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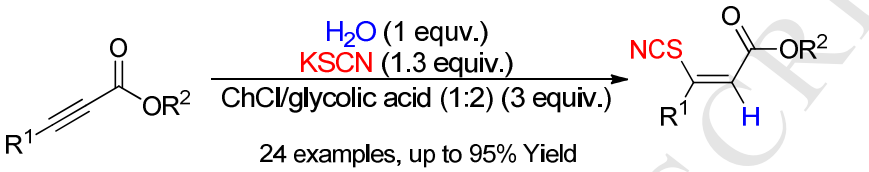


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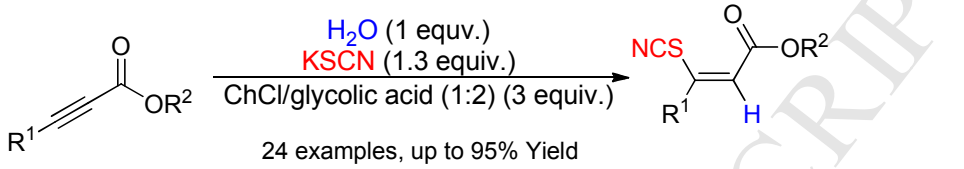


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# Deep eutectic solvent promoted hydrothiocyanation of alkynoates leading to Z-3-thiocyanatoacrylates

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ABSTRACT

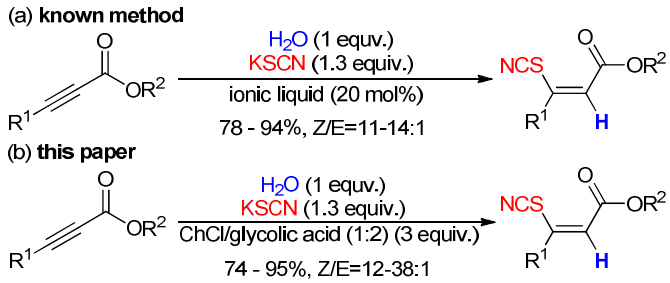
A mild and efficient protocol for the selective construction of Z-3-thiocyanatoacrylates is described. Various alkynoates reacted with KSCN and $H_2O$ by using cheap and recyclable deep eutectic solvent as the catalyst and reaction media to produce the corresponding products in excellent yields with mild reaction conditions and wide substrate scope.



## 1. Introduction

The organosulfur compounds are fundamental motifs in organic chemistry because they ubiquitously appear in natural products, pharmaceuticals and fine chemicals.[1,2] Among numerous sulfur-containing compounds, organic thiocyanates are a useful structural motif found in various biologically active natural products, unnatural drugs, and functional materials.[3] They also serve as versatile building blocks toward a broad range of organosulfur compounds.[4] Over the past years, a number of methods have been well-established for the synthesis of alkyl[5], alkenyl,[6] and aromatic thiocyanates[7]. However, the novel and practical protocol for the direct construction of thiocyanatoacrylate, particularly regio- and stereoselective synthesis of Z-3-thiocyanatoacrylates from simple and safe raw materials under environmentally friendly conditions is still remains rarely. For example, He and co-workers has pioneered a direct construction of Z-3-thiocyanatoacrylates through room-temperature ionic liquid-catalyzed catalyzed reaction of alkynoates[8], KSCN and water[9]. Although this methodology represents a remarkable advance, it still needs to use toxic and expensive ionic liquids and proceeds with moderate stereoselectivities (Scheme 1a). Improved protocols for the preparation selective regio- and stereoselective synthesis of Z-3-thiocyanatoacrylates are therefore highly desirable.

Green Chemistry emphasizes the establishment of environmentally friendly chemical reaction that avoids the usage of toxic reagents and the utilization of eco-friendly substances and nontoxic solvents.[10] Recently, deep eutectic solvents (DES) have attracted much attention from synthetic and pharmaceutical chemists.[11] DES not only has the close physico-chemical properties with ionic liquid, but also has a lot of advantages than ionic liquid, including nontoxicity, simple and green preparation, inexpensive and readily accessibility. A number of organic transformation with DES as catalyst or reaction media have been developed during the past few years.[12] However, a novel method for the regio- and stereoselective hydrothiocyanation of various alkynoates to access Z-3-thiocyanatoacrylates has never been reported. Herein, we report an environment-friendly method for the selective synthesis of Z-3-thiocyanatoacrylates through DES-catalyzed hydrothiocyanation of alkynoates (Scheme 1b). In this process, both the high efficiency and excellent selectivities were achieved with the help of hydrogen bond.



