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Transition-Metal-Promoted Direct C–H Cyanoalkylation and Cyanoalkoxylation of Internal Alkenes *via* Radical C–C Bond Cleavage of Cycloketone Oxime Esters

Jiang Lou,[a,b] Yuan He,[a,b] Yunlong Li,[a,b] and Zhengkun Yu[a,c,*]

[a] Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian, Liaoning 116023, People′s Republic of China
[b] University of Chinese Academy of Sciences, Beijing 100049, People′s Republic of China
[c] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, People′s Republic of China
Fax: +86-411-8437-9227
E-mail: zkyu@dicp.ac.cn

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Abstract. Transition-metal-catalyzed alkyl-Heck-type cross-coupling of olefinic C−H bonds has been a challenge in the C−H activation area. Herein, we report $FeCl_3$-promoted efficient direct C−H cyanoalkylation of internal alkenes, that is, ketene dithioacetals, with cycloketone oxime esters *via* radical C−C bond cleavage under the redox-neutral conditions. With $CuCl_2$ as the catalyst under a dioxygen atmosphere direct C−H cyanoalkoxylation of the same internal alkenes was achieved. The cyanoalkylated tetrasubstituted alkene products could be diversely transformed to cyanoalkyl-funtionalized *N*- and *S*-heterocyclic compounds. The mechanistic studies have revealed that these C−H cyanoalkylation and cyanoalkoxylation reactions proceed through a radical pathway.

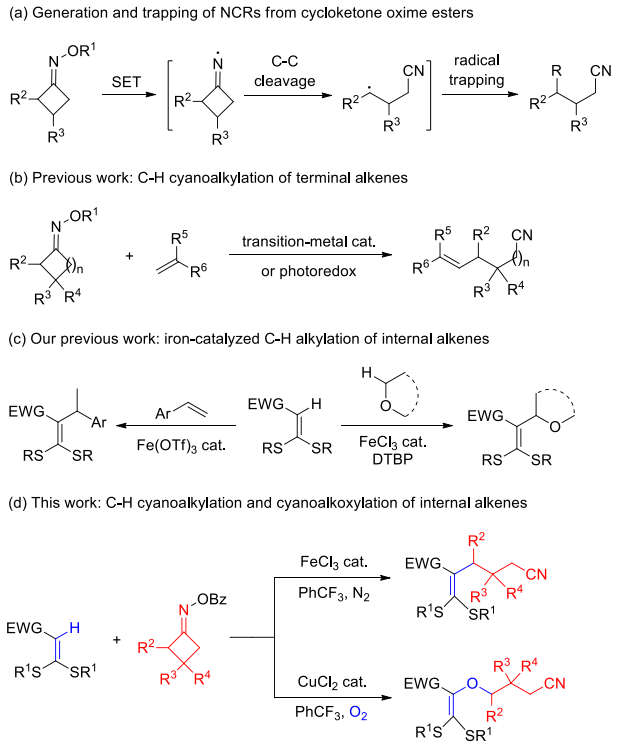
Keywords: cycloketone oxime esters; cyanoalkylation; cyanoalkoxylation; C−H functionalization; internal alkenes

Introduction

Transition-metal-catalyzed direct C−H functionalization is emerging as one of the most powerful and straightforward tools for the construction of C−C and C−heteroatom bonds.[1] In this regard, direct olefinic C−H functionalization seems to be a concise route to multisubstituted alkenes,[2] although the cross-coupling reactions of halo-,[3] oxygen-,[4] boron-,[5] silicon-,[6] and metal[7]-functionalized ketene units have been documented for the same goal. Direct C−H functionalization of olefinic C−H bonds has recently been paid much attention for the construction of multisubstituted alkenes.[2,8] However, the limitations are often encountered including functional group tolerance, substrate scopes, reaction types, time-consuming procedures, and/or use of expensive transition-metal catalysts. One of the challenges is the alkyl-Heck-type reactions of olefinic C−H bonds due to the inherent instability of the alkyl-metal species *in situ* generated from the alkylative coupling partners, which prefer *β*-H elimination over the insertion reaction with the alkene substrates.[9] Thus, new catalytic systems as well as versatile coupling partners are still highly desired for the direct olefinic C−H functionalization.

The cross-coupling of olefinic C−H bonds with alkyl radicals has recently been documented as a promising approach towards alkylated molecules *via* single-electron transfer (SET) processes.[10] Cyano-alkyl radicals generated from nitrogen-centered-radicals (NCRs), that is, iminyl radicals, have been utilized as the useful coupling partners for C−C cross-coupling reactions (Scheme 1a).[11] Such cyanoalkyl radicals resulted from transition-metal-catalyzed C–C bond cleavage of cycloketone oxime esters *via* a SET process can react with terminal alkenes or their surrogates, giving cyanoalkyl-functionalized alkenes (Scheme 1b).[12] Zard and coworkers reported the pioneering work on radical C−C bond cleavage of cyclobutanone derivatives.[13] Nishimura and Uemura, et al. documented iridium and palladium-catalyzed ring-opening reactions of cyclobutanone oxime esters through *β*-carbon scission.[14] Shi, Chen and Xiao groups reported copper-catalyzed and visible-light-driven intermolecular Heck-like coupling of cyclobutanone oxime esters with styrene derivatives, respectively.[15] Wu lab achieved a gallic acid-promoted SET process for cyclobutanone oxime activation and carbonylative alkylation of alkenes.[16] Guo, et al. Synthesized cyanoalkyl-functionalized alkenes,[17a] arenes,[17b] and *N*-heterocycles[17c,d] through iron, copper, or nickel-catalyzed C−H cyanoalkylation of *α,β*-unsaturated carboxylic acids, arenes, and *N*-heterocyclic compounds, with cycloketone oxime esters. Yu, et al.

