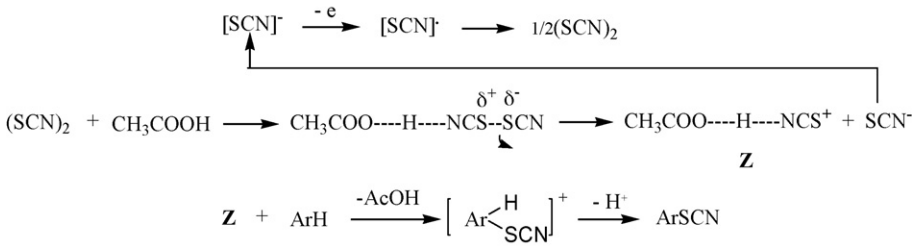
2.1.1.13. 1-Thiocyanatomethyl-2-methylbenzene. Oil; IR: a sharp peak of thiocyanate group at 2147 cm^{-1}; ^1H NMR (in $CDCl_3$, 200 MHz) δ: 2.42 (s, 3H, CH_3), 4.22 (s, 2H, CH_2SCN), 7.27–7.28 (m, 4H, ring protons), ^{13}C NMR (in $CDCl_3$, 200 MHz) δ: 18.9 (CH_3), 36.4 (CH_2SCN), 111.8 (SCN), 126.5, 129.2, 130.1, 131.2, 131.8, 136.7 (6 aromatic carbons); MS: *m*/*z* (%): M^+ 163 (5), 134 (3), 121 (3), 105 (100), 77 (20).

3. Results and discussion

Previously we have shown [21] that polar acidic solvents promote polarization of the S–S bond in the electrochemically generated thiocyanogen dimer $(SCN)_2$. The partial positively charged species could then attack aromatic substrates to yield the desired thiocyanation products, according to the mechanism outlined in Scheme 3.

It has been postulated that the reason for the selectivity of the thiocyanation of anisole to be both *regio*-selectivity (no *ortho* isomer) and *isomer*-selectivity (no isothiocyanate) could be attributed to the bulkiness and nature (it 'blocks' the nitrogen site), respectively, of the thiocyanation species 'Z' mentioned in Scheme 3. In addition, it is noteworthy that although the formal exhaustive electrolysis requires 1 F/mol NH_4SCN whereas in practice, 1.5–2 F have passed. As can be seen from Scheme 3, more electricity is consumed due to further oxidation of regenerated SCN^-.

In the present study, we have examined the *in situ* electrochemical thiocyanation of various aromatic compounds, including substituted methoxybenzenes and anilines in the presence of



Scheme 3. A plausible mechanism for electrochemical thiocyanation.

electrochemically generated thiocyanogen. The outcome of thiocyanation products emerged from the mono- and disubstituted aromatic substrates studied is summarized in Table 1. All substrates in entries 1–9 have peak potentials in the range of 1.35–2.2 V (vs. Ag/AgCl), well above the oxidation potential of the thiocyanate anion (~1 V vs. Ag/AgCl). As to the aniline derivatives in entries 10–12, see a relevant discussion later on. In general, the results indicate that a high *isomer*-selectivity was achieved because all products are exclusively thiocyanates with no formation of isothiocyanate isomers. This trend is in line with our previous observation in the case of anisole [21].

The electron density on the aromatic substituted ring plays an important role on the yield of the thiocyanation product. The presence of a strong electron-donating substituent such as a methoxy group, highly activates the aromatic ring to give a good yield of *para* substituted thiocyanate (Table 1, entry 1). However, the efficiency of the thiocyanation reaction decreases considerably when a weaker electron-donating substituent is employed (a methyl group, entry 2).

This finding could be accounted to the weak electrophilic nature of 'Z'.

In the case of disubstituted anisoles, the *para* position to one of the methoxy groups in 1,3-dimethoxybenzene is activated by both methoxy substituents towards an electrophilic attack. Therefore, as expected, of the three dimethoxybenzenes, the highest yield (74%) of the thiocyanate product has been obtained for this isomer (entry 3). However, in the case of 1,2-dimethoxybenzene, the *para* position is now activated by only one methoxy group (and deactivated by the other) and therefore, the yield of the thiocyanate product decreases (66%) (entry 4). For 1,4-dimethoxybenzene, the *para* position is occupied and all available *ortho* positions for electrophilic attack are activated and deactivated at the same time, in addition to the steric hindrance applied by the bulkiness of species 'Z'. As a result, a sharp decrease in the yield of the desired product (12%) (entry 5) takes place.

A similar trend should be expected for the three isomers of methylanisoles (entries 6–8), namely, when both substituents exert an inductive effect at two different sites of the aromatic nucleus, the more powerful activating group has a dominant influence, and that is why the thiocyanate group occupies the *para* position to the methoxy rather than to the methyl substituent in the case of *m*-methylanisole (entry 6). The same argument applies when the inductive effect of the two substituents opposes each other like in the case of *o*-methylanisole (entry 7).

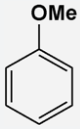
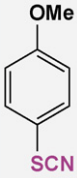
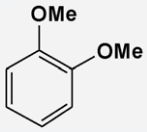
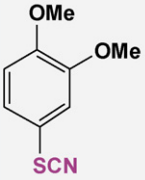
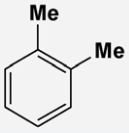
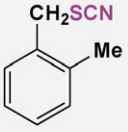
Surprisingly, the *ortho* isomer of methylanisole afforded a higher yield (60%) of the thiocyanate product compared to that obtained from the *meta* isomer (38%), in contrast to the trend observed for the corresponding dimethoxybenzene isomers. This result could be ascribed to the steric hindrance exerted by the methyl group at its *ortho* position (in addition to the bulkiness of 'Z' described in Scheme 3), which is not applicable in the case of 1,3-dimethoxybenzene (entry 3). It is noteworthy that the yield from each isomer (entries 6–8) is lower than that from the corresponding ones of the dimethoxybenzenes (entries 3–5). This outcome is attributed to the smaller activating effect of the methyl group with respect to the methoxy group (σ_p^+ values for methyl and methoxy groups are −0.31 and −0.78, respectively [27].