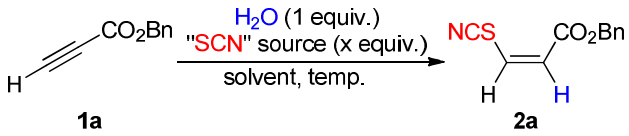

**Scheme 1.** Synthetic route of Z-3-thiocyanatoacrylates

## 2. Results and discussion

To find the optimized conditions for the construction of Z-3-thiocyanatoacrylates, the reaction of benzyl propiolate (**1a**), KSCN and water was selected as the model reaction. We first performed the hydrothiocyanation reaction using hydrochloric acid (1M) as the solvent at ambient temperature for 10 h, and a 20% yield of (*Z*)-benzyl 3-thiocyanatoacrylate (**2a**) was obtained with complex mixtures that included un-reacted substrate **1a**. Next, the effect of solvent on the hydrothiocyanation reaction efficiency was investigated (entires 2-10). These results revealed that deep eutectic ChCl/glycolic acid (1:2, 1 mL) was a superior

reaction medium with a 52% NMR yield (entry 5). Glycolic acid aqueous solution or ChCl aqueous aqueous solution alone gave low or no conversions of **1a** (entries 3 and 10). These obvious differences suggested that the synergetic function of glycolic acid and ChCl resulted in such an efficient conversion. Decreasing the loading of ChCl/glycolic acid to 3 equivalents had virtually no effect on the yield. Attempted to lower the reaction medium loading to 2 equivalents was unsuccessful and yield dropped to 45% (entry 13). Switching the thiocyanate salt from KSCN to NaSCN or $NH_4SCN$ led to a lower yield of **2a** by prolong the reaction time to 16 hour. Further optimization of the optimal amount of KSCN (entries 12 and 16-18) showed that 1.3 equivalents of KSCN (entry 16) was the suitable loading. Elevating the reaction temperature from room temperature to 50℃ not only resulted in an excellent yield of **2a** but also accelerated the reaction rate. Further increasing the reaction temperature to 60℃ did not improve the reaction efficiency (entry 20). No conversation of 1a was detected in the absence of deep eutectic ChCl/glycolic acid (entry 21).

**Table 1.** Optimization of reaction conditions[a]

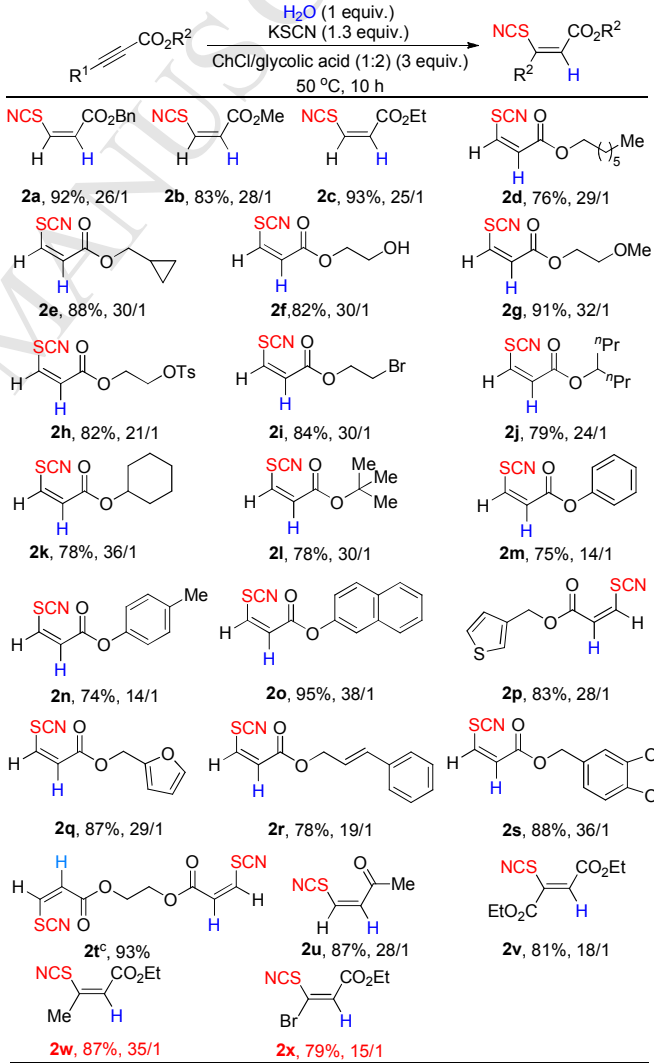



| Entry | Solvent | [SCN] (X equiv) | Yield[b] | Z/E[b] |
|---|---|---|---|---|
| 1 | HCl (1M, 1mL) | KSCN (1.5) | 20 | 10:1 |
| 2 | HOAc (1M, 1mL) | KSCN (1.5) | 15 | 10:1 |
| 3 | glycolic acid (1M, 1mL) | KSCN (1.5) | 28 | 11:1 |
| 4 | ChCl/glycolicacid(1:2)(1M, 1mL) | KSCN (1.5) | 40 | 23:1 |
| 5 | ChCl/glycolic acid(1:2)(1 mL) | KSCN (1.5) | 52 | 25:1 |
| 6 | ChCl/oxalic acid(1:1)(1 mL) | KSCN (1.5) | 20 | 22:1 |
| 7 | ChCl/citric acid(1:1)(1 mL) | KSCN (1.5) | 25 | 20:1 |
| 8 | ChCl/glycolic acid(1:1)(1mL) | KSCN (1.5) | 40 | 24:1 |
| 9 | ChCl/urea (1:1)(1mL) | KSCN (1.5) | trace | -- |
| 10 | ChCl (1 M, 1mL) | KSCN (1.5) | N.D. | -- |
| 11[c] | ChCl/glycolic acid(1:2) (5 equiv.) | KSCN (1.5) | 52 | >25:1 |
| 12 | ChCl/glycolic acid(1:2) (3 equiv.) | KSCN (1.5) | 52 | >25:1 |
| 13 | ChCl/glycolic acid(1:2) (2 equiv.) | KSCN (1.5) | 45 | >25:1 |
| 14 | ChCl/glycolic acid(1:2) (3 equiv.) | NaSCN (1.5) | 48 | >25:1 |
| 15 | ChCl/glycolic acid(1:2) (3 equiv.) | $NH_4SCN$ (1.5) | 43 | >25:1 |
| 16 | ChCl/glycolic acid(1:2) (3 equiv.) | KSCN (1.3) | 52 | >25:1 |
| 17 | ChCl/glycolic acid(1:2) (3 equiv.) | KSCN (1.2) | 48 | >25:1 |
| 18 | ChCl/glycolic acid(1:2) (3 equiv.) | KSCN (1.1) | 43 | >25:1 |
| **19**[d] | ChCl/glycolic acid(1:2) (3 equiv.) | **KSCN (1.3)** | **92** | >25:1 |
| 20[e] | ChCl/glycolic acid(1:2) (3 equiv.) | KSCN (1.3) | 89 | >25:1 |
| 21[d] | -- | KSCN (1.3) | N.D. | -- |