realized photoredox-catalyzed intermolecular C−H and C−C vinylation with vinyl boronic acids.[18] Very recently, Chen, Xiao, and Guo, et al. reported the three-component radical cross-couplings of cyclobutanone oxime esters with styrenes and boronic acids[19] or with $B_2(OH)_4$ and pinacol.[20] In all the C–H functiona-lization involved ring-opening reactions of cyclo-ketone oxime esters, a cyanoalkyl motif could be incorporated into a vinylic or aromatic C–H bond. Unfortunately, the alkene substrates are only limited to terminal alkenes (Scheme 1b), and direct C–H cyanoalkylation of internal alkenes has not yet been reported.



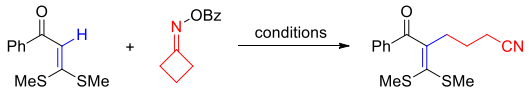
Scheme 1. C−H alkylation of alkenes.

During the ongoing investigation of direct C−H functionalization of internal alkenes, we have developed the effective strategy to activate an internal olefinic C−H bond by introducing an electron-withdrawing group (EWG), and one or two electron-donating alkylthio moieties at the two termini of an olefinic C=C bond, which has been successfully applied in the direct C−H functionalization of internal alkenes to construct C−C and C−X bonds.[21] In our hands, direct C−H alkylation of internal alkenes, that is, α-oxo ketene dithioacetals, with styrenes and activated alkanes was efficiently realized (Scheme 1c).[22] To extend the generality of such an olefinic C–H activation/functionalization strategy, we reasonably envisioned that the alkyl radicals generated from the ring-opening of strained carbocycles might be applied as the partners to be coupled with internal olefinic C–H bonds. Herein, we disclose $FeCl_3$-catalyzed direct cyanoalkylation as well as $CuCl_2$-catalyzed direct cyanoalkoxylation of internal alkenes α-oxo ketene dithioacetals *via* radical C−C bond cleavage of cycloketone oxime esters under the redox neutral conditions (Scheme 1d).

Results and Discussion

Initially, the reaction of α-benzoyl ketene di(methyl-thio)acetal (**1a**) with *O*-benzoyl cyclobutanone oxime ester **2a** was conducted to optimize the reaction conditions (Table 1). With 10 mol% $FeCl_2$ as the catalyst under a nitrogen atmosphere, the reaction of **1a** and **2a** in a 1:1.2 molar ratio underwent in 1,4-dioxane at 100 °C for 24 h, forming the target cyanoalkylation product **3a** in 31% yield (Table 1, entry 1). $FeCl_3$ exhibited a better catalytic activity

Table 1. Screening of cyanoalkylation conditions.[a]



1a 2a 3a

Entry	Catalyst	2a [equiv]	Solvent	Temp [°C]	Yield[b] [%]
1[c]	$FeCl_2$	1.2	1,4-dioxane	100	31
2	$FeBr_3$	1.2	1,4-dioxane	100	30
3	$FeCl_3$	1.2	1,4-dioxane	100	34
4	$FeCl_3$	1.2	MeCN	100	29
5	$FeCl_3$	1.2	$PhCF_3$	100	60
6	$FeCl_3$	1.2	Toluene	100	32
7	$FeCl_3$	1.5	$PhCF_3$	100	62
8	$FeCl_3$	1.8	$PhCF_3$	100	70
9	$FeCl_3$	2.0	$PhCF_3$	100	68
10	$FeCl_3$	1.8	$PhCF_3$	90	56
11	$FeCl_3$	1.8	$PhCF_3$	110	80
12	$FeCl_3$	1.8	$PhCF_3$	120	76
13[c,d]	$FeCl_3$	1.8	$PhCF_3$	110	79
14[c,e]	$FeCl_3$	1.8	$PhCF_3$	110	84 (79)[f]
15[c,g]	$FeCl_3$	1.8	$PhCF_3$	110	81
16[c,e]		1.8	$PhCF_3$	110	53

[a] Conditions: **1a** (0.1 mmol), **2a**, solvent (1.0 mL), catalyst (10 mol%), 0.1 MPa N_2, 24 h.
[b] Determined by ^1H NMR analysis using 1,3,5-trimethoxylbenzene as the internal standard.
[c] **1a** (0.3 mmol), **2a** (0.54 mmol).
[d] $PhCF_3$ (3.0 mL)
[e] $PhCF_3$ (1.5 mL).
[f] Isolated yield given in parentheses.
[g] $PhCF_3$ (1.0 mL).

