EurJOC

European Journal of Organic Chemistry

Chemistry Europe

European Chemical Societies Publishing

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202100647

Link to VoR: https://doi.org/10.1002/ejoc.202100647

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10.1002/ejoc.202100647

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FULL PAPER

Xanthates as thiol surrogates for nucleophilic substitution with aryl halides

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http://www.ibch.ru/en/structure/groups/heterocyclic

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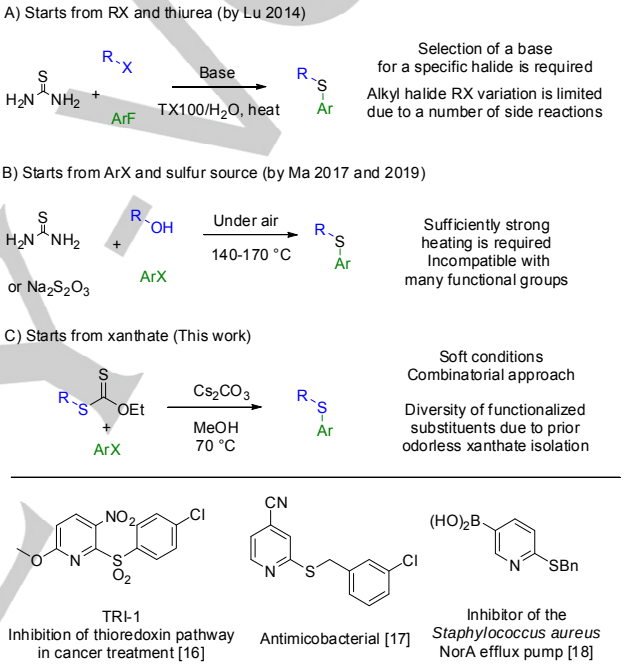
Abstract: We herein report an unprecedented xanthate-based protocol for the preparation of aryl-alkyl thioethers. Heating xanthates with aryl halides and namely cesium carbonate in methanol provides the target thioethers in generally good yields within short reaction times. This method allows one to avoid contact with odorous thiols and also to introduce substituents of which the corresponding thiols are virtually unavailable or inconvenient in use.

Introduction

Being the sixteenth most abundant element in the earth's crust and eighth most abundant element in the human body, sulfur significantly contributes to a diversity of organic chemistry. A number of organosulfur compounds are found naturally and demonstrate a wide range of biological properties. In this regard, designing novel approaches to arranging C-S bond in various organic compounds is a key challenge in the modern organic synthesis. Formation of a C-S bond in aromatic substrates is provided by a variety of metal-catalyzed methods,[1] although the direct nucleophilic substitution with thiols remains important once the reaction proceeds on an activated substrate. Generally, a thiol partner needs to be synthesized, which can be achieved by a number of synthetic approaches to thiols created. Most of them are associated with the use thioacids,[2] thiourea,[3] and other related compounds including xanthates and $Na_2S_2O_3$.[4] As a drawback, low- and medium molecular weight thiols are toxic, [5] and notorious for their extremely unpleasant odors, what makes the search for thiol surrogates an urgent task.

Thereby, reactions of aromatic nucleophilic substitution without the isolation of thiols have become more popular. Thiourea is a general reagent of choice in this case,[6] coupled with aryl halides and alkyl halides [7] or even alcohols[8](Scheme 1). Such protocols benefit from one-pot mixing three reagents, being almost odorless and fulfilling requirements of green chemistry, despite harsh conditions are required.



Scheme 1. Methods for thioether synthesis that do not require isolation of thiols. Examples of bioactive aryl-thioethers and their derivatives.

In this article, we would like to demonstrate that various xanthates can also be used for this purpose under much milder conditions. Although an extra step of xanthate synthesis is thus added, much greater scope of the reaction partners is expected. Unlike thiourea derivatives, xanthates can be obtained from a wide variety of halides (as well mesylates, tosylates, etc[9], including very inactive ones) by nucleophilic substitution,[10] from aromatic diazonium salts by ion-radical reaction,[11] from C-H acids and organometallic reagents by electrophilic xanthylation,[12] or even by direct C-H activation of alkanes.[13] Moreover, given the extensively explored by Prof. Samir Zard area of the xanthate radical addition across the double bond,[4b, 14] virtually any aliphatic xanthate is now available. Xanthates are almost odorless, bench-stable and provide thiols under relatively mild basic conditions.[15]

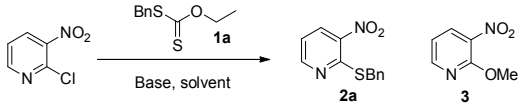
In this work, we have shown that, in the case of nucleophilic substitution in aromatic halides, xanthate can be used as thiol surrogates in the presence of cesium carbonate in methanol.

10.1002/ejoc.202100647

Results and Discussion

In the course of work on the preparation of thio derivatives, we found that heating of the mixture of a xanthates, 2-chloro-3-nitropyridine and a base in isopropanol leads to formation of a corresponding aryl-thioethers. Earlier, a similar reaction with potassium hydroxide in methanol was shown, but it was used only for intramolecular conversion, only in one example, and its yield turned out to be very low.[4b] Thus, we studied this transformation in more detail and showed (Table 1) that the best result can be achieved when cesium carbonate in methanol is used. Under optimized conditions, a non-target alkoxy derivative is formed in a minimal amount, and the yield of the target thioether is maximal. Probably, good solubility of cesium carbonate in methanol accounts for effective methoxide formation and subsequent xanthate alcoholysis.

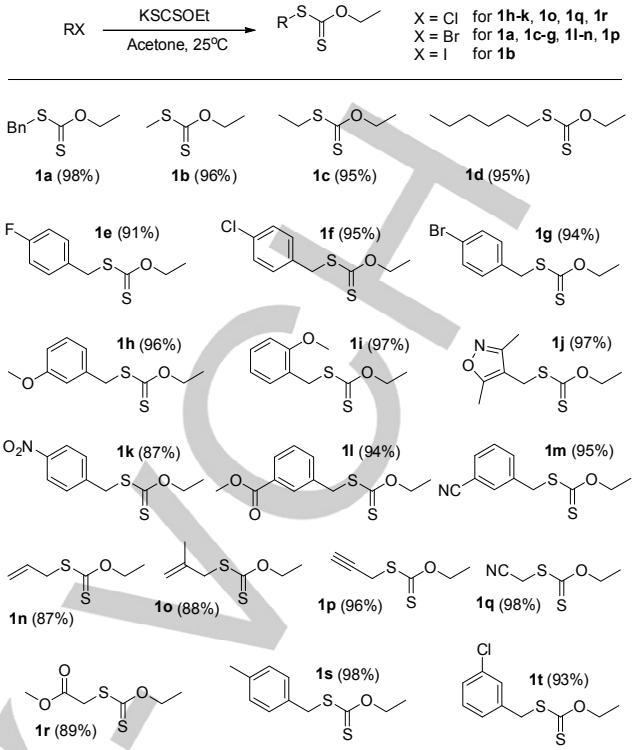
Table 1. Optimization of the reaction conditions



Entry	Solvent	Time	Base	Temp.	Result[b]
1	iPrOH	2 h	K_2CO_3	80 °C	Conversion<50%
2	EtOH	2 h	K_2CO_3	80 °C	Conversion<50%
3	MeOH	2 h	K_2CO_3	70 °C	**2a** 65%, **3** 20%
4	iPrOH	2 h	Cs_2CO_3	80 °C	**2a** 60%, numerous by-products
5	EtOH	2 h	Cs_2CO_3	80 °C	**2a** 40%, numerous by-products
6	MeOH	2 h	Cs_2CO_3	70 °C	**2a** 85%, **3** 5%
7	MeOH	24 h	Cs_2CO_3	25 °C	Conversion<50%
8	CH_3CN	2 h	Cs_2CO_3	70 °C	Conversion<10%
9	CH_3CN+water	2 h	Cs_2CO_3	70 °C	Complex mixture
10	water	2 h	Cs_2CO_3	70 °C	Complex mixture

[a] Reaction conditions: 1 mmol of 2-chloro-3-nitro-pyridine, 1.2 mmol of **1a**, 1.3 mmol of a base and 3 ml of corresponding solvent. [b] NMR determined.

