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Effective metal-free electrooxidative thiocyanation of anilines

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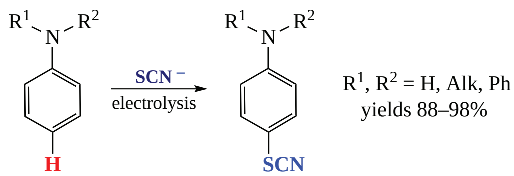
An original anodic C–H thiocyanation of anilines with NH_4SCN has been developed, allowing to obtain the products in 88–98% yields under potentiostatic diaphragm electrolysis on glassy carbon electrodes at E_{anode} = 0.60 V and moderate consumption of electricity. The preliminary voltammetric analysis included the assessment of the changes in the thiocyanate ion curve after the addition of aniline, as well as the measurements of the potentials of the reagents and products, which gave insight into mechanisms of the process (formation of thiocyanate radical and thiocyanogen) and was necessary for its optimization.



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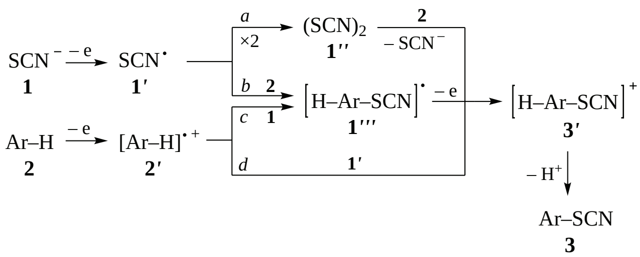
In recent years, the functionalization of aromatic C–H bonds has been developed using a cheap, affordable and environmentally promising electric current,[1–6] which is an attractive alternative to unrecyclable chemical oxidants[7,8] or metal catalysts.[9,10] In this regard, we are interested in the electrooxidative (anodic) C–H thiocyanation of arenes[11–21] including aniline derivatives.[11–15,17,20,21] The latter are the valuable structural components of pharmaceuticals[22] and dyes[23] while thiocyanato anilines have a pronounced antifungal activity.[17,24]

The currently documented electrosyntheses of thiocyanato anilines have certain disadvantages: the use of Pt electrodes,[11,13,14,20,21] impurities of dithiocyanates,[12] moderate or low yields,[11,12,15] or ~2–3-fold excess of electricity consumption.[12,14,20,21] In the latter two groups, the decomposition of anilines and (or) their thiocyanates could occur as a result of anodic oxidation (under galvanostatic electrolysis[12,14]) or cathodic reduction (in an undivided cell[11,12,14,15]).

Based on the above data, this work is devoted to the analysis of possible mechanisms of anodic thiocyanation of anilines, their study using cyclic voltammetry and the subsequent optimization of the electrolysis. According to developing original concepts,[1,6,13,15–19] the anodic C–H thiocyanation of arenes is carried out by the electrolysis of 'thiocyanate anion **1**/arene **2** mixture, which would proceed *via* the several probable mechanisms (Scheme 1) depending on the anodic potentials (E_p^{ox}) of arene **2** *vs.* thiocyanate ion **1** and on the conditions. The most common[11–21] is pathway *a*, involving the anodic generation of well-known[25–27] thiocyanogen **1′′**. The possibility of implementation of pathway *c* comprising radical cation **2′** (ECE mechanism) was also shown.[15,16,18,19]

However, it is not impossible to consider the reactions of thiocyanate radical **1′** with arene **2** (pathway *b*, the homolytic aromatic substitution[28]), or with radical cation **2′** (pathway *d*, EEC_rC_p mechanism[29]). For the thiocyanation of anilines, such pathways are equally probable due to the closeness of the anodic potentials (E_p^{ox}) of anilines and thiocyanate anion.[13] Accordingly, initial voltammetric studies were carried out, which made it possible to identify the most probable mechanisms of the process, to evaluate its efficiency, and to determine its optimal conditions.