than $FeCl_2$ (Table 1, entries 1-3). $PhCF_3$ as the solvent remarkably enhanced the yield to 60% (Table 1, entries 4-6). Increasing the loading of **2a** improved the reaction efficiency, and 70% yield was thus obtained for **3a** in the presence of 1.8 equiv of the oxime ester (Table 1, entries 7-9). Elevating the reaction temperature to 110 °C further increased the product yield to 80% (Table 1, entries 8 and 10-12). Scaling up the reaction to 0.3 mmol for **1a** yielded **3a**

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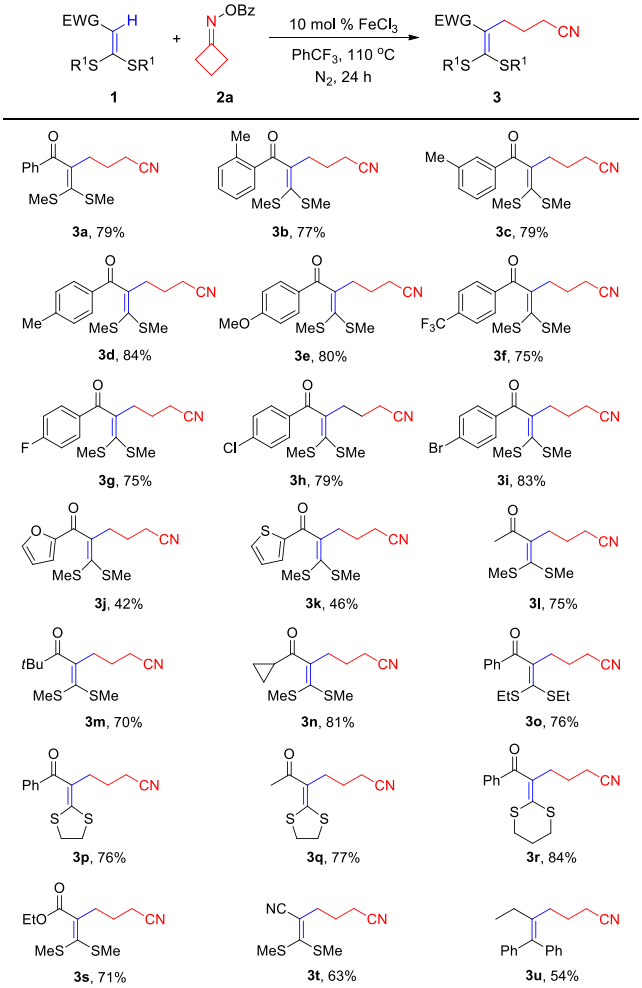
in a comparable yield (79%) (Table, entry 13), and the suitable substrate concentration was found to be 0.2 M for **1a**, leading to the target product **3a** in 79% isolated yield (Table 1, entries 13-15). It is noteworthy that the reaction also underwent in the absence of the iron salt, forming the product in 53% yield upon simple heating (Table 1, entry 16), and microwave-promoted homolytic cleavage of the N–O bond of cycloketone oxime esters could also occur in the absence of a transition-metal catalyst.[23]

Under the optimized conditions, the scope of ketene dithioacetals (**1**) was explored (Table 2). The analogs of **1a**, that is, substituted α-oxo ketene dithioacetals, exhibited diverse reactivities to form the target cyanoalkylation products of type **3** in good to excellent yields. No obvious steric effects were observed for the methyl-substituted α-benzoyl ketene dithioacetal substrates, and their reactions with **2a** afforded products **3b-d** (77-84%). The electronic effects were not obvious either between the methoxy

Table 2. Scope of ketene dithioacetals (**1**).[a]

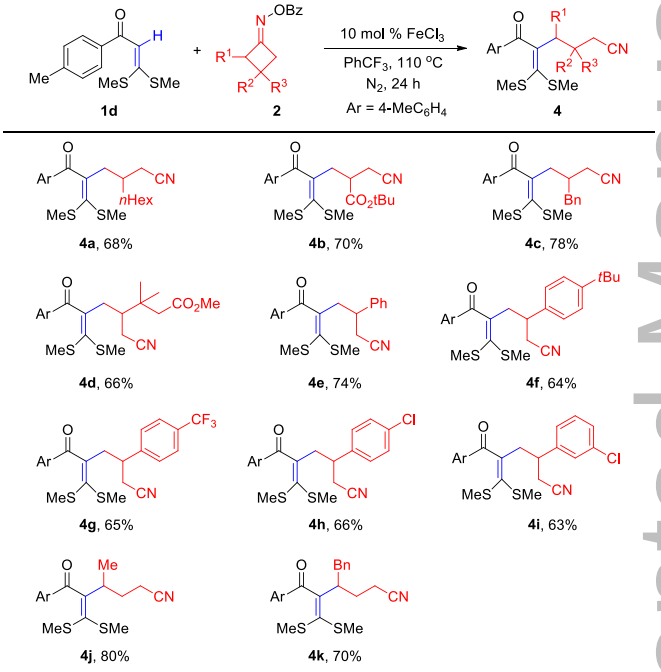


[a] Conditions: **1a** (0.3 mmol), **2a** (0.54 mmol), $FeCl_3$ (0.03 mmol), $PhCF_3$ (1.5 mL), 110 °C, 0.1 MPa N_2, 24 h. Yields refer to the isolated products.