[a] Reaction conditions: **1a** (0.3 mmol), "SCN"source, water (0.3mmol), rt.
[b] NMR yields based on **1a**. The Z/E ratios was estimated by $^1$H NMR. of glycolic acid.
[c] 5 equiv. of deep eutectic ChCl/glycolic acid(1:2) composes of 5 equiv. of ChCl and 10 equiv. of glycolic acid.
[d] At 50℃
[e] At 60℃

With the optimal reaction conditions in hand (Table 1, entry19), we proceeded to evaluate the substrate scope of the three-component reaction and these results are shown in Table 2. To our delight, a series of alkynoates bearing varied carbon chain lengths and diverse isomeric structures employed for hydrothiocyanation to provide the desired Z-β-thiocyanate acrylates in 74–95% yields with excellent stereoselectivities (**2a-2k**). All primary, secondary and tertiary alkyl alcohol esters were compatible under the standard reaction conditions. The present method also works well with aromatic, polycyclic aromatic and heteroaromatic alcohol esters, delivering the corresponding products in good to excellent yields (**2l - 2p**). Propargylic carboxylates containing natural alcohol, such as furfuryl alcohol, cinnamyl alcohol and piperonyl alcohol, were also well-tolerated under optimal conditions, leading to the corresponding products in good yields (**2q - 2s**). The (2Z,2'Z)-ethane-1,2-diyl bis(3-thiocyanatoacrylate) **2t** was obtained in 93% yield by direct double thiocyanation under the optimal conditions. Furthermore, the relatively low activity of internal alkynoates, such as but-3-yn-2-one and diethyl acetylenedicarboxylate can also be used as the substrates, furnishing the desired thiocyanation products (**2u - 2w**) in good yields and excellent stereoselectivities. However, when 4,4,4-trifluorobut-2-ynoate or 3-phenylpropiolate were used as reaction substrates, only a trace amount of the desired product could be observed.

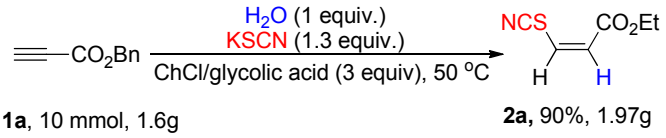
**Table 2.** Substrate scope[a, b]




[a] Reaction conditions: **1** (0.3 mmol), KSCN (0.39 mmol), ChCl/glycolic acid（0.27 g）, water (6 mg), 50°C, 10 h.
[b] Isolated yields based on **1**.
[c] 0.78 mmol of KSCN was used.

It is well known that the scalability and reusability of a catalytic reaction system are of significant importance from the views of green chemistry and industrial manufacturing. In order

to demonstrate the scalability of the hydrothiocyanation reaction, a large-scale reaction (10 mmol) was conducted under the optimal reaction conditions (Scheme 2). The experimental result showed that a 90% yield of **2a** was obtained, suggesting that the present reaction system is easy to scale up. The reusability of deep eutectic ChCl/glycolic acid (1:2) was then investigated. Generally, after completion of the reaction, the product was extracted for the determination of yield by $^1$H NMR and the deep eutectic ChCl/glycolic acid (1:2) was reused directly. Empolying substrate **1a** as example, the experimental results revealed that the deep eutectic solvent could be reused without significant reduction in catalytic activity in five consecutive runs.



