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Electrooxidative C–H thiocyanation of hetarenes: voltammetric assessment of thiocyanogen reactivity

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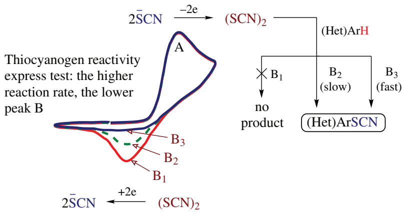
The height of thiocyanogen reduction peak on cyclic voltammograms of thiocyanate ion can serve as the criterion for thiocyanogen reactivity towards hetarenes present in the electrolyte. This allows one to predict the efficiency of anodic thiocyanation of various hetarenes.



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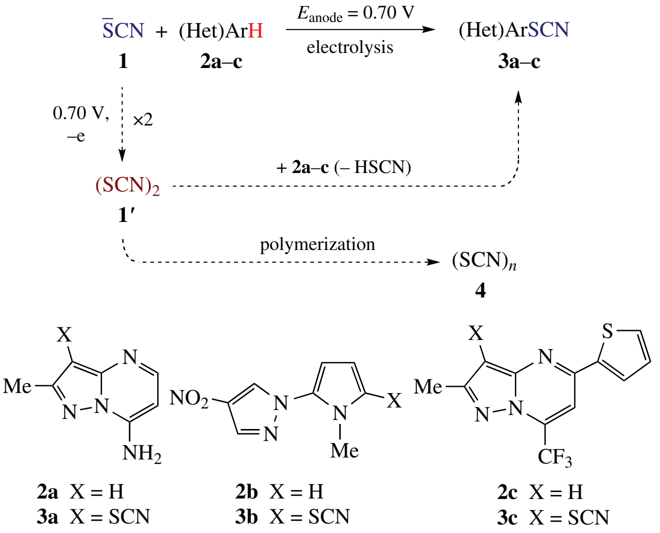
Direct C–H functionalization is the most popular methodology for modifying arenes to obtain a wide range of practically useful structures.[1] One of the most promising methods for this purpose is the electrooxidative (anodic) C–H (An) functionalization of arenes, with the anode serving as 'green oxidizing agent'.[2] Previously, we applied this approach for thiocyanation of various (het)arenes[3] *via* the electrogeneration of known[4] thiocyanogen $(SCN)_2$. Typically, the controlled potential electrolysis (CPE) of thiocyanate ion/(het)arene mixture was carried out in an undivided cell with Pt electrodes in MeCN at potential value corresponding to the oxidation peak of thiocyanate ion (E_p^{ox} = 0.70 V *vs*. SCE). This value was derived from cyclic voltammetry (CV) data.

Taking into account the data[5] and our concepts,[3(*b*),(*e*)] C–H (An) thiocyanation of aromatic systems proceeds according to Scheme 1. Electrooxidation (EO) of thiocyanate ion **1** at the stage **1** → **1′** leads to thiocyanogen **1′**. The latter either reacts with hetarenes **2a–c** at the stage **1′** → **3**, forming the target hetaryl thiocyanates **3a–c**, or would polymerize at the stage **1′** → **4** with the formation[6] of yellow sediment flakes.



Scheme 1

Earlier, we noted[3] that the higher oxidation potential (E_p^{ox}) of (het)arenes, the lower their reactivity towards thiocyanogen, and the efficiency of C–H (An) thiocyanation would drop. This prompted us to distinguish three arbitrary groups of (het)arenes in respect of their efficiency in thiocyanation depending on the 'proximity' of the E_p^{ox} (het)arene to the E_p^{ox} thiocyanate ion (0.70 V). Moreover, we expected that a comparison of the CV data[†] obtained in this work with the thiocyanation outcome in respect of readily and hardly oxidizable (het)arenes would help to derive CV criteria for the efficiency of the electrosynthesis.

Of the above three arbitrary groups of (het)arenes, group 1 includes the most reactive amino(het)arenes and alkyl(alkoxy) indoles[3(*b*)–(*e*)] having E_p^{ox} in the range ~1.0–1.3 V. A set of typical CV curves for this group describing the thiocyanation pattern using 2-methylpyrazolo[1,5-*a*]pyrimidin-7-amine **2a** as an example is shown in Figure 1. Curve *1* is a typical voltammogram of thiocyanate ion with peak A_1 (E_p^{ox} = 0.70 V) of its one-electron EO. The irreversibility of peak A_1 is caused by the thiocyanogen formation,[3(*b*),(*e*),5(*a*)] which is fixed on the reverse scan as the cathodic peak B_1 (E_p^{red} = 0.34 V). Peaks A_2 (E_p^{ox} = 1.10 V) and A_3 (E_p^{ox} = 1.35 V) correspond to EO of the initial hetarene **2a** and its thiocyanato product **3a** (see Figure 1).