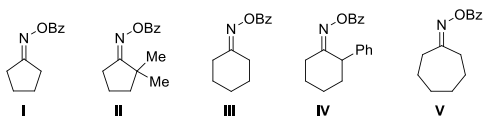
and trifluoromethyl-substituted α-benzoyl-based substrates, giving the corresponding products **3e** and **3f** in 75-80% yields. The halo-substituted α-benzoyl ketene di(methylthio)acetals efficiently underwent the reactions with **2a**, affording compounds **3g-i** in 75-83% yields. α-Heteroaroyl, that is, 2-furoyl and 2-thienoyl-bearing ketene dithioacetals reacted with **2a** less efficiently, only yielding **3j** and **3k** in 42-46% yields. Aliphatic α-acetyl, *tert*-butylcarbonyl, and cyclopropylcarbonyl-functionalized ketene di(methylthio)acetals reacted well to produce **3l-n** in 70–81% yields. α-Benzoyl ketene di(ethylthio)acetal and the cyclic α-benzoyl and α-acetyl ketene dithioacetals also efficiently reacted with **2a** to form products **3o-r** (76-84%). It is noteworthy that the α-ester, and cyano-functionalized ketene di(methylthio)acetals, and 1,1-diphenyl-1-butene could smoothly undergo the reactions with **2a**, affording the target products **3s-u** in moderate to good yields (54-71%).

Next, the protocol generality was investigated by performing the reactions of α-oxo ketene dithioacetals **1** with a variety of cyclobutanone oxime esters **2** (Table 3). Under the optimal conditions, the

Table 3. Scope of cycloketone oxime esters (**2**).[a]



[a] Conditions: **1d** (0.3 mmol), **2** (0.54 mmol), $FeCl_3$ (0.03 mmol), $PhCF_3$ (1.5 mL), 110 °C, 0.1 MPa N_2, 24 h. Yields refer to the isolated products.



reaction of α-(4-methyl)benzoyl ketene di(methylthio)acetal (**1d**) reacted with 3-hexylcyclobutanone oxime ester **2b** to afford the target cyanoalkylation product **4a** (68%). *tert*-Butyl 3-((benzoyloxy)imino)-cyclobutanecarboxylate (**2c**) did not exhibit an obvious electronic effect, and its reaction with **1d** gave compound **4b** in 70% yield. 3-Benzyl substituted cyclobutanone oxime ester **2d** underwent the reaction smoothly, efficiently yielding product **4c**

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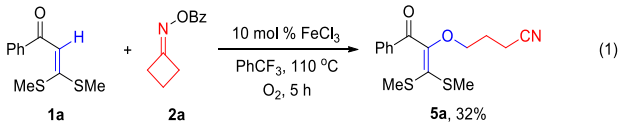
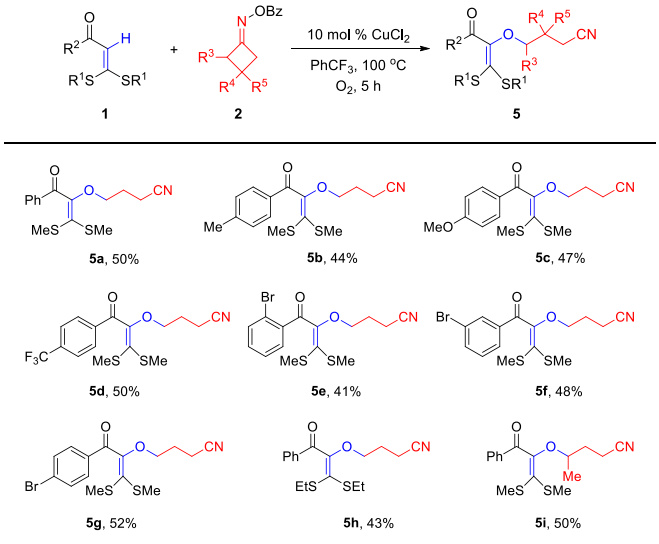
(78%). Bulky substituted *tert*-butyl and phenyl groups at the 3-position of cyclobutanone oxime esters rendered formation of products **4d** (66%) and **4e** (74%), respectively. 3-(4-*tert*-Butyl), 3-(4-trifluoromethyl), 3-(4-chloro), and 3-(3-chloro)-substituted phenyl-bearing cyclobutanone oxime esters exhibited no obvious steric/electronic effects on the reaction efficiency, and the related reactions formed **4f-i** in 63-66% yields. Unsymmetrical cyclobutanone oxime esters such as 2-methyl and 2-benzyl-substituted cyclobutanone oxime esters **2k** and **2l** could also smoothly react with **1d** to give the target products **4j** (80%) and **4k** (70%), respectively. It should be noted that the five to seven-membered *O*-benzoyl cycloketone oxime esters **I-V** could not undergo the same type of cyanoalkylation reactions under the stated conditions, which is presumably attributed to the lower reactivity of the less-strained rings than the cyclobutanone oxime esters to the iron catalysts.