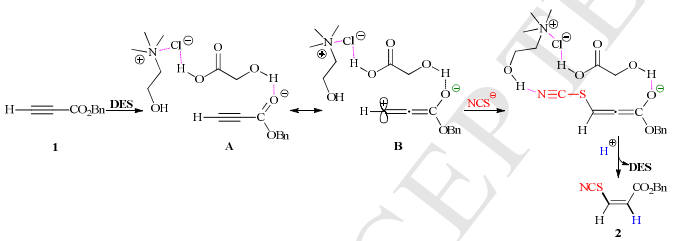

**1a**, 10 mmol, 1.6g

**2a**, 90%, 1.97g

1st run **90**%; 2nd run **88**%; 3rd run **85**%; 4th run **83**%; 5th run **80**%

**Scheme 2.** Large-scale synthesis and reusable experiment.

Based on these results obtained in Table 1 and previous reports, [13] a reasonable mechanism for the regio- and stereoselective hydrothiocyanation reaction is depicted in Scheme 3. Stronger hydrogen bond capabilities of deep eutectic ChCl/glycolic acid activated alkynoates to in situ generate an allenolate intermediate **A** through the formation of an intermolecular hydrogen bond between glycolic acid and substrate **1a**. Then, the thiocyanate anion nucleophilic attacked the β-carbon atom of intermediate **B** to deliver the intermediate **C**. Meanwhile, an intramolecular hydrogen bond between the hydroxyl group of ChCl and the nitrogen atom of "SCN" motif was formed in this intermediate. Finally, the trapping of a proton (in situ generated from ionization of water) occurs from the less hindered face, trans to "SCN", thus resulted in the production of (Z)-benzyl 3-thiocyanatoacrylate **2a**.




**Scheme 3.** Possible reaction mechanism.

## 3. Conclusion

In summary, we have developed a practical and environment-friendly protocol for the selective synthesis of Z-3-thiocyanatoacrylates through deep eutectic solvent-catalyzed hydrothiocyanation reaction. Both the high efficiency (74-95% yield) and excellent stereoselectivities (Z:E > 12:1) were achieved through intramolecular and intermolecular hydrogen bond. In this process, the inexpensive and green deep eutectic ChCl/glycolic acid not only acts as recycled reaction media, but also serves as catalyst. The present reaction could be readily scaled up to a large scale, providing a good opportunity for applications in synthetic chemistry and industry production.

## 4. Experimental Section

### 4.1. General methods and materials

Ethyl acetate (ACS grade), hexanes (ACS grade) were purchased from J&K Scientific Ltd. and used without further purification. Commercially available reagents were used without further purification. Reactions were monitored by TLC. Flash column chromatography was performed over silica gel (200-300 mesh). $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AV-II 500 MHz NMR spectrometer. High-resolution mass spectra were performed on a Q-TOF microspectrometer.

### 4.2. General Procedure for the Synthesis of 2.

In a vial was placed alkyne (0.3 mmol), ChCl/glycolic acid (1:2) (270 mg, 0.9 mmol), KSCN (38 mg, 0.39 mmol), water (0.3 mmol), and then the contents were reacted at 50 ℃. Upon completion, the reaction mixture was purified by column chromatography on silicagel (eluent: hexanes/ethyl acetate) to afford 2.

### 4.3. Larger-scale Synthesis of 2a

In a vial was placed benzyl propiolate (1.6 g, 10 mmol), ChCl/glycolic acid (1:2) (9 g, 30 mmol), KSCN (1.26 g, 13 mmol), water (10 mmol), and then the contents were reacted at 50 ℃. Upon completion, the reaction mixture was purified by column chromatography on silica gel (eluent: hexanes/ethyl acetate) to afford 2a.

### 4.4. Recycling research of ChCl/glycolic acid (1:2)

In a vial was consecutively placed benzyl propiolate (1.6 g, 10 mmol), ChCl/glycolic acid (1:2) (9 g, 30 mmol), KSCN (1.26 g, 13 mmol) and $H_2O$ (0.18 g, 10 mmol), then the mixtures were stired at 50 ℃ for 10 h. Upon completion, the reaction mixture was extracted with cyclpentyl methyl ether (10 mL × 3). The extraction was product with high purity. The yield was estimated by gas chromatography. To the recycled ChCl/glycolic acid (1:2), only 10 mmol of **1a**, 13 mmol of KSCN, 10 mmol of $H_2O$ were added to the filter residue, and the next cycle was carried out under the same reaction conditions.

### 4.5. Characterization of the compounds

*4.5.1. (Z)-benzyl 3-thiocyanatoacrylate (**2a**).*[9]

Colorless oil (60.4 mg, 92%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.42 – 7.33 (m, 5H), 7.17 (d, *J* = 9.3, 1H), 6.30 (d, *J* = 9.3, 1H), 5.22 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.17, 138.92, 134.87, 128.89, 128.87, 128.71, 119.75, 112.36, 67.53.

*4.5.2. (Z)-methyl 3-thiocyanatoacrylate (**2b**).*[9]

Colorless oil (35.6 mg, 83%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.15 (d, *J* = 9.3, 1H), 6.26 (d, *J* = 9.3, 1H), 3.79 (s, 3H).$^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.74, 138.61, 119.54, 112.24, 52.46.

*4.5.3. (Z)-ethyl 3-thiocyanatoacrylate (**2c**).*[9]

Colorless oil (40.5 mg, 86%);$^1$H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 9.2 Hz, 1H), 6.26 (d, *J* = 9.2 Hz, 1H), 4.25 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.42, 138.25, 120.01, 112.55, 61.81, 14.25.