At the first stage, curves of NH_4SCN **1**, aniline **2a**, 4-thiocyanatoaniline **3a**, and equimolar mixture of thiocyanate anion and aniline (Figure 1) were studied. On the one hand, after the addition of aniline **2a** to thiocyanate anion **1**, the cathodic peak B_1 (E_p^{red} = 0.34 V *vs.* SCE) of thiocyanogen disappeared [Figure 1(*a*), curves *2* (*3*) and *1*], which indicates[13,16,18,19] its consumption *via* pathway *a* with high rate (see Scheme 1). On the other hand, a significant growth (~33%) of the anodic peak A_1 of thiocyanate anion is observed for the first time (curves *2* and *1*), which is consistent with the oxidation of both thiocyanate anion **1** and radical **1′′′** in the course of pathway *b*. Moreover, the peak A_2 (E_p^{ox} = 0.92 V) of aniline **2a** significantly decreased (see



Scheme 1

† Deceased.

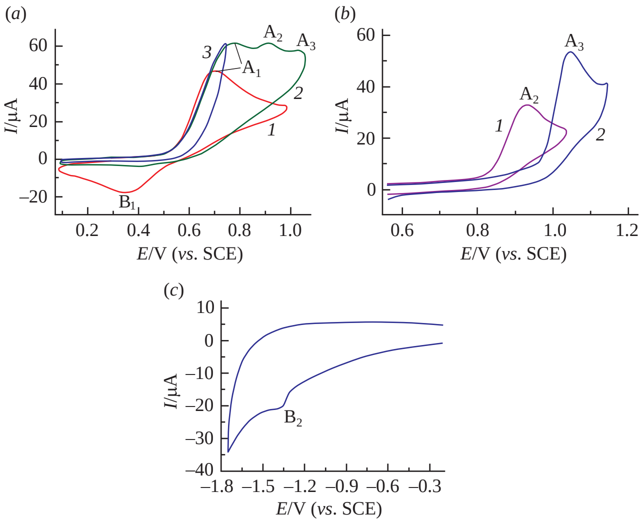


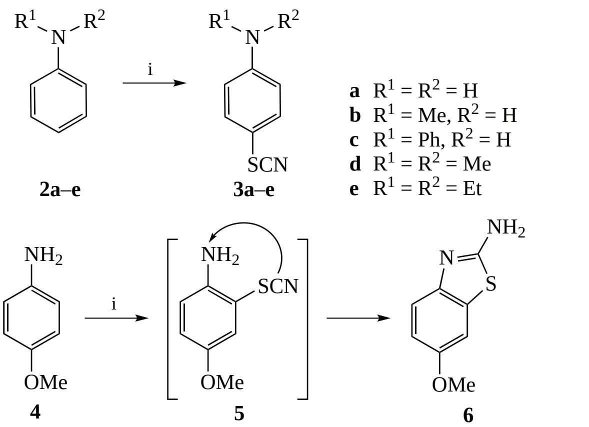
Figure 1 CV curves on glassy carbon working electrode, 0.1 M $NaClO_4$ in MeCN, $\nu = 0.10$ V s^{-1}. (*a*) Initial anodic scan for: (*1*) NH_4SCN **1** (0.002 M), (*2*) NH_4SCN **1**/aniline **2a** (1 : 1) mixture, (*3*) the same on the reverse scan from 0.75 V; (*b*) initial anodic scan for: (*1*) aniline **2a** (0.002 M), (*2*) 4-thiocyanatoaniline **3a** (0.002 M); (*c*) initial cathodic scan for 4-thiocyanatoaniline **3a** (0.002 M).

part *a*, curve *2* and part *b*, curve *1*), which is also consistent with pathways *a*, *b* and inconsistent with pathways *c*, *d*. Finally, curve *3* [see Figure 1(*a*)] shows the anodic peak A_3 of 4-thiocyanatoaniline **3a** (E_p^{ox} = 1.04 V, *cf.* part *b*, curve *2*), while part *c* shows the curve with its cathodic peak B_2 (E_p^{red} = –1.38 V). It is important to note that the irreversibility of peaks A_2, A_3, and B_2 most likely indicates the decomposition of aniline **2a** and 4-thiocyanatoaniline **3a** during anodic and cathodic processes, which should not be ignored.