Next, we carried out the synthesis of an extended series of xanthates **1**. The synthesis was performed using the classical approach employing potassium xanthate and halides in acetone. The yields for such a transformation were often almost quantitative (Scheme 2). Isolation of substances did not require complex column purification. Filtration through a short pad of silica was sufficient to achieve more than 90% purity, which was satisfactory for the next stage.



Scheme 2. Synthesis of xanthates.

The reaction of these xanthates with 2-chloro-3-nitropyridine proceeded in high yields in almost all cases (Scheme 3). Using this approach, we synthesized a thiomethyl derivative **2b**, which otherwise requires the use of gaseous methylthiol, and cyanomethyl derivative **2r**, for which the corresponding thiol does not exist at all. Reaction yields are decreased for allyl, metallyl, caroboxymethyl and cyanomethyl derivatives. Probably, these substrates underwent certain side reactions under the basic medium. Due to the similar reason, the yield turned out to be extremely low in case of propargyl and nitrobenzyl derivatives. In these cases we were unable to isolate the target products from the obtained mixture.

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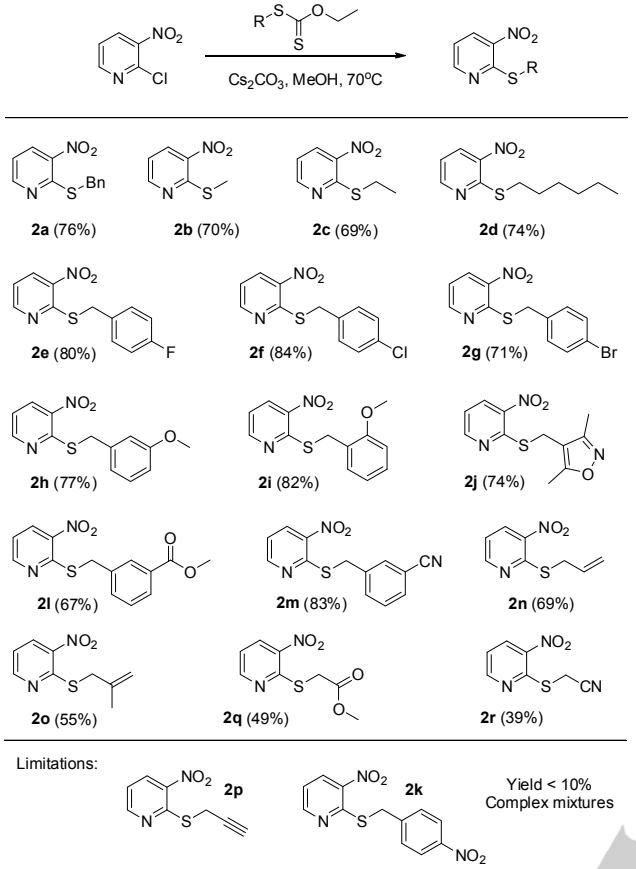
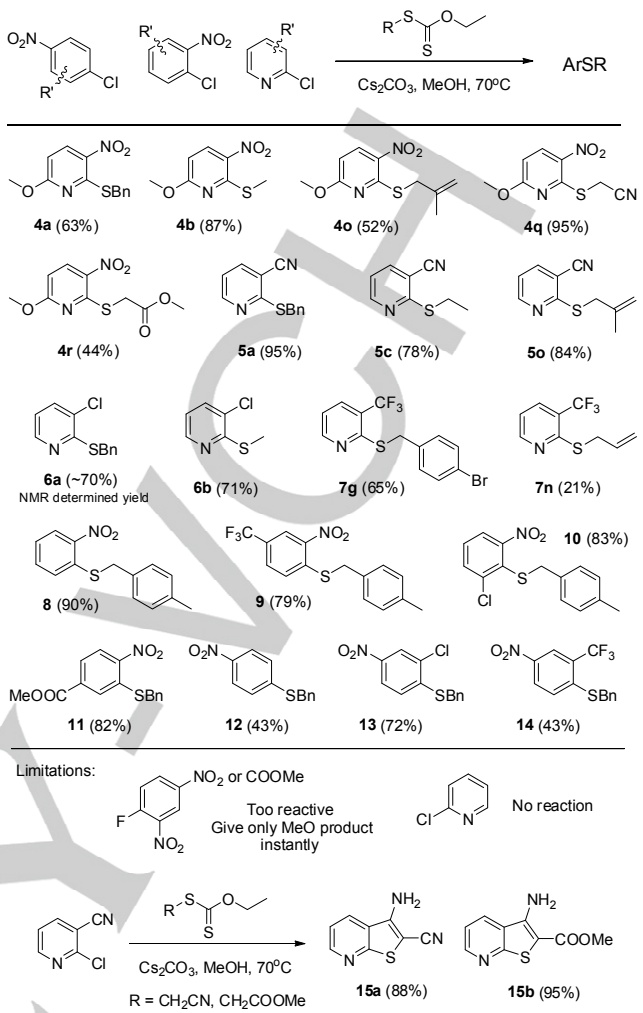


Scheme 3. Scope of 2-chloro-3-nitro-pyridine reaction with various xanthates.

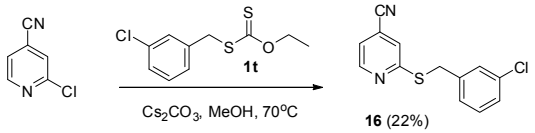
The next step, we expanded the scope of the activated aryl halides, including simple *o*- and *p*-chloronitrobenzenes (Scheme 4). We showed that proposed technique can be used for less active derivatives, but it required prolonged reaction time (up to 40 hours).



Scheme 4. Scope of various aryl halides reaction.

The limitations of the approach are bound by the active aryl halides (e.g., dinitrofluorobenzene), which react with methanol readily before the S-nucleophile is released. In addition, less reactive 2-chloropyridine cannot be involved in the reaction, since methanol media cannot maintain sufficient temperature for the reaction to begin. Meanwhile, the reaction with functionalized xanthates **1q** and **1r** does not stop after the nucleophilic substitution step for 2-chloro-nicotinonitrile. In this case, 3-aminothieno[2,3-*b*]pyridines **15** are obtained in good yields. Although this condition could be regarded as the limitation of the devised protocol, such substances otherwise are available through more sophisticated pathways according to literature procedures and used for the further synthesis of many important biologically active compounds.[19]

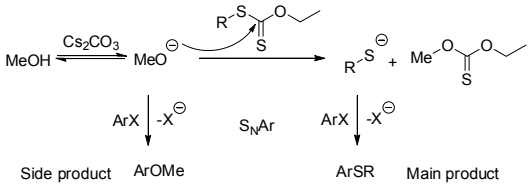
We also have shown that the approach proposed by us can be used for the synthesis of the above-mentioned (Scheme 1) antimicobacterial compounds on example of compound **16**,[17] although this specific reaction may require further optimization (Scheme 5).



Scheme 5. Scale-up experiments and bio-active compound synthesis

The proposed reaction set-up is almost odorless, except for the cases of less active substrates, or incomplete reaction when formation of thiols and disulfides is clearly observed. This

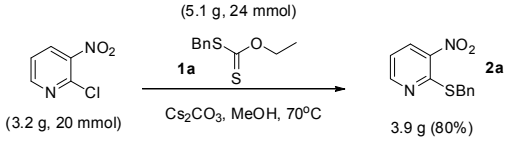
confirms that the above-described process is likely to proceed *via* cesium thiolate formation (Scheme 6).



Scheme 6. Proposed reaction mechanism

Nevertheless, reaction workup consists only of evaporation and immediate column purification. This technology minimizes contacts with an unpleasant odor since thiols are in a non-volatile anionic form all the time.