[†] Cyclic voltammetry studies were performed in a 10 ml temperature-controlled (25 °C) glass cell under nitrogen using an Elins P30JM potentiostat. The scan rate was 0.10 V s^{-1}. A Pt disc 1 mm in diameter in a Teflon casing was used as the working electrode. A saturated calomel electrode (SCE) separated by a salt bridge filled with the supporting electrolyte (0.1 M $NaClO_4$ in MeCN) was used as the reference electrode. A Pt plate (S = 3 cm^2) was used as the counter electrode. The synthesis and some CV data for hetarenes **2a–c** of groups 1–3 were described in our previous works.[3]

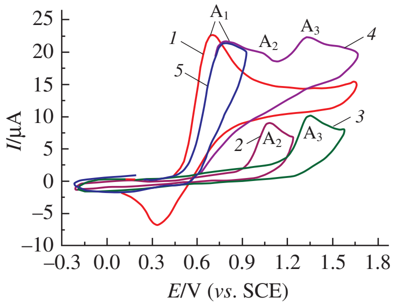


Figure 1 CV curves on Pt working electrode, 0.1 м $NaClO_4$ in MeCN, ν = 0.10 V s^{-1}: (*1*) NH_4SCN (0.002 м), (*2*) hetarene **2a** (0.002 м), (*3*) product **3a**, (*4*) NH_4SCN/**2a** mixture (1 : 1), (*5*) the same on the reverse scan from 0.90 V.

A characteristic voltammetric behaviour of (het)arenes from group 1 is the absence of the cathodic peak of thiocyanogen B_1 (E_p^{red} = 0.34 V) on the CV of their mixtures with thiocyanate ion. For example, after addition an equimolar amount of hetarene **2a** to the thiocyanate solution (see Figure 1, curve *4*), peak B_1 on the reverse scan completely disappears. At the same time, peak A_2 (EO of the initial hetarene) decreases and the peak A_3 (EO of the target aryl thiocyanate) grows (curve *4*). According to the mechanism given in Scheme 1, such results indicate that thiocyanogen and compound **2a** (stage **1′** → **3**) react quickly. This confirms the high (89%) yield of the target product during electrolysis at E_p^{ox} of thiocyanate ion.[3(*e*)] Note also that the peak B_1 on the reverse scan from 0.90 V (before the peak A_2 of studied hetarene, E_p^{ox} = 1.10 V) is absent (curve *5*). This eliminates other possible mechanisms (see below) for implementing the target process.

Group 2 includes the studied (het)arenes (E_p^{ox} ~ 1.30–1.70 V) with moderate reactivity. They are alkyl- or alkoxy-substituted 5- and 6-membered (het)arenes.[3] The key difference between the thiocyanation of the (het)arenes of group 2 from those of group 1 is that on the CV curve of the thiocyanate ion/(het)arene mixture peak B_1 (reduction of thiocyanogen) does not completely disappear, but only decreases; for example, peak B_1 on the CV curve of the 1 : 1 mixture of thiocyanate ion and 1-(1-methyl-1*H*-pyrrol-2-yl)-4-nitro-1*H*-pyrazole **2b** (Figure 2, curve *2*). This effect is also retained during reverse scan from 0.95 V (curve *3*). This indicates (see Scheme 1) the incomplete consumption of the electrogenerated thiocyanogen **1′** in the course of its reaction with hetarene **2** at stage **1′** → **3**. Curve *2* also has peak A_4 (E_p^{ox} = 1.43 V) of unreacted hetarene **2b** and peak A_5 (E_p^{ox} = 1.69 V) of the target product **3b**. Note that peak A_4 completely disappears only with the application of 5-fold excess of thiocyanate ion, but not with 2-fold one, like peak A_2 in Figure 1. This reflects a rather low reaction rate of thiocyanogen with (het)arenes from group 2. As a result, the thiocyanation of compound **2b** provides[3(*d*)] 48% yield of product **3b** (*cf.* 89% yield in the above case of **2a**[3(*e*)]).