At the second step, based on the above results and on E_p^{ox} of initial anilines **2a–e** and **4** and preliminary obtained[14,24,30] samples of target products **3a–e**, **6** (Scheme 2, Table 1), the C–H thiocyanation of anilines **2a–e**, **4** was carried out at the anodic potential (E_{anode}) of 0.60 V in a divided cell equipped with glassy carbon electrodes.[‡] Such E_{anode} and type of cell were chosen to slow down the possible decomposition of substrates or products on the electrodes. In cases of anilines **2a–e**, thiocyanation occurred at the *para*-position to afford products **3a–e** (see Scheme 2) in 88–98% yields. In the case of 4-methoxyaniline **4** with occupied *para*-position, aminothiazole **6** was obtained (yield 92%) as a result of heterocyclization of initially formed *ortho*-thiocyanato derivative **5**. The electricity consumption (Q) in all cases did not exceed the theoretical value (Q_t) more than 1.5 fold.

Note that diphenylamine **2c** selectively gave mono-thiocyanate **3c**, in contrast to the work[12] where the corresponding bis-thiocyanated product was formed, apparently, by electrooxidation of compound **3c** *via* pathways *c* and *d* (see Scheme 1) during the galvanostatic electrolysis. In addition, according to current and previous[19] results, the use of an undivided cell led to a decrease in yields by ~30–40% in all cases.

In conclusion, we carried out the complex of voltammetric investigations (see Figure 1), which made it possible not only to choose the most probable mechanisms of the electrooxidative (anodic) C–H thiocyanation of aniline and its derivatives, but also to evaluate the efficiency of the process and to determine the optimal conditions for its implementation. Accordingly, the original procedure was accomplished, involving the initial potentiostatic (E_{anode} = 0.60 V) electrogeneration of thiocyanate radical or thiocyanogen in the anodic compartment of a divided cell, followed by their effective interaction with arenes **2a–e**, **4** (see Schemes 1, 2 and Table 1). High yields (88–98%), moderate electricity consumption (Q/Q_t = 1–1.5), mild conditions, available materials, and valuable applied properties of the target products make the proposed method promising for the further use and development.



Scheme 2 *Reagents and conditions*: i, NH_4SCN (4 mmol), aniline **2a–e** or **4** (1 mmol), glassy carbon electrodes, divided cell, 0.1 M $NaClO_4$ in MeCN (85 ml), E_{anode} = 0.60 V (*vs.* SCE), Q/Q_t = 1–1.5 (Q_t = 194 C).

Table 1 Electrooxidative (anodic) C–H thiocyanation of anilines.

Aniline	E_p^{ox}/V	Q/Q_t	Product	E_p^{ox}/V	Yield (%)
2a	0.92	1	**3a**	1.04	88
2b	0.78	1	**3b**	0.99	98
2c	0.95	1.5	**3c**	1.07	97
2d	0.75	1	**3d**	0.98	94
2e	0.72	1.5	**3e**	0.96	96
4	0.61	1.5	**6**	0.67	92

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.01.030.

[‡] Electrolysis was carried out using potentiostat P30JM and 0.1 M solution of $NaClO_4$ in MeCN (85 ml) as supporting electrolyte in a glass temperature-controlled (25 °C) divided cell equipped with a tracing-paper diaphragm and glassy carbon electrodes (10 cm^2 anode and 3 cm^2 cathode). A solution of NH_4SCN (4 mmol) and aniline **2a–e**, **4a** (1 mmol) in the supporting electrolyte (70 ml) was placed into the anodic compartment, and the supporting electrolyte (15 ml) was placed into the cathodic compartment. The process was performed at E_{anode} = 0.60 V (*vs.* SCE) by passing 194–298 C of electricity. The anolyte was concentrated *in vacuo*, the residue was diluted with H_2O (15 ml) and extracted with CH_2Cl_2 (4 × 20 ml). The combined extracts were dried (Na_2SO_4), filtered and concentrated *in vacuo*. Column chromatography (SiO_2, CH_2Cl_2) gave pure products **3a–e**, **6a**, which were identical in their ^{1}H NMR and HRMS characteristics with the reported ones.[14,24,30]

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