*4.5.4. (Z)-propyl 3-thiocyanatoacrylate (**2d**).*

White solid (39.0 mg, 76%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.13 (d, *J* = 9.2, 1H), 6.25 (d, *J* = 9.2, 1H), 4.17 (t, *J* = 6.8, 2H), 1.67 – 1.63 (m, 2H), 1.38 – 1.21 (m, 10H), 0.87 (t, *J* = 7.0, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.48, 138.18, 120.01, 112.50, 65.93, 31.76, 28.94, 28.55, 25.85, 22.66, 14.16. HRMS Calcd (EI) m/z for $C_7H_9NO_2S$: $[M]^+$ 171.0354, found: 171.0356.

*4.5.5.(Z)-cyclopropylmethyl 3-thiocyanatoacrylate (**2e**).*[9]

Colorless oil (48.3 mg, 88%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.15 (d, *J* = 9.3, 1H), 6.29 (d, *J* = 9.3, 1H), 4.02 (d, *J* = 7.4, 2H), 0.87-0.81 (m, 1H), 0.64 – 0.57 (m, 2H), 0.34-0.29 (m, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.49, 138.27, 120.10, 112.56, 70.70, 29.85, 9.78.

*4.5.6. (Z)-2-hydroxyethyl 3-thiocyanatoacrylate(**2f**).*[9]

Colorless oil (42.3 mg, 82%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.23 (d, *J* = 9.3, 1H), 6.35 (d, *J* = 9.3, 1H), 4.37 – 4.30 (m, 2H), 3.91 – 3.86 (m, 2H), 2.67 (s, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.43, 138.96, 119.56, 112.26, 66.94, 60.63.

*4.5.7. (Z)-2-methoxyethyl 3-thiocyanatoacrylate (**2g**).*[9]

Colorless oil (51.1 mg, 91%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 9.4, 1H), 6.30 (d, *J* = 9.4, 1H), 4.33 – 4.31 (m, 2H), 3.62 – 3.59 (m, 2H), 3.37 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.23, 138.76, 119.66, 112.25, 70.10, 64.55, 59.07.

*4.5.8. (Z)-2-(tosyloxy)ethyl 3-thiocyanatoacrylate (**2h**).*[9]

White solid (80.4 mg, 82%); $^1$H NMR (500 MHz, Chloroform-*d*) δ = 7.79 (d, *J*=8.4, 2H), 7.36 (d, *J*=7.9, 2H), 7.18 (d, *J*=9.4, 1H), 6.20 (d, *J*=9.3, 1H), 4.37 – 4.35 (m, 2H), 4.27 – 4.25 (m, 2H), 2.46 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.69, 145.40, 139.56, 132.75, 130.12, 128.10, 119.20, 111.95, 67.10, 62.78, 21.83.

*4.5.9. (Z)-2-bromoethyl 3-thiocyanatoacrylate (**2i**)* [9]

Light yellow solid (60.0 mg, 85%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 9.2, 1H), 6.31 (d, *J* = 9.2, 1H), 4.50 (t, *J* = 6.0, 2H), 3.54 (t, *J* = 6.0, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.73, 139.58, 119.25, 112.04, 64.84, 28.10.

*4.5.10. (Z)-heptan-4-yl 3-thiocyanatoacrylate(**2j**).*

White solid (40.5 mg, 79%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.12 (d, *J* = 9.2, 1H), 6.24 (d, *J* = 9.2, 1H), 4.97 (tt, *J* = 7.3, 5.2, 1H), 1.58 – 1.51 (m, 4H), 1.35 – 1.28 (m, 4H), 0.90 (t, *J* = 7.3, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.29, 137.97, 120.40, 112.68, 76.17, 36.27, 18.65, 14.05. HRMS Calcd (EI) m/z for $C_7H_9NO_2S$: $[M]^+$ 171.0354, found: 171.0352.

*4.5.11. (Z)-cyclohexyl 3-thiocyanatoacrylate (**2k**).*[9]

Colorless oil (49.4 mg, 78%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.11 (dd, *J* = 9.3, 4.3, 1H), 6.23 (dd, *J* = 9.3, 4.3, 1H), 4.89 – 4.76 (m, 1H), 1.92 – 1.84 (m, 2H), 1.77 – 1.71 (m, 2H), 1.51 – 1.30 (m, 6H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.92, 137.84, 120.56, 112.66, 74.67, 31.64, 25.32, 23.77.

*4.5.12. (Z)-tert-butyl 3-thiocyanatoacrylate (**2l**).*

Colorless oil (43.3 mg, 78%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.04 (d, *J* = 9.3, 1H), 6.16 (d, *J* = 9.3, 1H), 1.49 (s, 9H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.78, 136.71, 121.76, 112.93, 83.12, 28.18.

*4.5.13. (Z)-phenyl 3-thiocyanatoacrylate (**2m**).*[9]

Colorless oil (46.1 mg, 75%); $^1$H NMR (500 MHz, Chloroform-*d*) δ = 7.46 – 7.39 (m, 2H), 7.35 (d, *J*=9.3, 1H), 7.29 (t, *J*=7.5, 1H), 7.17 – 7.12 (m, 2H), 6.51 (d, *J*=9.3, 1H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 164.74, 149.88, 140.73, 129.64, 126.54, 121.15, 119.15, 111.84.