The observation that *m*-xylene gave a low yield of a thiocyanate product (13%, entry 9) with a complex mixture of side-chain products and parathiocyanogen $(SCN)_n$ suggests that intermediate 'Z' is a weak electrophile. In addition, the electrophilic thiocyanation process could be sensitive not only to the electron-donating ability of the substituent, but also to steric hindrance (Me vs. OMe). Therefore, stronger activating groups, or at least as strong as the methoxy substituent, are to be examined. Accordingly, amino substituents (σ_p^+ values for NH_2 and NMe_2 groups are −1.3 and −1.7, respectively) appear to be good candidates for this purpose. However, a drawback of their use stem from the fact that aniline, and its N-alkyl and N,N-dialkyl substituted derivatives are oxidized in the range of 0.7–1 V [28] and therefore, all compete with the oxidation of the thiocyanate anion. Consequently, for this very reason and others (e.g., transformation of the substrates to other types of products [29]), the yield of the thiocyanate products is not expected to be high. Indeed, N,N-dimethylaniline gave only 42% of p-SCN-$C_6H_4NMe_2$ (entry 10). In the case of aniline and N-ethylaniline (entries 11 and 12), in addition to the competition problem, both substrates undergo hydroformylation (whenever formic acid is present) presumably prior to thiocyanation, which cause the aromatic ring to be less susceptible towards an electrophilic attack. This further diminishes the yield of the desired products. Apparently, in both cases the major products were C_6H_4NHCOH and $C_6H_4N(Et)COH$, respectively. N-ethylaniline afforded only 15% of p-NCS-C_6H_4NHEt whereas aniline itself yielded 15% of the respective hydroformylated products, p-NCS-C_6H_4NHCOH (it is likely that the hydroformylation took place prior the initial thiocyanation reaction, causing a deactivation of the aromatic nucleus towards thiocyanation). Notably that thiocyanation of N-ethylaniline and toluidines was previously carried out under different experimental conditions (constant current, aqueous ethanol–HCl solution and low temperature) in a two-step reaction (first electrochemical generation of thiocyanogen and then addition of the substrate) afforded good yields (~60%) of the desired thiocyanation products [30].

Finally, it is noteworthy that whenever the yield of the thiocyanation product goes down, the yield of parathiocyanogen goes up, as evidenced by the color change in the solution (from colorless to pale yellow to yellow to orange).

Attempts to investigate the electrochemical thiocyanation process by carrying out electrolyses under constant current conditions are described in Table 2 for some selective examples. Whereas similar *regio*- and *isomer*-selectivities have been observed as in the use of the CPE technique, the reaction has certainly become less efficient now. Entries 1–3 are confined to anisole at different current densities but with the same electricity consumption. Clearly, the yield of the product *p*-thiocyanatoanisole increases (from 31 to 64%) with decreasing charge density (from 1 to 10 mA/cm^2). However, the low current density and duration (about 17 h) of electrolysis of 2 mmol of thiocyanate anion by consuming just 1.5 F/mol (entry 3) is far from being practical. With higher electricity con-

Table 2
Constant current electrochemical thiocyanation of anisole and some representative disubstituted aromatic derivatives[a].

Entry	Substrate	Product	Current density (mA/cm^2)	Charge (Coulombs) [F/mol]	Yield (%)
1			10	300 [1.5]	31
2			4	300 [1.5]	58
3			1	300 [1.5]	64
4			1	450 [2.25]	75
5			4	300 [1.5]	29
6			4	300 [1.5]	13

[a] In a mixture of acetic and formic acids (1:1), 0.1 M $LiClO_4$ employing Pt electrodes and a divided cell; 5 mmol substrate and 2 mmol NH_4SCN were used.

sumption (entry 4) the product's yield increases to 75% but again, about 26 h were required to get it. Anyway, just for comparison, *o*-dimethoxybenzene (entry 5) and *o*-xylene (entry 6) were electrolyzed under the same conditions used for anisole in entry 3, and the results show that the yield of products were 29% (ring-thiocyanation) and 13% (side-chain thiocyanation, respectively, considerably lower than what was achieved by controlled potential electrolysis for these substrates (Table 1). The lower yields could be attributed to the simultaneous oxidation of the substrate and the thiocyanate anion, which may lead to other types of products besides the thiocyanation of the aromatic nucleus.

4. Conclusions

An environmentally friendly electrochemical thiocyanation (that avoids the use of toxic oxidizing agents) of various aromatic compounds has been described. Electrochemical thiocyanation of monosubstituted aromatic compounds in acetic or formic acids was *regio*-selective (no *ortho* isomer was detected) and isomer selective (no isothiocyanate isomer was detected). However, the thiocyanation reaction was efficient only for anisole. In the case of disubstituted aromatic compounds, a high isomer-selectivity was found in organic acids because no isothiocyanate isomers were detected. The reaction has been found to be efficient when a methoxy group is the substituent. A stronger electron-donating substituents like an amine, N-alkyl- or N,N-dialkyl amines, cause the aromatic nucleus to compete with the oxidation of the thiocyanate anion, and as a result, the yield of the thiocyanation product decreased. From a preparative point of view, it has been found that the CPE technique employed for the electrochemical thiocyanation process is superior over constant current electrolysis.

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