Finally we performed the scale-up experiment using 2-chloro-3-nitropyridine and xanthate **1a** (Scheme 7, SI). The yields of reaction even slightly increase upon increase of scale.



Scheme 7. Scale-up experiment

Conclusion

Thus, in this paper, we proposed a new protocol for the synthesis of aryl-alkyl thioethers. The novelty of the protocol consists in the use of S-alkylated xanthates, which acts as the thiol surrogates. The joint heating of xanthates, arylhalides and caesium carbonate in methanol leads to the formation of aryl-thioethers in high yield. This technique allows avoiding contact with unpleasant thiol odors and also introducing substituents of which the corresponding thiols are hardly obtainable, gaseous, or do not exist at all.

Experimental Section

General Considerations: Commercially available reagents were used without additional purification. E. Merck Kieselgel 60 was used for column chromatography. Thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} glass-backed plates (MERCK). Visualization was performed using UV light (254 or 312 nm) and staining with $KMnO_4$. NMR spectra were recorded on a 700 MHz Bruker Avance III NMR at 303°K, Avance III 800 (with a 5-mm CPTXI cryoprobe) and Bruker Fourier 300. Chemical shifts are reported relative to residue peaks of $CDCl_3$ (7.27 ppm for ^{1}H and 77.0 ppm for 13C) or DMSO-d_6 (2.51 ppm for ^{1}H and 39.5 ppm for ^{13}C). Melting points were measured on a SMP 30 apparatus without correction. High-resolution mass spectra (HRMS) spectra were recorded on AB Sciex TripleTOF® 5600+ System using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage – 5500 V); mass range from m/z 50 to m/z 3000; external or internal calibration was done with ESI Tuning Mix, Agilent. A syringe injection was used for solutions in acetonitrile, methanol, or water (flow rate 20 µl/min). Nitrogen was applied as a dry gas; interface temperature was set at 180°C. Elemental analysis was performed on vario MICRO Cube (Elementar), these data are presented only for hardly ionisable compounds, for which HRMS data were insufficient – compounds **9**, **10**, **12-14**. IUPAC compound names were generated using ChemDraw Software.

General procedure for the synthesis of S-substituted-O-ethyl-carbonodithioates (xanthates 1): Potassium ethyl xanthate (3.84 g, 24 mmol) was dissolved in acetone (100 mL). A corresponding halide (20 mmol) was added to the solution. The resulting mixture was stirred at room temperature for 4 hours (in case of allyl, propargyl, and benzyl halides) or 24 hours (in case of alkyl halides). The solvent was evaporated; EtOAc (100 mL) and water (30 mL) were added. The mixture was shaken untill all solids dissolved. Water phase was discarded and organic phase was washed with brine (3x30 mL). The solution was dried over Na_2SO_4. The solvents were removed under reduced pressure. The crude product was dissolved in EtOAc (20 mL) and filtered through a pad of silica gel (approx. 20 mL). The silica gel pad was additionally washed with EtOAc (50 mL). The solvent was evaporated to afford desired xanthates with 90%+ purity in almost quantitative yields. This purity was found to be suitable for the next step. Moreover, deeper purification (column chromatography engaging weakly polar eluents) leads to considerable losses of the product and does not always significantly increase the purity.

Preparation of the xanthates **1a**,[20] **1b**,[21] **1c**,[22] **1d**,[13] **1f**,[23] **1k**,[24] **1n**,[25] **1p**,[26] **1q**,[27] **1r**[27] asd **1s**,[23] have already been described in the literature.

***S*-benzyl *O*-ethyl carbonodithioate (1a)**.[20] Light yellowish oil (4.16 g, 98%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.38 (d, *J*=7.4 Hz, 2H), 7.33 (t, *J*=7.4 Hz, 2H), 7.27 (t, *J*=7.3 Hz, 1H), 4.63 (q, *J*=7.3 Hz, 2H), 4.40 (s, 2H), 1.35 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.1, 135.9, 128.9, 128.4, 127.3, 70.2, 39.2, 13.4; HRMS (ESI): m/z calcd for $C_{10}H_{13}OS_2^+$: 213.0402 [M+H]$^+$; found: 213.0401.

***O*-ethyl *S*-methyl carbonodithioate (1b)**.[21] Light yellowish oil (2.62 g, 96%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.63 (q, *J*=7.1 Hz, 2H), 2.55 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=215.3, 70.0, 18.4, 13.5; HRMS (ESI): m/z calcd for $C_4H_9OS_2^+$: 137.0089 [M+H]$^+$; found: 137.0091.

***O*-ethyl *S*-ethyl carbonodithioate (1c)**.[22] Light yellowish oil (2.85 g, 95%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.63 (q, *J*=7.1 Hz, 2H), 3.11 (q, *J*=7.4 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H), 1.27 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=214.2, 69.8, 29.4, 13.5, 13.4; HRMS (ESI): m/z calcd for $C_5H_{11}OS_2^+$: 151.0246 [M+H]$^+$; found 151.0249.

***O*-ethyl *S*-hexyl carbonodithioate (1d)**. Light yellowish oil (3.92 g, 95%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.63 (q, *J*=7.1 Hz, 2H), 3.11 (t, *J*=7.4 Hz, 2H), 1.65-1.59 (m, 2H), 1.38-1.33 (m, 5H), 1.30-1.23 (m, 4H), 0.86 (q, *J*=7.4 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=214.3, 69.8, 35.1, 30.7, 28.0, 27.9, 21.9, 13.7, 13.4; HRMS (ESI): m/z calcd for $C_9H_{19}OS_2^+$: 207.0872 [M+H]$^+$; found: 207.0875.

***O*-ethyl *S*-4-fluorobenzyl carbonodithioate (1e)**. Light yellowish oil (4.19 g, 91%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.45-7.39 (m, 2H), 7.16 (t, *J*=8.8 Hz, 2H), 4.63 (q, *J*=7.1 Hz, 2H), 4.39 (s, 2H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.0, 161.4 (d, *J*=243.6 Hz), 132.2, 130.9 (d, *J*=8.2 Hz), 115.2 (d, *J*=21.6 Hz), 70.2, 38.3, 13.4; HRMS (ESI): m/z calcd for $C_{10}H_{12}FOS_2^+$: 231.0308 [M+H]$^+$; found: 231.0307.

***O*-ethyl *S*-4-chlorobenzyl carbonodithioate (1f)**.[23] Light yellowish oil (4.68 g, 95%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.42-7.37 (m, 4H), 4.62 (q, *J*=7.1 Hz, 2H), 4.39 (s, 2H), 1.35 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d6) δ=212.8, 135.2, 132.0, 130.7, 128.3, 70.3, 38.3, 13.4; HRMS (ESI): m/z calcd for $C_{10}H_{12}ClOS_2^+$: 247.0013 [M+H]$^+$; found: 247.0009.

***O*-ethyl *S*-4-bromobenzyl carbonodithioate (1g)**. Yellow solid (5.47 g, 94%); M.p 28-29°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.52 (d, *J*=8.4 Hz, 2H), 7.33 (d, *J*=8.4 Hz, 2H), 4.62 (q, *J*=7.1 Hz, 2H), 4.37 (s, 2H), 1.34 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.7, 135.6, 131.2, 131.0, 120.5, 70.3, 38.3, 13.4; HRMS (ESI): m/z calcd for $C_{10}H_{12}BrOS_2^+$: 290.9507 [M+H]$^+$; found: 290.9509.

***O*-ethyl *S*-3-methoxybenzyl carbonodithioate (1h)**. Light yellowish oil (4.65 g, 96%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.25 (t, *J*=8.2 Hz, 1H),

6.96-6.92 (m, 2H), 6.85 (brd, *J*=7.4 Hz, 1H), 4.63 (q, *J*=7.1 Hz, 2H), 4.37 (s, 2H), 3.74 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.1, 159.2, 137.3, 129.5, 121.1, 114.5, 112.8, 70.2, 54.9, 39.2, 13.4; HRMS (ESI): m/z calcd for $C_{11}H_{15}O_2S_2^+$: 243.0508 [M+H]$^+$; found: 243.0504.