*4.5.14. (Z)-p-tolyl 3-thiocyanatoacrylate(**2n**).*

Colorless oil (48.6 mg, 74%); $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.32 (d, *J* = 9.3, 1H), 7.20 (d, *J* = 9.0, 2H), 7.01 (d, *J* = 8.6, 2H), 6.49 (d, *J* = 9.0, 1H), 2.36 (s, 3H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 165.07, 147.78, 140.66, 136.41, 130.23, 120.91, 119.33, 112.04, 21.02. HRMS Calcd (EI) m/z for $C_{11}H_9NO_2S$: $[M]^+$ 219.0354,found: 219.0352.

*4.5.15. (Z)-naphthalen-2-yl 3-thiocyanatoacrylate (**2o**).*[9]

White solid (72.7 mg, 95%); $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.92 – 7.80 (m, 3H), 7.65 – 7.61 (m, 1H), 7.55 – 7.47 (m, 2H), 7.37 (d, *J* = 9.3, 1H), 7.28 – 7.25 (m, 1H), 6.56 (d, *J* = 9.3, 1H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 165.01, 147.62, 141.01, 133.73, 131.82, 129.85, 127.96, 127.88, 127.00, 126.27, 120.46, 119.30, 118.47, 111.95.

*4.5.16. (Z)-thiophen-3-ylmethyl 3-thiocyanatoacrylate(**2p**).*

White solid (56.0 mg, 83%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.36 – 7.31 (m, 2H), 7.16 (d, *J*=9.3, 1H), 7.13-7.08 (m, 1H), 6.28 (d, *J*=9.3, 1H), 5.22 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.04, 138.83, 135.66, 127.72, 126.68, 125.37, 119.69, 112.24, 62.24. HRMS Calcd (EI) m/z for $C_9H_7NO_2S_2$: $[M]^+$ 224.9918, found: 224.9915.

*4.5.17. (Z)-furan-2-ylmethyl 3-thiocyanatoacrylate (**2q**).*[9]

White solid (54.5 mg, 87%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.44 (dd, *J* = 1.8, 0.9, 1H), 7.17 (d, *J* = 9.3, 1H), 6.48 – 6.44 (m, 1H), 6.38 (dd, *J* = 3.3, 1.8, 1H), 6.27 (d, *J* = 9.3, 1H), 5.17 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.89, 148.45, 143.84, 139.14, 119.56, 112.23, 111.68, 110.86, 59.02.

*4.5.18. (Z)-cinnamyl 3-thiocyanatoacrylate (**2r**).*[9]

Colorless oil (57.3 mg, 78%); $^1$H NMR (400 MHz, $CDCl_3$) δ = 7.47 – 7.29 (m, 5H), 7.19 (d, *J* = 9.3, 1H), 6.72 (dd, *J* = 15.9, 1.5, 1H), 6.37 – 6.24 (m, 2H), 4.87 (dd, *J* = 6.7, 1.3, 2H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ 166.14, 138.77, 135.87, 135.52, 128.78, 128.50, 126.79, 121.97, 119.72, 112.39, 66.29.

*4.5.19. (Z)-benzo[d][1,3]dioxol-5-ylmethyl 3-thiocyanatoacrylate (**2s**).*[9]

White solid (69.4 mg, 88%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 9.4, 1H), 6.88 – 6.82 (m, 2H), 6.79 (d, *J* = 8.4, 1H), 6.27 (d, *J* = 9.4, 1H), 5.97 (s, 2H), 5.11 (s, 2H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.10, 148.17, 148.05, 138.82, 128.60, 122.89, 119.79, 112.28, 109.37, 108.48, 101.42, 67.50, 29.82.

*4.5.20. (2Z,2'Z)-ethane-1,2-diyl bis(3-thiocyanatoacrylate) (2t).*

White solid (79.2 mg, 93%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.22 (d, *J* = 9.3, 2H), 6.29 (d, *J* = 9.3, 2H), 4.44 (s, 4H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.91, 139.69, 119.24, 111.95, 62.90. HRMS Calcd (EI) m/z for $C_{10}H_8N_2O_4S_2$: $[M]^+$ 283.9925, found: 283.9924.

*4.5.21. (Z)-4-thiocyanatobut-3-en-2-one (**2u**).*[9]

Colorless oil (33.1 mg, 87%); $^1$H NMR (500 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 8.8, 1H), 6.67 (d, *J* = 8.8, 1H), 2.33 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 198.28, 138.34, 124.88, 113.58, 30.03.

*4.5.22. diethyl 2-thiocyanatofumarate (**2v**).*[9]

White solid (55.6 mg, 81%); $^1$H NMR (500 MHz, Chloroform-*d*) δ = 6.84 (s, 1H), 4.42 (q, *J*=7.1, 2H), 4.29 (q, *J*=7.2, 2H), 1.41 (t, *J*=7.2, 3H), 1.33 (t, *J*=7.2, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 164.64, 161.56, 138.28, 126.50, 108.91, 64.17, 62.43, 14.20, 14.04.