(1)

During the screening of reaction conditions for the C−H cyanoalkylation of α-oxo ketene dithioacetal **1a** with oxime ester **2a**, the reaction was tested under an oxygen atmosphere. Unexpectedly, a C−H cyanoalkoxylation process occurred to form compound **5a** (32%) as the major product [Eq. (1)]. Encouraged by this finding, the conditions for the C−H cyanoalkoxylation reaction was further optimized to be 10 mol % $CuCl_2$ as the catalyst, $PhCF_3$ as the solvent, and the reaction was performed at 100 °C under an oxygen atmosphere (see the Supporting Information for details). It is noteworthy that the cyanoalkoxylation reaction could not occur without the transition-metal catalyst.

Table 4. Cyanoalkoxylation of ketene dithioacetals.[a]



[a] Conditions: **1** (0.3 mmol), **2** (0.6 mmol), $CuCl_2$ (0.03 mmol), $PhCF_3$ (3.0 mL), 100 °C, 0.1 MPa O_2, 5 h. Yields refer to the isolated products.

A variety of α-oxo ketene dithioacetals **1** were applied in the copper catalysis system with cyclobutanone oxime esters **2** as the coupling partners (Table 4). α-Benzoyl ketene dithioacetal **1a** reacted with **2a** to form the target product **5a** in 50% yield. *p*-Methyl, *p*-methoxy, and *p*-trifluoromethyl-substituted α-benzoyl ketene dithioacetals underwent the reactions smoothly, giving the corresponding products **5b-d** in 44-50% yields. *o*-, *m*-, and *p*-Bromo-functionalized α-benzoyl ketene di(methylthio)acetals reacted with **2a** to afford compounds **5e-g**

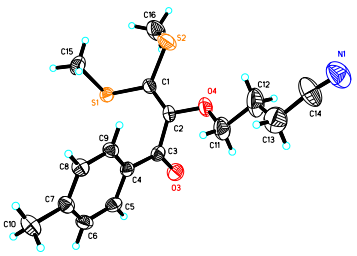
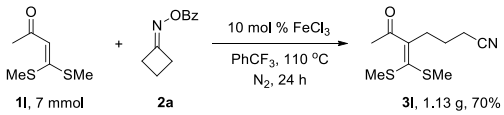


Figure 1. Molecular structure of compound **5b**.

(41-52%). α-Benzoyl ketene di(ethylthio)acetal also reacted well with **2a** to yield the target product **5h** (43%). 2-Methyl cyclobutanone oxime ester **2k** did not exhibit an obvious steric effect, its reaction with **2a** produced compound **5i** in 50% yield. The molecular structure of compound **5b** was further confirmed by the X-ray single crystallographic determination (Figure 1, see the Supporting Information for details). It is noteworthy that the cyanoalkylation products of types **3** and **4** were always accompanied as the byproducts in the reactions of **1** and **2** under an oxygen atmosphere, which



(2)

led to a tedious isolation procedure for compounds **5**, and thus diminished their isolation yields.

To demonstrate the applicability of the present synthetic protocol, gram-scale preparation of compound **3l** was carried out by means of the reaction of **1l** (7 mmol) with **2a**. Under the standard conditions, the target products **3l** was obtained in 70% yield [Eq. (2)]. The potential applications of the resultant tetrasubstituted alkene products were also explored. Treatment of compound **3a** with excess of hydrazine hydrate in refluxing toluene afforded 4-cyanoalkylpyrazole **6** in 81% yield [Eq. (3)]. In the presence of NaOH base, tetrasubstituted α-alkenoyl ketene dithioacetal **7** was produced (90%) from the condensation of compound **3l** and benzaldehyde [Eq. (4)]. Compound **7** underwent [5C+1S] annulation with $Na_2S·9H_2O$ to form cyanoalkylated 2,3-dihydrothiopyran-4-one **8** in 75% yield [Eq. (5)]. With $Pd(PPh_3)_2Cl_2$ as the catalyst in the presence of Ph_3SiH

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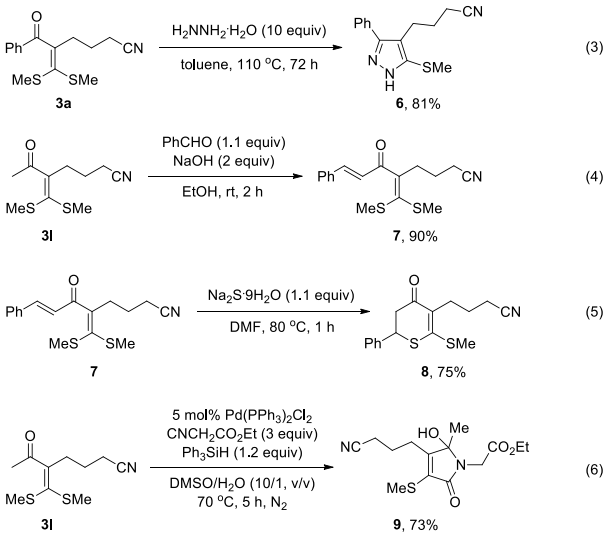
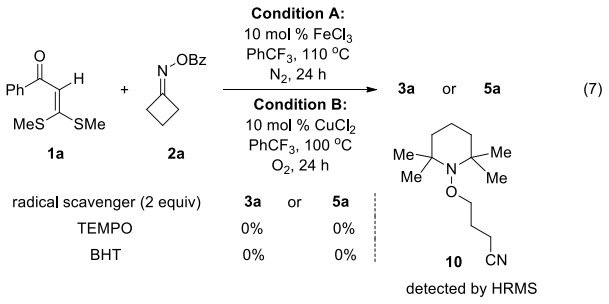
compound **3l** reacted with ethyl isocyanoacetate to yield cyanoalkyl-functionalized 5-hydroxy-α,β-unsaturated γ-lactam **9** (73%) *via* C−S bond activation/cleavage and migratory isocyanide insertion [Eq. (6)].