Group 3 includes poorly reactive (het)arenes (E_p^{ox} > ~1.7 V). All of them (anisole,[3(*a*)] furan, thiophene,[3(*b*)] and pyrazolo[1,5-*a*]-pyrimidines with electron withdrawing substituents[3(*c*),(*e*)]) do not react with thiocyanogen or give trace amounts of thiocyanato products. To this, peak B_1 of thiocyanogen remained unchanged (Figure 3, *cf.* curves *1* and *2*) both on the CV of NH_4SCN and on the CV of the equimolar mixture of NH_4SCN and 2-methyl-5-thiophen-2-yl-7-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidine **2c** on reverse scan from 1.20 V (lower than peak A_6 of this hetarene, E_p^{ox} = 1.75 V).

Therefore, thiocyanogen practically does not react with the initial hetarene **2c**, which is also confirmed[3(*e*)] by the unsuccessful attempted preparative CPE at 0.70 V. At the reverse scan from 2.1 V (see Figure 3, curve *3*), peak B_1 became noticeably lower (*cf.* curves *3* and *5*) and a low-intensity peak A_7 (E_p^{ox} = 1.95 V) of the target product **3c** appeared. Moreover, CPE[3(*e*)] at the potential peak A_6 (E_p^{ox} = 1.75 V) of the initial arene EO resulted in an increase in the yield of the target aryl thiocyanate to 65%. All these data indicate the implementation of the EO process in a different way as compared to that in Scheme 1. Thus, thiocyanation of (het)arenes (E_p^{ox} = 1.70–1.90 V) of group 3 proved to be more effective during CPE at E_p^{ox} of (het)arene and implementing the possible ECE mechanism *via* the interaction between hetarene radical cation and thiocyanate ion.[3(*e*)]

The results of the studies showed that, in contrast to the E_p^{ox} values, a more objective and rigorous criterion for assigning (het)arenes to a particular group is the height of peak B_1 (thiocyanogen reduction current) on the CV of the equimolar mixture of the thiocyanate ion/(het)arene compared to peak B_1 on CV of thiocyanate ion of the same concentration (*e.g.*, *cf.* curves *4* and *1* in Figure 1). In this case, the current of peak B_1 on the CV of thiocyanate ion at given concentration is the limiting value (B_1^{lim}).

In this context, the group 1 should include (het)arenes that intensively interact with the thiocyanogen. For this assignment, now we have proposed not a roughly selected range of E_p^{ox} ~ 1.0–1.3 V, but a more stringent criterion. This is the absence of peak B_1 on the CV curves of thiocyanate ion/(het)arene mixtures (see, *e.g.*, Figure 1, curve *4*). Group 2 included (het)arenes with moderate reactivity. The criterion for their assignment to this group has also becomes more stringent, namely, the presence on the CV curves of (het)arenes (when recording the corresponding mixtures) of B_1 peaks different in height, but smaller than the peak B_1^{lim} (see, *e.g.*, Figure 2, curve *2*). Finally, group 3 includes non-reactive (het)arenes. In this case, the heights of peaks B_1 on the CV curves of the corresponding mixtures are the same and agree with the limit value B_1^{lim} (see, *e.g.*, Figure 3, curve *2*). Note also that for CV curves of mixtures of (het)arenes from groups 1 and 2 with thiocyanate ion, it is typical that disappearance or

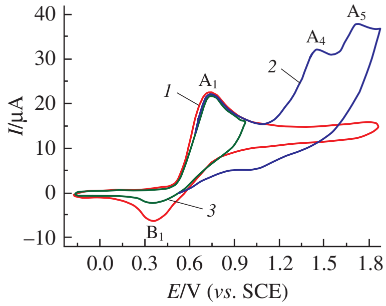


Figure 2 CV curves on Pt working electrode, 0.1 м $NaClO_4$ in MeCN, ν = 0.10 V s^{-1}: (*1*) NH_4SCN (0.002 м), (*2*) NH_4SCN/hetarene **2b** mixture (1 : 1), (*3*) the same on the reverse scan from 0.95 V.