***O*-ethyl *S*-2-methoxybenzyl carbonodithioate (1i)**. Light yellowish oil (4.70 g, 97%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.35 (brd, *J*=7.5 Hz, 1H), 7.29 (brt, *J*=8.0 Hz, 1H), 7.02 (d, *J*=8.0 Hz, 1H), 6.91 (t, *J*=7.4 Hz, 1H), 4.64 (q, *J*=7.1 Hz, 2H), 4.33 (s, 2H), 3.81 (s, 3H), 1.37 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.7, 157.1, 130.3, 129.2, 123.2, 120.1, 110.8, 70.0, 55.4, 34.6, 13.4; HRMS (ESI): m/z calcd for $C_{11}H_{15}O_2S_2^+$: 243.0508 [M+H]$^+$; found: 243.0507.

***S*-((3,5-dimethylisoxazol-4-yl)methyl) *O*-ethyl carbonodithioate (1j)**. Light yellowish oil (4.49 g, 97%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.67 (q, *J*=7.2 Hz, 2H), 4.22 (s, 2H), 2.39 (s, 3H), 2.19 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.8, 166.7, 159.0, 108.4, 70.3, 27.4, 13.5, 10.8, 9.7; HRMS (ESI): m/z calcd for $C_9H_{14}NO_2S_2^+$: 232.0460 [M+H]$^+$; found: 232.0458.

***S*-4-nitrobenzyl *O*-ethyl carbonodithioate (1k)**.[24] Yellow solid (4.47 g, 87%); m.p. 61-63°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.20 (d, *J*=8.8 Hz, 2H), 7.67 (d, *J*=8.8 Hz, 2H), 4.62 (q, *J*=7.1 Hz, 2H), 4.53 (s, 2H), 1.34 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.4, 146.6, 144.6, 130.1, 123.5, 70.6, 38.1, 13.4; HRMS (ESI): m/z calcd for $C_{10}H_{12}NO_3S_2^+$; 258.0253 [M+H]$^+$; found: 258.0250.

Methyl 3-(((ethoxycarbonothioyl)thio)methyl)benzoate (1l). Light yellowish oil (5.08 g, 94%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.99 (brs, 1H), 7.85 (brd, *J*=7.8 Hz, 1H), 7.66 (brd, *J*=7.6 Hz, 1H), 7.49 (t, *J*=7.6 Hz, 1H), 4.61 (q, *J*=7.1 Hz, 2H), 4.47 (s, 2H), 3.85 (s, 3H), 1.35 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.7, 165.8, 137.1, 133.6, 129.8, 129.6, 128.7, 128.0, 70.3, 51.9, 38.5, 13.3; HRMS (ESI): m/z calcd for $C_{12}H_{15}O_3S_2^+$: 271.0457 [M+H]$^+$; found: 271.0457.

***S*-3-cyanobenzyl *O*-ethyl carbonodithioate (1m)**. White solid (4.51 g, 95%); m.p. 69-71°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.84 (brs, 1H), 7.76-7.12 (m, 2H), 7.55 (t, *J*=7.8 Hz, 1H), 4.61 (q, *J*=7.1 Hz, 2H), 4.44 (s, 2H), 1.34 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.6, 138.3, 133.8, 132.5, 131.1, 129.6, 118.5, 111.4, 70.5, 38.0, 13.4; HRMS (ESI): m/z calcd for $C_{11}H_{12}NOS_2^+$: 238.0355 [M+H]$^+$; found: 238.0350.

***S*-allyl *O*-ethyl carbonodithioate (1n)**.[25] Light yellowish oil (2.82 g, 87%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=5.58 (ddt, *J*=17.0, 9.9, 6.9 Hz, 1H), 5.31 (brd, *J*=17.0 Hz, 1H), 5.17 (brd, *J*=9.9 Hz, 1H), 4.63 (q, *J*=7.1 Hz, 2H), 3.81 (brd, *J*=6.9 Hz, 2H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.2, 132.0, 118.8, 70.1, 37.7, 13.4; HRMS (ESI): m/z calcd for $C_6H_{11}OS_2^+$: 163.0246 [M+H]$^+$; found: 163.0245.

***O*-ethyl *S*-(2-methylallyl) carbonodithioate (1o)**. Light yellowish oil (3.10 g, 88%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=5.01 (brs, 1H), 4.90 (brs, 1H), 4.62 (q, *J*=7.1 Hz, 2H), 3.82 (s, 2H), 1.76 (s, 3H), 1.36 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.4, 139.3, 114.7, 70.1, 41.8, 21.0, 13.4; HRMS (ESI): m/z calcd for $C_7H_{13}OS_2^+$: 177.0402 [M+H]$^+$; found: 177.0405.

***O*-ethyl *S*-prop-2-yn-1-yl carbonodithioate (1p)**.[26] Light yellowish oil (3.07 g, 96%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.66 (q, *J*=7.1 Hz, 2H), 3.97 (d, *J*=2.7 Hz, 2H), 3.21 (t, *J*=2.7 Hz, 1H), 1.37 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=211.7, 78.3, 73.9, 70.5, 23.6, 13.4; HRMS (ESI): m/z calcd for $C_6H_9OS_2^+$: 161.0089 [M+H]$^+$; found: 161.0091.

***S*-(cyanomethyl) *O*-ethyl carbonodithioate (1q)**.[27] Light yellowish oil (3.16 g, 98%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.70 (q, *J*=7.2 Hz, 2H), 4.26 (s, 2H), 1.40 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=209.8, 116.6, 71.3, 20.8, 13.3; HRMS (ESI): m/z calcd for $C_5H_8NOS_2^+$: 162.0042 [M+H]$^+$; found: 162.0045.

Methyl 2-((ethoxycarbonothioyl)thio)acetate (1r).[27] Light yellowish oil (3.46 g, 89%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=4.61 (q, *J*=7.1 Hz, 2H), 4.06 (s, 2H), 3.67 (s, 3H), 1.34 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.6, 168.1, 70.7, 52.4, 36.9, 13.4; HRMS (ESI): m/z calcd for $C_6H_{11}O_3S_2^+$: 195.0144 [M+H]$^+$; found: 195.0149.

***O*-ethyl S-4-methylbenzyl carbonodithioate (1s)**.[23] Light yellowish solid (4.44 g, 98%); m.p. 24-26°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.25 (d, *J*=8.0 Hz, 2H), 7.13 (d, *J*=8.0 Hz, 2H), 4.63 (q, *J*=7.3 Hz, 2H), 4.35 (s, 2H), 2.27 (s, 3H), 1.36 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=213.3, 136.6, 132.7, 129.0, 128.8, 70.1, 39.0, 20.6, 13.4; HRMS (ESI): m/z calcd for $C_{11}H_{15}OS_2^+$: 227.0559 [M+H]$^+$; found: 227.0559.

***O*-ethyl *S*-3-chlorobenzyl carbonodithioate (1t)**. Light yellowish oil (4.58 g, 93%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.46 (brs, 1H), 7.38 – 7.32 (m, 3H), 4.62 (q, *J*=7.1 Hz, 2H), 4.40 (s, 2H), 1.35 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=212.8, 139.0, 132.9, 130.3, 128.8, 127.7, 127.3, 70.5, 38.2, 13.5; HRMS (ESI): m/z calcd for $C_{10}H_{12}ClOS_2^+$: 247.0013 [M+H]$^+$; found: 247.0002.