The control experiments were conducted to probe

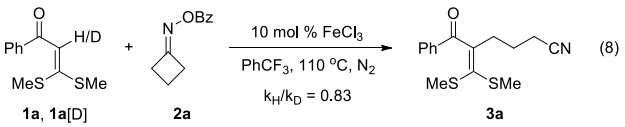


into the reaction mechanism. Addition of 2 equiv of a radical scavenger, that is, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT), into the reaction system could completely inhibit the cyanoalkylation/cyanoalkoxylation reaction of **1a** and **2a** under the standard conditions [Eq. (7)]. The adduct of the possible cyanoalkyl radical intermediate with TEMPO, that is,



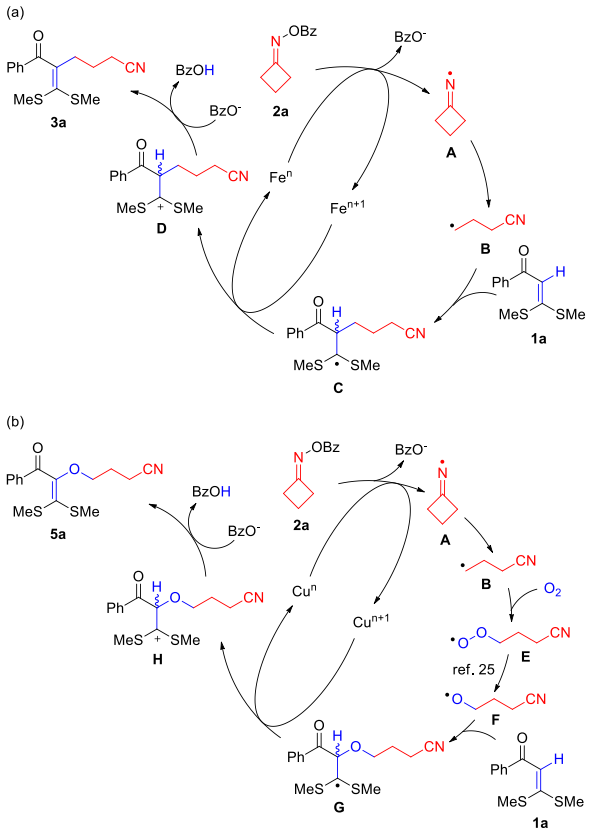
compound **10**, was detected in the reaction mixtures by high resolution mass spectrometry (see the Supporting Information for details). It should be noted that compounds of type **10** could be prepared under microwave irridiation conditions.[23] These results have implicated that both the two reactions may proceed through a radical pathway. The kinetic isotope effect (KIE) experiments of cyanoalkylation were explored by conducting the reactions of **1a** and its deuterated form **1a**[D] with **2a** under the standard conditions, respectively [Eq. (8)]. A secondary isotope effect[24] was observed with k_H/k_D = 0.83, suggesting that cleavage of the internal olefinic C−H bond in **1a** is not involved in the rate-determining step of the overall catalytic cycle.

On the basis of the present experimental results as well as previous works,[14-19,25] plausible reaction mechanisms for the cyanoalkylation and cyanoalkoxylation reactions are proposed in Scheme 2. The reaction may start with the formation of a reduced Fe^n or Cu^n catalyst, which is generated from the reduction of the $FeCl_3$ or $CuCl_2$ precatalyst under the stated conditions.[11h] In addition, simple heating facilitated the homolytic N–O bond cleavage of the cyclobutanone oxime ester to form a nitrogen-centered-radical,[23] which may initiate the catalytic



time:	10 min	20 min	30 min
for **1a**[H]	^{1}H NMR yield of **3a**:	6.5%	8.4%	15.2%
for **1a**[D]	^{1}H NMR yield of **3a**:	6.1%	10.7%	16.6%

cycle to some extent (Table 1, entry 16). For the cyanoalkylation (path a): Initially, interaction of an iron or copper catalyst with *O*-benzoyl oxime ester **2a** undergoes a single-electron transfer (SET) process to generate iminyl radical **A** and release BzO^- anion, followed by ring-opening to form γ-cyanoalkyl radical **B** *via* homolytic α,β-C−C cleavage. Addition of radical **B** to the ketene moiety of internal alkene **1a** produces a more stabilized, less reactive, and readily oxidizable radical **C**. Such a radical is further oxidized by Fe^{n+1} species to form cation **D** with concomitant regeneration of the catalytically active Fe^n