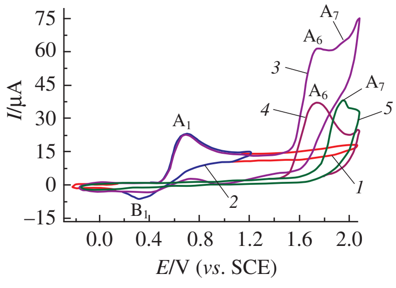


Figure 3 CV curves on Pt working electrode, 0.1 м $NaClO_4$ in MeCN, ν = 0.10 V s^{-1}: (*1*) NH_4SCN (0.002 м), (*2*) NH_4SCN/hetarene **2c** mixture (1 : 1) on the reverse scan from 1.20 V, (*3*) the same on the reverse scan from 2.10 V, (*4*) the initial hetarene, (*5*) its thiocyanation product.

diminution of the peaks B_1 is usually accompanied by disappearance or diminution of the anodic peaks of the initial (het)arenes and by the appearance of anodic peaks of the target products.

An analysis of the results of this and previous[3] studies leads to the conclusion that the possibility, effectiveness and the supposed mechanism of anodic C–H thiocyanation of (het)arenes with thiocyanate ion can be easily pre-tested by voltammetry *via* monitoring the heights of the cathodic peaks of thiocyanogen in the reaction mixtures. Thus, CV data make it possible to pre-optimize the procedure conditions, namely, to choose the proper potential of the electrosynthesis and consider some other parameters of the process.

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References

1 (*a*) V. N. Charushin and O. N. Chupakhin, *Russ. Chem. Bull., Int. Ed.*, 2019, **68**, 453 (*Izv. Akad. Nauk, Ser. Khim.*, 2019, 453); (*b*) H. M. L. Davies and D. Morton, *J. Org. Chem.*, 2016, **81**, 343; (*c*) H. M. L. Davies and D. Morton, *Angew. Chem., Int. Ed.*, 2014, **53**, 10256; (*d*) J. Yamaguchi, A. D. Yamaguchi and K. Itami, *Angew. Chem., Int. Ed.*, 2012, **51**, 8960.

2 (*a*) V. A. Petrosyan, *Mendeleev Commun.*, 2011, **21**, 115; (*b*) M. D. Karkas, *Chem. Soc. Rev.*, 2018, **47**, 5786; (*c*) Q.-L. Yang, P. Fang and T.-S. Mei, *Chin. J. Chem.*, 2018, **36**, 338; (*d*) S. R. Waldvogel, S. Lips, M. Selt, B. Riehl and C. J. Kampf, *Chem. Rev.*, 2018, **118**, 6706.

3 (*a*) A.V. Burasov and V. A. Petrosyan, *Russ. Chem. Bull., Int. Ed.*, 2008, **57**, 1321 (*Izv. Akad. Nauk, Ser. Khim.*, 2008, 1296); (*b*) V. A. Kokorekin, V. L. Sigacheva and V. A. Petrosyan, *Tetrahedron Lett.*, 2014, **55**, 4306; (*c*) V. A. Kokorekin, R. R. Yaubasarova, S. V. Neverov and V. A. Petrosyan, *Mendeleev Commun.*, 2016, **26**, 413; (*d*) R. R. Yaubasarova, V. A. Kokorekin, G. V. Ramenskaya and V. A. Petrosyan, *Mendeleev Commun.*, 2019, **29**, 334; (*e*) V. A. Kokorekin, R. R. Yaubasarova, S. V. Neverov and V. A. Petrosyan, *Eur. J. Org. Chem.*, 2019, 4233.

4 (*a*) R. G. Guy, in *Cyanates and Their Thio Derivatives*, ed. S. Patai, John Wiley & Sons, New York, 1977, vol. 2, pp. 819–886; (*b*) J. L. Wood, in *Organic Reactions*, ed. R. Adams, John Wiley & Sons, New York, 1946, vol. 3, pp. 240–266.

5 (*a*) G. Cauquis and G. Pierre, *C. R. Acad. Sci., Ser. C*, 1971, **272**, 609; (*b*) A. Gitkis and J. Y. Becker, *Electrochim. Acta*, 2010, **55**, 5854; (*c*) L. Fotouhi and K. Nikoofar, *Tetrahedron Lett.*, 2013, **54**, 2903; (*d*) X. Zhang, C. Wang, H. Jiang and L. Sun, *RSC Adv.*, 2018, **8**, 22042.

6 F. Cataldo, *J. Inorg. Organomet. Polym.*, 1997, **7**, 35.

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