General procedures for the synthesis of compounds 2-15: A corresponding 2-chloro-pyridine (2 mmol), cesium carbonate (850 mg, 2.6 mmol), a corresponding xanthate (2.4 mmol) and methanol (6 ml) were mixed in a screw-capped tube. The mixture was stirred for 1-1.5 hours (for 3-nitro, 3-cyano pyridines and nitrobenzenes) or 10-40 hours (for less active 3-chloro and 3-trifluoromethyl pyridines) at 70°C in the oil bath. Reaction progress was monitored by TLC (eluent – EtOAc/hexane, 1:10). After the complete consumption of starting 2-chloro-pyridine or chloro-nitrobenzene, the solvent was evaporated and the crude product was purified by flash column chromatography using gradient elution with a mixture of hexane/toluene (3:1 to 1:3).

Thioesters **2a**,[28] **2b**,[29] **5c**,[30] **6a**,[8b] **6b**,[31] **7n**,[32] **8**,[7] **11**,[33] **12**,[34] as well as aminothieno[2,3-b]pyridines **15a**,[35] **15b**[19b] and 2-Methoxy-3-nitropyridine **3**[36] have already been prepared in the literature by other methods.

2-Methoxy-3-nitropyridine (3, main sideproduct for 2-chloro-3-nitropyridine).[36] Brownish solid; m.p. 57-59°C (lit - 56°C[36]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.51 (dd, *J*=4.8, 1.7 Hz, 1H), 8.44 (dd, *J*=7.8, 1.7 Hz, 1H), 7.44 (dd, *J*=7.8, 4.8 Hz, 1H), 4.03 (s, 3H); ^{1}H NMR (700 MHz, $CDCl_3$) δ=8.41 (dd, *J*=4.8, 1.7 Hz, 1H), 8.28 (dd, *J*=7.8, 1.7 Hz, 1H), 7.06 (dd, *J*=7.8, 4.8 Hz, 1H), 4.13 (s, 3H); HRMS (ESI): m/z calcd for $C_6H_7N_2O_3^+$: 155.0451 [M+H]$^+$; found: 155.0455.

2-(Benzylthio)-3-nitropyridine (2a).[28] Yellow solid (420 mg, 85%); m.p. 63-65°C (lit – 66-67°C[28]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.87 (dd, *J*=4.6, 1.7 Hz, 1H), 8.62 (dd, *J*=8.2, 1.7 Hz, 1H), 7.47 (dd, *J*=8.2, 4.6 Hz, 1H), 7.44 (brd, *J*=7.2 Hz, 2H), 7.32 (brt, *J*=7.4 Hz, 2H), 7.25 (brt, *J*=7.4 Hz, 1H), 4.49 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 155.8, 153.7, 141.4, 136.8, 134.3, 129.2, 128.4, 127.1, 120.0, 34.3; HRMS (ESI): m/z calcd for $C_{12}H_{11}N_2O_2S^+$: 247.0536 [M+H]$^+$; found: 247.0536.

2-(Methylthio)-3-nitropyridine (2b). Yellow solid (238 mg, 70%); m.p. 102-104°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.85 (dd, *J*=4.6, 1.6 Hz, 1H), 8.61 (dd, *J*=8.4, 1.6 Hz, 1H), 7.44 (dd, *J*=8.4, 4.6 Hz, 1H), 2.55 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=156.8, 153.7, 141.8, 134.1, 119.5, 13.8; HRMS (ESI): m/z calcd for $C_6H_7N_2O_2S^+$: 171.0223 [M+H]+; found: 171.0225.

2-(Ethylthio)-3-nitropyridine (2c). Yellow solid (254 mg, 69%); m.p. 61-63°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.83 (dd, *J*=4.6, 1.5 Hz, 1H), 8.58 (dd, *J*=8.2, 1.5 Hz, 1H), 7.44 (dd, *J*=8.2, 4.6 Hz, 1H), 3.20 (q, *J*=7.3 Hz, 2H), 1.30 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=156.2, 153.7,

141.8, 134.3, 119.6, 24.1, 13.7; HRMS (ESI): m/z calcd for $C_7H_9N_2O_2S^+$: 185.0379 $[M+H]^+$; found: 185.0385.

2-(Hexylthio)-3-nitropyridine (2d). Light yellowish oil (355 mg, 74%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.81 (dd, *J*=4.6, 1.5 Hz, 1H), 8.58 (dd, *J*=8.2, 1.5 Hz, 1H), 7.43 (dd, *J*=8.2, 4.6 Hz, 1H), 3.19 (t, *J*=7.4 Hz, 2H), 1.66-1.61 (m, 2H), 1.44-1.37 (m, 2H), 1.31-1.26 (m, 4H), 0.86 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=156.3, 153.6, 141.8, 134.2, 119.5, 30.8, 29.7, 28.1, 21.9, 13.8; HRMS (ESI): m/z calcd for $C_{11}H_{17}N_2O_2S^+$: 241.1005 $[M+H]^+$; found: 241.1005.

2-((4-Fluorobenzyl)thio)-3-nitropyridine (2e). Yellow solid (423 mg, 80%); m.p. 108-110°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.87 (dd, *J*=4.6, 1.5 Hz, 1H), 8.62 (dd, *J*=8.2, 1.5 Hz, 1H), 7.49-7.45 (m, 3H), 7.13 (t, *J*=8.8 Hz, 2H), 4.48 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=161.3 (d, *J*=243.5 Hz), 155.7, 153.7, 141.4, 134.4, 133.2 (d, *J*=3.1 Hz), 131.2 (d, *J*=8.2 Hz), 120.1, 115.1 (d, *J*=21.5 Hz), 33.4; HRMS (ESI): m/z calcd for $C_{12}H_{10}FN_2O_2S^+$: 265.0442 $[M+H]^+$; found: 265.0443.

2-((4-Chlorobenzyl)thio)-3-nitropyridine (2f). Yellow solid (471 mg, 84%); m.p. 95-97°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.85 (dd, *J*=4.6, 1.5 Hz, 1H), 8.61 (dd, *J*=8.4, 1.5 Hz, 1H), 7.49-7.42 (m, 3H), 7.36 (d, *J*=8.6 Hz, 2H), 4.48 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=155.5, 153.7, 141.5, 136.3, 134.4, 131.7, 131.0, 128.3, 120.2, 33.3; HRMS (ESI): m/z calcd for $C_{12}H_{10}ClN_2O_2S^+$: 281.0146 $[M+H]^+$; found: 281.0144.

2-((4-Bromobenzyl)thio)-3-nitropyridine (2g). Yellow solid (461 mg, 71%); m.p. 97-99°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.85 (dd, *J*=4.6, 1.5 Hz, 1H), 8.62 (dd, *J*=8.4, 1.5 Hz, 1H), 7.50 (d, *J*=8.4 Hz, 2H), 7.46 (dd, *J*=8.4, 4.6 Hz, 1H), 7.40 (d, *J*=8.4 Hz, 2H), 4.48 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=155.5, 153.7, 141.4, 136.7, 134.4, 131.4, 131.2, 120.2, 120.1, 33.4; HRMS (ESI): m/z calcd for $C_{12}H_{10}BrN_2O_2S^+$: 324.9641 $[M+H]^+$; found: 324.9644.

2-((3-Methoxybenzyl)thio)-3-nitropyridine (2h). Yellow solid (425 mg, 77%); m.p. 82-84°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.87 (dd, J = 4.6, 1.6 Hz, 1H), 8.62 (dd, J = 8.3, 1.6 Hz, 1H), 7.47 (dd, J = 8.3, 4.6 Hz, 1H), 7.23 (t, J = 7.8 Hz, 1H), 7.03 – 6.98 (m, 2H), 6.83 (dd, J = 8.3, 2.5 Hz, 1H), 4.46 (s, 2H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=159.2, 155.9, 153.7, 141.4, 138.3, 134.3, 129.5, 121.4, 120.0, 114.9, 112.6, 54.9, 34.3; HRMS (ESI): m/z calcd for $C_{13}H_{13}N_2O_3S^+$: 277.0641 $[M+H]^+$; found: 277.0641.