Scheme 2. Proposed mechanisms: (a) cyanoalkylation; (b) cyanoalkoxylation.

species. Subsequently, the cationic intermediate **D** undergoes hydrogen abstraction by BzO^- anion to afford the Heck-like cyanoalkylation product **3a**. However, heat-induced radical chain propagation mechanism involving iminyl radical generation under the stated conditions could not be ruled out.[12d,23] For the cyanoalkoxylation (path b): Under an oxygen atmosphere, radical **B** is readily captured by O_2 molecule to form peroxy radical **E** which is presumably reduced by Cu^n species through the Fenton-type mechanism to give alkoxy radical **F**. Addition of species **F** to internal alkene **1a** leads to radical **G**. This radical intermediate can be further oxidized by Cu^{n+1} species to give cationic intermediate **H** with concomitant regeneration of the catalytically active Cu^n species. Eventually, intermediate **H** undergoes hydrogen abstraction by BzO^- anion to provide the Heck-like cyanoalkoxylation product **5a**. It is noteworthy that the cyanoalkoxylation process is always accompanied by the cyanoalkylation product of type **3** or **4** as the byproduct under an oxygen atmosphere.

Conclusions

In summary, efficient iron-promoted C–H cyanoalkylation and copper-catalyzed C–H cyanoalkoxylation of internal alkenes with *O*-benzoyl cyclobutanone oxime esters have been realized to access multifunctionalized alkenes. The diversity of the functionality including alkene categories, carbonyl and alkylthio groups, makes these compounds good candidates to serve as precursors for further synthetic transformations. The present work has provided a strategy for alkyl-Heck-type cross-coupling of internal alkenes and offers a concise route to tetrasubstituted alkenes.

Experimental Section

General Considerations

^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a 400 MHz spectrometer and all chemical shift values refer to $CDCl_3$ ($\delta(^1H)$, 7.26 ppm and $\delta(^{13}C)$, 77.16 ppm). X-Ray crystallographic analysis was achieved by the Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Sciences. The HRMS analysis was obtained by ESI on a GC-TOF mass spectrometer. Column chromatographic purifications were performed on silica gel. All the chemical reagents were purchased from commercial sources and used as received unless otherwise indicated.

General procedure for the synthesis of cyanoalkylated ketene dithioacetals (3)

Under a nitrogen atmosphere a mixture of ketene dithioacetals (**1**) (0.30 mmol), *O*-benzoyl cyclobutanone oxime ester (**2a**) (102 mg, 0.54 mmol), and $FeCl_3$ (4.9 mg, 0.03 mmol) in 1.5 mL $PhCF_3$ was stirred at 110 °C for 24 h. After cooled to ambient temperature, EtOAc and saturated aqueous $NaHCO_3$ (10 mL each) were successively added. The organic phase was separated and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic phase was washed with water (3×10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resultant mixture was subjected to purification by column chromatography on silica gel (eluent: petroleum ether (60-90 °C)/ethyl acetate = 20:1, v/v) to afford the target product **3a**.

5-Benzoyl-6,6-bis(methylthio)hex-5-enenitrile (3a): 69 mg, 79% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86, 7.57 and 7.47 (m each, 2:1:2 H, aromatic CH), 2.79 (dd, *J* = 8.6 and 6.9 Hz, 2 H, $(C=O)CCH_2$), 2.39 (m, 5 H, CH_2CN and SMe), 2.07 (s, 3 H, SMe), 1.84 (m, 2 H, CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.59 (Cq, C=O), 144.7, 136.8 and 136.5 (Cq), 133.5, 129.0 and 128.8 (aromatic CH), 119.3 (CN), 32.8 ($(C=O)CCH_2$), 24.3 (CH_2CH_2CN), 17.2 and 16.4 (SMe), 16.9 (CH_2CN). HRMS Calcd for $C_{15}H_{17}NOS_2$ $[M+H]^+$: 292.0830; Found:292.0829.

5-(2-Methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3b): 71.2 mg, 77% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.7 Hz, 1 H, aromatic CH), 7.36 (m, 1 H, aromatic CH), 7.26 (m, 1 H, aromatic CH), 7.21 (t, *J* = 7.5 Hz, 1 H, aromatic CH), 2.81 (m, 2 H, $(C=O)CCH_2$), 2.59 (s, 3 H, Me), 2.42 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.36 (s, 3 H, SMe), 1.92 (m, 5 H, SMe and CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.6 (Cq, C=O), 146.3, 140.2, 139.3 and 137.4 (Cq), 132.2, 131.7, 129.5 and 125.3 (aromatic CH), 119.4 (CN), 33.2 ($(C=O)CCH_2$), 24.4 (CH_2CH_2CN), 21.5 (Me), 17.0 and 16.5 (SMe), 16.7 (CH_2CN). HRMS Calcd for $C_{16}H_{19}NOS_2$ $[M+H]^+$: 306.0986; Found: 306.0989.