*4.5.23. (Z)-ethyl 3-thiocyanatobut-2-enoate (**2w**).*[9]

Colorless oil (44.6 mg, 87%); $^1$H NMR (500 MHz, Chloroform-*d*) δ = 6.13 (d, *J*=1.4, 1H), 4.21 (q, *J*=7.1, 2H), 2.47

(d, *J*=1.4, 3H), 1.29 (t, *J*=7.1, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 166.13, 146.78, 117.48, 110.45, 61.33, 25.96, 14.29.

*4.5.24. (E)-ethyl 3-bromo-3-thiocyanatoacrylate (**2x**).*[8]

White solid (55.7 mg, 79%); $^1$H NMR (500 MHz, Chloroform-*d*) δ = 6.73 (s, 1H), 4.24 (q, *J*=7.2, 2H), 1.31 (t, *J*=7.1, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 165.17, 126.31, 125.02, 109.60, 62.09, 14.21.

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**Supplementary data**

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.****

**References and notes**

(1) (a) Mishra, C. B.; Kumari, S.; Tiwari, M. *Eur. J. Med. Chem.* **2015**, *92*, 1; (b) Feng, M.; Tang, B.; H. Liang, S.; Jiang, X. *Curr. Top. Med. Chem.* **2016**, *16*, 1200; (c) Xie, L.-Y.; Peng, S.; Tan, J.-X.; Sun, R.-X.; Yu, X.; Dai, N.-N.; Tang, Z.-L.; Xu, X.; He, W.-M. *ACS Sustainable Chem. Eng.* **2018**, *6*, 16976; (d) Liang, Q.; Zhang, Y.; Huang, M.; Xiao, Y.; Xiao, F. *Mol. Med. Rep.* **2019**, *19*, 1256; (e) Li, G.; Gan, Z.; Kong, K.; Dou, X.; Yang, D. *Adv. Synth. Catal.* **2019**, 361, 1808; (f) Zong, Y.; Lang, Y.; Yang, M.; Li, X.; Fan, X.; Wu, J. *Org. Lett.* **2019**, *21*, 1935; (g) Bao, W.-H.; He, M.; Wang, J.-T.; Peng, X.; Sung, M.; Tang, Z.; Jiang, S.; Cao, Z.; He, W.-M. *J. Org. Chem.* **2019**, *84*, 6065.

(2) (a) Elhalem, E.; Bailey, B. N.; Docampo, R.; Ujváry, I.; Szajnman, S. H.; Rodriguez, J. B. *J. Med. Chem.* **2002**, *45*, 3984; (b) Kokorekin, V. A.; Terent'ev, A. O.; Ramenskaya, G. V.; Grammatikova, N. É.; Rodionova, G. M.; Ilovaiskii, A. I. *Pharm. Chem. J.* **2013**, *47*, 422; (c) Chao, M. N.; Storey, M.; Li, C.; Rodríguez, M. G.; Di Salvo, F.; Szajnman, S. H.; Moreno, S. N. J.; Docampo, R.; Rodriguez, J. B. *Biorg. Med. Chem.* **2017**, *25*, 6435; (d) Liang, Q.; Zhang, Y.; Zeng, M.; Guan, L.; Xiao, Y.; Xiao, F. *Toxicol. Res.* **2018**, *7*, 521.

(3) (a) Falck, J. R.; Gao, S.; Prasad, R. N.; Koduru, S. R. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1768; (b) Zhen, L.; Yuan, K.; Li, X.-y.; Zhang, C.; Yang, J.; Fan, H.; Jiang, L. *Org. Lett.* **2018**, *20*, 3109; (c) Maity, R.; Naskar, S.; Mal, K.; Biswas, S.; Das, I. *Adv. Synth. Catal.* **2017**, *359*, 4405.

(4) (a) Tao, Z.-K.; Li, C.-K.; Zhang, P.-Z.; Shoberu, A.; Zou, J.-P.; Zhang, W. *J. Org. Chem.* **2018**, *83*, 2418; (b) Yang, H.; Duan, X.-H.; Zhao, J.-F.; Guo, L.-N. *Org. Lett.* **2015**, *17*, 1998.

(5) (a) Jiang, G.; Zhu, C.; Li, J.; Wu, W.; Jiang, H. *Adv. Synth. Catal.* **2017**, *359*, 1208; (b) Dong, D.-Q.; Gao, X.; Li, L.-X.; Hao, S.-H.; Wang, Z.-L. *Res. Chem. Intermed.* **2018**, *44*, 7557; (c) Lu, L.-H.; Zhou, S.-J.; Sun, M.; Chen, J.-L.; Xia, W.; Yu, X.; Xu, X.; He, W.-M. *ACS Sustainable Chem. Eng.* **2019**, *7*, 1574; (d) Wu, D.; Qiu, J.; Karmaker, P. G.; Yin, H.; Chen, F.-X. *J. Org. Chem.* **2018**, *83*, 1576.