2-((2-Methoxybenzyl)thio)-3-nitropyridine (2i). Yellow solid (453 mg, 82%); m.p. 126-128°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.88 (dd, *J*=4.6, 1.6 Hz, 1H), 8.60 (dd, *J*=8.3, 1.6 Hz, 1H), 7.45 (dd, *J*=8.3, 4.6 Hz, 1H), 7.40 (dd, *J*=7.4, 1.7 Hz, 1H), 7.30 – 7.25 (m, 1H), 7.02 (d, *J*=8.2 Hz, 1H), 6.89 (t, *J*=7.4 Hz, 1H), 4.45 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=157.4, 156.5, 153.7, 141.4, 134.3, 130.7, 128.9, 124.0, 120.2, 119.7, 110.9, 55.5, 29.4; HRMS (ESI): m/z calcd for $C_{13}H_{13}N_2O_3S^+$: 277.0641 $[M+H]^+$; found: 277.0644.

3,5-Dimethyl-4-(((3-nitropyridin-2-yl)thio)methyl)isoxazole (2j). Yellow solid (392 mg, 74%); m.p. 123-125°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.88 (dd, *J*=4.6, 1.6 Hz, 1H), 8.61 (dd, *J*=8.3, 1.6 Hz, 1H), 7.47 (dd, *J*=8.3, 4.6 Hz, 1H), 4.26 (s, 2H), 2.44 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=166.7, 159.3, 155.5, 153.5, 141.7, 134.5, 120.1, 109.5, 22.3, 10.9, 9.8; HRMS (ESI): m/z calcd for $C_{11}H_{12}N_3O_3S^+$: 266.0594 $[M+H]^+$; found: 266.0593.

Methyl 3-(((3-nitropyridin-2-yl)thio)methyl)benzoate (2l). Yellow solid (407 mg, 67%); m.p. 96-98°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.85 (dd, *J*=4.6, 1.6 Hz, 1H), 8.61 (dd, *J*=8.3, 1.6 Hz, 1H), 8.05 (brs, 1H), 7.83 (brd, *J*=7.8 Hz, 1H), 7.73 (brd, *J*=7.7 Hz, 1H), 7.49 – 7.45 (m, 2H), 4.57 (s, 2H), 3.85 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=166.0, 155.5, 153.7, 141.5, 138.1, 134.4, 134.1, 129.8, 129.7, 128.8, 127.8, 120.2, 52.1, 33.7; HRMS (ESI): m/z calcd for $C_{14}H_{13}N_2O_4S^+$: 305.0591 $[M+H]^+$; found: 305.0594.

3-(((3-Nitropyridin-2-yl)thio)methyl)benzonitrile (2m). Yellow solid (450 mg, 83%); m.p. 150-152°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.86 (dd, *J*=4.6, 1.6 Hz, 1H), 8.62 (dd, *J*=8.2, 1.6 Hz, 1H), 7.91 (brs, *J*=1.8 Hz, 1H), 7.80 (brd, *J*=7.9 Hz, 1H), 7.71 (brd, *J*=7.7 Hz, 1H), 7.52 (t, *J*=7.7 Hz, 1H), 7.48 (dd, *J*=8.3, 4.6 Hz, 1H), 4.54 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=155.2, 153.7, 141.5, 139.4, 134.5, 134.2, 132.7, 130.8, 129.5, 120.3, 118.6, 111.3, 33.2; HRMS (ESI): m/z calcd for $C_{13}H_{10}N_3O_2S^+$: 272.0488 $[M+H]^+$; found: 272.0489.

2-(Allylthio)-3-nitropyridine (2n). Yellow solid (271 mg, 69%); m.p. 54-56°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ 8.83 (dd, *J*=4.6, 1.6 Hz, 1H), 8.60 (dd, *J*=8.2, 1.6 Hz, 1H), 7.45 (dd, *J*=8.3, 4.6 Hz, 1H), 5.95 (ddt, *J*=17.0, 10.0, 6.9 Hz, 1H), 5.34 (dq, *J*=17.0, 1.5 Hz, 1H), 5.15 – 5.11 (m, 1H), 3.90 (brd, *J*=6.9 Hz, 2H).^{13}C NMR (75 MHz, DMSO-d_6) δ=155.5, 153.6, 141.7, 134.3, 133.2, 119.9, 118.4, 32.6; HRMS (ESI): m/z calcd for $C_8H_9N_2O_2S^+$: 197.0379 $[M+H]^+$; found: 197.0381.

2-((2-Methylallyl)thio)-3-nitropyridine (2o). Light yellow oil (231 mg, 55%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.82 (dd, *J*=4.6, 1.6 Hz, 1H), 8.60 (dd, *J*=8.2, 1.6 Hz, 1H), 7.44 (dd, *J*=8.2, 4.6 Hz, 1H), 5.05 (brs, 1H), 4.89 (brs, 1H), 3.93 (s, 2H), 1.80 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=155.7, 153.6, 141.9, 140.3, 134.3, 119.9, 114.4, 36.4, 21.5; HRMS (ESI): m/z calcd for $C_9H_{11}N_2O_2S^+$: 211.0536 $[M+H]^+$; found: 211.0539.

2-((3-Nitropyridin-2-yl)thio)acetonitrile (2q). Brown solid (152 mg, 39%); m.p. 104-106°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.94 (dd, *J*=4.6, 1.5 Hz, 1H), 8.72 (dd, *J*=8.3, 1.6 Hz, 1H), 7.59 (dd, *J*=8.3, 4.6 Hz, 1H), 4.28 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=154.0, 153.1, 141.6, 134.8, 121.2, 118.0, 16.1; HRMS (ESI): m/z calcd for $C_7H_6N_3O_2S^+$: 196.0175 $[M+H]^+$; found: 196.0180.

Methyl 2-((3-nitropyridin-2-yl)thio)acetate (2r). Orange solid (224 mg, 49%); m.p. 59-61°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.77 (dd, *J*=4.6, 1.6 Hz, 1H), 8.64 (dd, *J*=8.3, 1.6 Hz, 1H), 7.46 (dd, *J*=8.3, 4.6 Hz, 1H), 4.08 (s, 2H), 3.64 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=169.3, 155.0, 153.7, 141.5, 134.5, 120.3, 52.2, 32.6; HRMS (ESI): m/z calcd for $C_8H_9N_2O_4S^+$: 229.0278 $[M+H]^+$; found: 229.0281.

2-(Benzylthio)-6-methoxy-3-nitropyridine (4a). Yellow solid (348 mg, 63%); m.p. 103-105°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.51 (d, *J*=9.0 Hz, 1H), 7.44 (brd, *J*=7.2 Hz, 2H), 7.35 (brt, *J*=7.6 Hz, 2H), 7.28 (brt, *J*=7.4 Hz, 1H), 6.78 (d, *J*=9.0 Hz, 1H), 4.53 (s, 2H), 4.02 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.2, 157.6, 137.3, 136.4, 135.5, 129.0, 128.5, 127.2, 106.9, 54.9, 34.8; HRMS (ESI): m/z calcd for $C_{13}H_{13}N_2O_3S^+$: 277.0641 $[M+H]^+$; found: 277.0644.

6-Methoxy-2-(methylthio)-3-nitropyridine (4b). Yellow solid (348 mg, 87%); m.p. 134-136°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.50 (d, *J*=9.0 Hz, 1H), 6.75 (d, *J*=9.0 Hz, 1H), 4.06 (s, 3H), 2.57 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.2, 158.7, 137.3, 135.9, 106.4, 54.8, 14.0; HRMS (ESI): m/z calcd for $C_7H_9N_2O_3S^+$: 201.0328 $[M+H]^+$; found: 201.0332.

2-(2-Methylallyl)-6-methoxy-3-nitropyridine (4o). Yellow solid (249 mg, 52%); m.p. 76-78°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.49 (d, *J*=9.0 Hz, 1H), 6.76 (d, *J*=9.0 Hz, 1H), 5.05 (brs, 1H), 4.93 (brs, 1H), 4.04 (s, 3H), 3.95 (brs, 2H), 1.83 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.1, 157.5, 140.2, 137.4, 135.9, 114.2, 106.8, 54.8, 36.8, 21.6; HRMS (ESI): m/z calcd for $C_{10}H_{13}N_2O_3S^+$: 241.0641 $[M+H]^+$; found: 241.0645.

2-((6-Methoxy-3-nitropyridin-2-yl)thio)acetonitrile (4q). Yellow solid (426 mg, 95%); m.p. 149-151°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.56 (d, *J*=9.0 Hz, 1H), 6.89 (d, *J*=9.0 Hz, 1H), 4.31 (s, 2H), 4.16 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.6, 154.9, 137.5, 135.8, 118.2, 108.0, 55.2, 16.5; HRMS (ESI): m/z calcd for $C_8H_8N_3O_3S^+$: 226.0281 $[M+H]^+$; found: 226.0280.

Methyl 2-((6-methoxy-3-nitropyridin-2-yl)thio)acetate (4r). Yellow solid (226 mg, 44%); m.p. 115-117°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.51 (d, *J*=9.0 Hz, 1H), 6.78 (d, *J*=9.0 Hz, 1H), 4.11 (s, 2H), 3.96 (s, 3H), 3.65 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=169.4, 164.4, 156.8, 137.3, 135.7, 107.3, 54.8, 52.2, 33.0; HRMS (ESI): m/z calcd for $C_9H_{11}N_2O_5S^+$: 259.0383 $[M+H]^+$; found: 259.0385.

2-(Benzylthio)nicotinonitrile (5a). Yellowish solid (430 mg, 95%); m.p. 72-74°C; ^{1}H NMR (700 MHz, DMSO-d6) δ=8.74 (dd, *J*=5.0, 1.8 Hz, 1H), 8.22 (dd, *J*=7.7, 1.8 Hz, 1H), 7.43 (brd, *J*=6.9 Hz, 2H), 7.36 – 7.29 (m, 3H), 7.25 (brt, *J*=7.4 Hz, 1H), 4.55 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=160.9, 152.6, 141.7, 137.1, 129.0, 128.4, 127.3, 119.7, 115.5, 106.1, 33.4; HRMS (ESI): m/z calcd for $C_{13}H_{11}N_2S^+$: 227.0637 $[M+H]^+$; found: 227.0641.

2-(Ethylthio)nicotinonitrile (5c).[30] Yellowish oil (256 mg, 78%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.70 (dd, *J*=4.9, 1.8 Hz, 1H), 8.20 (dd, *J*=7.7, 1.8 Hz, 1H), 7.30 (dd, *J*=7.7, 4.9 Hz, 1H), 3.25 (q, *J*=7.3 Hz, 2H), 1.32 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=161.5, 152.7, 141.7, 119.3, 115.6, 106.4, 23.9, 14.4; HRMS (ESI): m/z calcd for $C_8H_9N_2S^+$: 165.0481 $[M+H]^+$; found: 165.0483.

2-((2-Methylallyl)thio)nicotinonitrile (5o). Yellowish oil (319 mg, 84%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.70 (dd, *J*=4.9, 1.8 Hz, 1H), 8.21 (dd, *J*=7.8, 1.8 Hz, 1H), 7.32 (dd, *J*=7.8, 4.9 Hz, 1H), 5.03 (brs, 1H), 4.88 (brs, 1H), 3.98 (brs, 2H), 1.79 (brs, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=160.9, 152.6, 141.7, 140.2, 119.7, 115.5, 114.4, 106.6, 35.9, 21.2; HRMS (ESI): m/z calcd for $C_{10}H_{11}N_2S^+$: 191.0637 $[M+H]^+$; found: 191.0638.

2-(Benzylthio)-3-chloropyridine (6a).[8b] Yellowish oil (~70%, determined from NMR of 80-90% purity product); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.49 (dd, *J*=4.8, 1.3 Hz, 1H), 7.87 (dd, *J*=7.8, 1.5 Hz, 1H), 7.43 (bd, *J*=7.4 Hz, 2H), 7.31 (bt, *J*=7.8 Hz, 2H), 7.25 (bt, *J*=7.3 Hz, 1H), 7.21 (dd, *J*=7.8, 4.8 Hz, 1H), 4.46 (s, 2H).

2-(Methylthio)-3-chloropyridine (6b).[31] Yellowish oil (225 mg, 71%); ^{1}H NMR (800 MHz, DMSO-d_6) δ=8.46 (dd, *J*=4.7, 1.5 Hz, 1H), 7.84 (dd, *J*=7.9, 1.5 Hz, 1H), 7.18 (dd, *J*=7.9, 4.7 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (201 MHz, DMSO-d_6) δ=156.6, 147.6, 136.2, 128.1, 120.4, 12.8; HRMS (ESI): m/z calcd for $C_6H_7ClNS^+$: 159.9982 $[M+H]^+$; found: 159.9977.

2-((4-Bromobenzyl)thio)-3-(trifluoromethyl)pyridine (7g). Yellowish oil (451 mg, 65%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.73 (brd, *J*=4.8 Hz, 1H), 8.09 (brd, *J*=7.9 Hz, 1H), 7.49 (d, *J*=8.4 Hz, 2H), 7.39 (d, *J*=8.4 Hz, 2H), 7.36 (dd, *J*=7.8, 4.9 Hz, 1H), 4.52 (s, 2H); ^{13}C NMR (176 MHz, DMSO-d_6) δ=156.0, 152.3, 137.0, 135.2 (q, *J*=5.2 Hz), 131.2, 131.2, 123.3 (q, *J*=273.1 Hz), 121.9 (q, *J*=32.2 Hz), 120.2, 119.6, 32.5; HRMS (ESI): m/z calcd for $C_{13}H_{10}BrF_3NS^+$: 347.9664 $[M+H]^+$; found: 347.9670.

2-(Allylthio)-3-(trifluoromethyl)pyridine (7n). Yellowish oil (90 mg, 21%); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.71 (brd, *J*=4.6 Hz, 1H), 8.09 (brd, *J*=7.8 Hz, 1H), 7.35 (dd, *J*=7.8, 4.8 Hz, 1H), 5.93 (ddt, *J*=16.9, 10.1, 6.8 Hz, 1H), 5.31 (dq, *J*=17.0, 1.5 Hz, 1H), 5.11 (brd, *J*=10.0 Hz, 1H), 3.95 (brd, *J*=6.8 Hz, 2H); ^{13}C NMR (201 MHz, DMSO-d_6) δ=156.1, 152.3, 135.2 (q, *J*=5.2 Hz), 133.4, 122.7 (q, *J*=274.2 Hz), 122.2 (q, *J*=32.4 Hz), 119.4, 118.2, 31.9; HRMS (ESI): m/z calcd for $C_9H_9F_3NS^+$: 220.0402 $[M+H]^+$; found: 220.0402.

(4-methylbenzyl)(2-nitrophenyl)sulfane (8).[7] Yellow solid (466 mg, 90%); m.p. 101-104°C (lit – 101-103°C[7]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.18 (dd, *J*=8.3, 1.4 Hz, 1H), 7.74 (d, *J*=8.2 Hz, 1H), 7.70 (t, *J*=8.3 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.32 (d, *J*=8.0 Hz, 2H), 7.15 (d, *J*=7.8 Hz, 2H), 4.32 (s, 2H), 2.28 (s, 3H).^{13}C NMR (75 MHz, DMSO-d_6) δ=145.3, 136.7, 136.6, 134.1, 132.4, 129.2, 129.1, 127.6, 125.8, 125.3, 35.8, 20.7; HRMS (ESI): m/z calcd for $C_{14}H_{13}NNaO_2S^+$: 282.0559 $[M+Na]^+$; found: 282.0555.