(6) (a) Yang, D.; Yan, K.; Wei, W.; Li, G.; Lu, S.; Zhao, C.; Tian, L.; Wang, H. *J. Org. Chem.* **2015**, *80*, 11073; (b) Sun, N.; Che, L.; Mo, W.; Hu, B.; Shen, Z.; Hu, X. *Org. Biomol. Chem.* **2015**, *13*, 691; (c) Jiang, H.; Yu, W.; Tang, X.; Li, J.; Wu, W. *J. Org. Chem.* **2017**, *82*, 9312; (d) Chen, Y.; Wang, S.; Jiang, Q.; Cheng, C.; Xiao, X.; Zhu, G. *J. Org. Chem.* **2018**, *83*, 716; (e) Gao, Y.; Liu, Y.; Wan, J.-P. *J. Org. Chem.* **2019**, *84*, 2243; (f) Lu, L.-H.; Zhou, S.-J.; Sun, M.; Chen, J.-L.; Xia, W.; Yu, X.; Xu, X.; He, W.-M. *ACS Sustainable Chem. Eng.* **2019**, *7*, 1574; (g)Teng, F.; Yu, J.-T.; Yang, H.; Jiang, Y.; Cheng, J. *Chem. Commun.* **2014**, *50*, 12139; (h) Chen, Q.; Lei, Y.; Wang, Y.; Wang, C.; Wang, Y.; Xu, Z.; Wang, H.; Wang, R. *Org. Chem. Front.* **2017**, *4*, 369; (i) Yu, J.-T.; Teng, F.; Cheng, J. *Adv. Synth. Catal.* **2017**, *359*, 26.

(7) (a) Lu, G.-p.; Cai, C.; Chen, F.; Ye, R.-l.; Zhou, B.-j. *ACS Sustainable Chem. Eng.* **2016**, *4*, 1804; (b) Li, W.; Yin, G.; Huang, L.; Xiao, Y.; Fu, Z.; Xin, X.; Liu, F.; Li, Z.; He, W. *Green Chem.* **2016**, *18*, 4879; (c) Wei, W.; Wang, L.; Yue, H.; Jiang, Y.-Y.; Yang, D. *Org. Biomol. Chem.* **2018**, *16*, 7001; (d) Yan, K.; Yang, D.; Wei, W.; Wang, F.; Shuai, Y.; Li, Q.; Wang, H. *J. Org. Chem.* **2015**, *80*, 1550.

(8) Wu, C.; Lu, L.-H.; Peng, A.-Z.; Jia, G.-K.; Peng, C.; Cao, Z.; Tang, Z.; He, W.-M.; Xu, X. *Green Chem.* **2018**, *20*, 3683.

(9) (a) Liu, K.-J.; Jiang, S.; Lu, L.-H.; Tang, L.-L.; Tang, S.-S.; Tang, H.-S.; Tang, Z.; He, W.-M.; Xu, X. *Green Chem.* **2018**, *20*, 3038; (b) Yang, J.; Mei, F.; Fu, S.; Gu, Y. *Green Chem.* **2018**, *20*, 1367; (c) Li, J.; Tang, W.; Ren, D.; Xu, J.; Yang, Z. *Green Chem.* **2019**; (d) Liu, Q.; Wang, L.; Yue, H.; Li, J.-S.; Luo, Z.; Wei, W. *Green Chem.* **2019**; (e) Bao, P.; Wang, L.; Liu, Q.; Yang, D.; Wang, H.; Zhao, X.; Yue, H.; Wei, W. *Tetrahedron Lett.* **2019**, *60*, 214; (f) Lu, L.-H.; Wang, Z.; Xia, W.; Cheng, P.; Zhang, B.; Cao, Z.; He, W.-M. *Chin. Chem. Lett.* **2019**, *30*, 1237; (g) Xie, L.-Y.; Peng, S.; Liu, F.; Liu, Y.-F.; Sun, M.; Tang, Z.-L.; Jiang, S.; Cao, Z.; He, W.-M. *ACS Sustainable Chem. Eng.* **2019**, *7*, 7193; (h) Dong, D.-Q.; Chen, W.-J.; Yang, Y.; Gao, X.; Wang, Z.-L. *ChemistrySelect* **2019**, *4*, 2480.

(10) (a) Clarke, C. J.; Tu, W.-C.; Levers, O.; Bröhl, A.; Hallett, J. P. *Chem. Rev.* **2018**, *118*, 747; (b) Liu, P.; Hao, J.-W.; Mo, L.-P.; Zhang, Z.-H. *RSC Adv.* **2015**, *5*, 48675; (c) Alonso, D. A.; Baeza, A.; Chinchilla, R.; Guillena, G.; Pastor, I. M.; Ramón, D. J. *Eur. J. Org. Chem.* **2016**, 612.

(11) (a) Xu, J.; Huang, W.; Bai, R.; Queneau, Y.; Jérôme, F.; Gu, Y. *Green Chem.* **2019**; (b) Yang, J.; De Oliveira Vigier, K.; Gu, Y.; Jérôme, F. *ChemSusChem* **2014**, *8*, 269; (c) Ma, C.-T.; Liu, P.; Wu, W.; Zhang, Z.-H. *J. Mol. Liq.* **2017**, *242*, 606; (d) Liu, P.; Hao, J.-W.; Liang, S.-J.; Liang, G.-L.; Wang, J.-Y.; Zhang, Z.-H. *Monatsh. Chem.* **2016**, *147*, 801.

(12) Xie, P.; Wang, J.; Liu, Y.; Fan, J.; Wo, X.; Fu, W.; Sun, Z.; Loh, T.-P. *Nat. Commun.* **2018**, *9*, 1321.