(4-methylbenzyl)(2-nitro-4-(trifluoromethyl)phenyl)sulfane (9). Yellow solid (517 mg, 79%); m.p. 136-138°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.46 (d, *J*=2.1 Hz, 1H), 8.04 (dd, *J*=8.6, 2.1 Hz, 1H), 7.94 (d, *J*=8.6 Hz, 1H), 7.35 (d, *J*=8.0 Hz, 2H), 7.17 (d, *J*=7.7 Hz, 2H), 4.42 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm144.7, 142.3, 137.0, 131.8, 129.9 (q, *J*=3.9 Hz), 129.3, 129.1, 128.7, 125.3 (q, *J*=33.7 Hz), 123.1 (q, *J* =272.4Hz), 122.9 (q, *J*=3.7 Hz), 35.8, 20.6; elemental analysis calcd (%) for $C_{15}H_{12}F_3NO_2S$: C 55.04; H 3.70; N 4.28; found C 55.14; H 3.69; N 4.27.

(2-Chloro-6-nitrophenyl)(4-methylbenzyl)sulfane (10). Yellow solid (487 mg, 83%); m.p. 83-84°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=7.86 (dd, *J*=8.1, 1.3 Hz, 1H), 7.77 (dd, *J*=8.0, 1.3 Hz, 1H), 7.59 (t, *J*=8.1 Hz, 1H), 7.04 (d, *J*=7.8 Hz, 2H), 6.99 (d, J=8.0 Hz, 2H), 4.11 (s, 2H), 2.24 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=156.0, 140.5, 136.7, 133.3, 133.0, 131.4, 129.0, 128.7, 125.0, 122.0, 38.8, 20.7; elemental analysis calcd (%) for $C_{14}H_{12}ClNO_2S$: C 57.24; H 4.12; N 4.77; found C 57.33; H 4.11; N 4.76.

Methyl 4-(benzylthio)-3-nitrobenzoate (11).[33] Yellow solid (497 mg, 82%); m.p. 142-145°C (lit – 138-139°C[33]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.63 (d, *J*=2.0 Hz, 1H), 8.16 (dd, *J*=8.5, 1.9 Hz, 1H), 7.90 (d, *J*=8.5 Hz, 1H), 7.47 (d, *J*=6.9 Hz, 2H), 7.37 (t, *J*=7.6 Hz, 2H), 7.31 (t, *J*=7.4 Hz, 1H), 4.45 (s, 2H), 3.90 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.3, 144.4, 143.0, 134.9, 133.4, 129.3, 128.7, 127.8, 127.7, 126.3, 126.1, 52.6, 36.1; HRMS (ESI): m/z calcd for $C_{15}H_{13}NNaO_4S^+$: 326.0457 $[M+Na]^+$; found: 326.0466.

Benzyl(4-nitrophenyl)sulfane (12).[34] Yellow solid (211 mg, 43%); m.p. 125-127°C (lit - 126-127°C[34]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.12 (d, *J*=9.0 Hz, 2H), 7.55 (d, *J*=9.0 Hz, 2H), 7.45 (d, *J*=7.3 Hz, 2H), 7.33 (t, *J*=7.7 Hz, 2H), 7.27 (t, *J*=7.4 Hz, 1H), 4.43 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=147.3, 144.5, 136.1, 128.9, 128.6, 127.4, 126.4, 123.8, 35.1; elemental analysis calcd (%) for $C_{13}H_{11}NO_2S$: C 63.65; H 4.52; N 5.71; found C 63.74; H 4.50; N 5.70.

Benzyl(2-chloro-4-nitrophenyl)sulfane (13). Yellow solid (403 mg, 72%); m.p. 105-107°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.28 (d, *J*=2.5 Hz, 1H), 8.15 (dd, *J*=8.8, 2.5 Hz, 1H), 7.69 (d, *J*=8.8 Hz, 1H), 7.48 (d, *J*=7.3 Hz, 2H), 7.37 (t, *J*=7.6 Hz, 2H), 7.30 (t, *J*=7.4 Hz, 1H), 4.48 (s, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ=146.3, 144.5, 135.2, 129.7, 129.0, 128.7, 127.7, 126.1, 123.9, 122.4, 35.2; elemental analysis calcd (%) for $C_{13}H_{10}ClNO_2S$: C 55.82; H 3.60; N 5.01; found C 55.93; H 3.59; N 5.00.

Benzyl(4-nitro-2-(trifluoromethyl)phenyl)sulfane (14). Yellow solid (269 mg, 43%); m.p. 89-91°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.39 (dd, J=8.8, 2.6 Hz, 1H), 8.37 (d, J=2.5 Hz, 1H), 7.92 (d, J=8.8 Hz, 1H), 7.47 (d, J=6.8 Hz, 2H), 7.35 (t, J=7.6 Hz, 2H), 7.29 (t, J=7.4 Hz, 1H), 4.57 (s, 2H). ^{13}C NMR (176 MHz, DMSO-d_6) δ=146.2, 144.1, 135.0, 129.0, 128.6, 128.6, 127.7, 126.9, 125.8 (q, *J*=31.6 Hz), 122.6 (q, *J*=273.9 Hz), 121.8 (q, *J*=6.1 Hz), 35.8; elemental analysis calcd (%) for $C_{14}H_{10}F_3NO_2S$: C 53.67; H 3.22; N 4.47; found C 53.73; H 3.21; N 4.46.

3-Aminothieno[2,3-*b*]pyridine-2-carbonitrile (15a).[35] Orange solid (308 mg, 88%); m.p. 215-217°C (lit – 218-219°C [35]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.71 (dd, *J*=4.6, 1.6 Hz, 1H), 8.50 (dd, *J*=8.2, 1.6 Hz, 1H), 7.52 (dd, *J*=8.2, 4.6 Hz, 1H), 7.31 (s, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=159.6, 150.9, 150.4, 131.3, 124.2, 119.9, 115.7, 71.4; HRMS (ESI): m/z calcd for $C_8H_6N_3S^+$: 176.0277 $[M+H]^+$; found: 176.0279.

Methyl 3-aminothieno[2,3-*b*]pyridine-2-carboxylate (15b).[19b] Yellow solid (396 mg, 95%); m.p. 190-191°C (lit – 191°C [19b]); ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.68 (dd, *J*=4.6, 1.6 Hz, 1H), 8.54 (dd, *J*=8.1, 1.6 Hz, 1H), 7.46 (dd, *J*=8.1, 4.6 Hz, 1H), 7.30 (brs, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ=164.8, 159.7, 150.7, 147.8, 131.5, 125.6, 119.4, 93.3, 51.4; HRMS (ESI): m/z calcd for $C_9H_9N_2O_2S^+$: 209.0379 $[M+H]^+$; found: 209.0384.

2-((3-chlorobenzyl)thio)isonicotinonitrile (16). Yellowish solid (115 mg, 22%); m.p. 97-99°C; ^{1}H NMR (700 MHz, DMSO-d_6) δ=8.69 (brd, *J*=5.1 Hz, 1H), 7.88 (brs, 1H), 7.56 (dd, J=5.1, 1.4 Hz, 1H), 7.49 (s, 1H), 7.39 (brd, *J*=7.5 Hz, 1H), 7.34 (t, *J*=7.7 Hz, 1H), 7.31 (dt, *J*=8.0, 1.6 Hz, 1H), 4.47 (s, 2H); ^{13}C NMR (201 MHz, DMSO-d_6) δ=159.7, 150.4, 140.2, 132.9, 130.3, 128.6, 127.6, 127.1, 123.6, 121.2, 119.9, 116.4, 32.5; HRMS (ESI): m/z calcd for $C_{13}H_{10}ClN_2S^+$: 261.0248 $[M+H]^+$; found: 261.0244.

Acknowledgements

The authors gratefully acknowledge support from the Russian Foundation for a Basic Research Grant 20-33-70266.

Keywords: Nucleophilic substitution • Sulfur • Thioethers • Thiols • Xanthates

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10.1002/ejoc.202100647

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A new protocol for the synthesis of aryl-alky thioethers based on the use of S-alkylated xantathes, which appear the thiol surrogates, is proposed. This technique allows to avoid contact with unpleasant thiols odor and allows to introduce substituents for which the corresponding thiols are hardly obtainable, gaseous, or do not exist at all.