5-(3-Methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3c): 72.4 mg, 79% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.7 Hz, 1 H, aromatic CH), 7.36 (m, 1 H, aromatic CH), 7.26 (d, *J* = 7.5 Hz, 1 H, aromatic CH), 7.21 (t, *J* = 7.5 Hz, 1 H,aromatic CH), 2.82 (m, 2 H, $(C=O)CCH_2$), 2.59 (s, 3 H, Me), 2.42 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.36 (s, 3 H, SMe), 1.90 (m, 5 H, SMe and CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.6 (Cq, C=O), 146.4, 140.2, 139.3 and 137.4 (Cq), 132.2, 131.7, 129.5 and 125.3 (aromatic CH), 119.4 (CN), 33.2 ($(C=O)CCH_2$), 24.4 (CH_2CH_2CN), 21.5 (Me), 17.0 and 16.5 (SMe), 16.7 (CH_2CN). HRMS Calcd for $C_{16}H_{19}NOS_2$ $[M+H]^+$: 306.0986; Found: 306.0984.

5-(4-Methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3d): 77.7 mg, 84% yield, yellow solid, m.p.: 42-43 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2 H, aromatic CH), 7.20 (d, *J* = 7.9 Hz, 2 H, aromatic CH), 2.70 (m, 2 H, $(C=O)CCH_2$), 2.32 (m, 8 H, CH_2CN, SMe and Me), 2.02 (s, 3 H, SMe), 1.76 (m, 2 H, CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.2 (Cq, C=O), 145.0, 144.5, 136.0 and 133.8 (Cq), 129.5 and 129.2 (aromatic CH), 119.3 (CN), 32.8 ($(C=O)CCH_2$), 24.2 (CH_2CH_2CN), 21.8 (Me), 17.2 and 16.3 (SMe), 16.8 (CH_2CN). HRMS Calcd for $C_{16}H_{19}NOS_2$ $[M+H]^+$: 306.0986; Found: 306.0986.

5-(4-Methoxybenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3e): 78 mg, 80% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 2 H, aromatic CH), 6.94 (d, *J* = 8.8 Hz, 2 H, aromatic CH), 3.86 (s, 3 H, OMe), 2.76 (m, 2 H, $(C=O)CCH_2$), 2.36 (m, 5 H, CH_2CN and

SMe), 2.10 (s, 3 H, SMe), 1.82 (m, 2 H, CH_2CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.3 (Cq, C=O), 163.9, 145.1, 135.4 and 129.1 (Cq), 131.4 and 114.1 (aromatic CH), 119.3 (CN), 55.6 (OMe), 32.8 ((C=O)CCH_2), 24.2 (*C*H$_2$CH$_2$CN), 17.2 and 16.3 (SMe), 16.7 (*C*H$_2$CN). HRMS Calcd for $C_{16}H_{19}NO_2S_2$ [M+H]$^+$: 322.0935; Found: 322.0936.

6,6-Bis(methylthio)-5-(4-(trifluoromethyl)benzoyl)-hex-5-enenitrile (3f): 81 mg, 75% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.1 Hz, 2 H, aromatic CH), 7.73 (d, *J* = 8.2 Hz, 2 H, aromatic CH), 2.80 (m, 2 H, (C=O)CCH_2), 2.40 (m, 5 H, CH_2CN and SMe), 2.05 (s, 3 H, SMe), 1.85 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.4 (Cq, C=O), 143.5, 139.8 and 139.1 (Cq), 134.4 (q, *J* = 32.4 Hz, *i*-C of $CF_3C_6H_4$), 129.1 (aromatic CH), 125.8 (q, *J* = 3.7 Hz, *o*-C of $CF_3C_6H_4$), 123.7 (q, *J* = 271.0 Hz, CF_3), 119.2 (CN), 32.9 ((C=O)C*C*H$_2$), 24.3 (*C*H$_2$CH$_2$CN), 17.1 and 16.4 (SMe), 16.9 (*C*H$_2$CN). HRMS Calcd for $C_{16}H_{16}NOF_3S_2$ [M+H]$^+$: 360.0704; Found: 360.0701.

5-(4-Fluorobenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3g): 70.5 mg, 75% yield, yellow solid, m.p.: 74-75 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 and 7,13 (m each, 2:2 H, aromatic CH), 2.77 (m, 2 H, (C=O)CCH_2), 2.38 (m, 5 H, CH_2CN and SMe), 2.08 (s, 3 H, SMe), 1.83 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.0 (Cq, C=O), 166.0 (d, *J* = 254 Hz, *i*-C of FC_6H_4), 144.2 and 137.1 (Cq), 132.8 (d, *J* = 2.9 Hz, *p*-C of FC_6H_4), 131.6 (d, *J* = 9.4 Hz, *m*-C of FC_6H_4), 119.3 (CN), 116.0 (d, *J* = 21.9 Hz, *o*-C of FC_6H_4), 32.8 ((C=O)C*C*H$_2$), 24.3 (*C*H$_2$CH$_2$CN), 17.1 and 16.3 (SMe), 16.8 (*C*H$_2$CN). HRMS Calcd for $C_{15}H_{16}NOFS_2$ [M+H]$^+$: 310.0736; Found: 310.0737.

5-(4-Chlorobenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3h): 77.5 mg, 79% yield, yellow solid, m.p.: 54-55 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.5 Hz, 2 H, aromatic CH), 7.43 (d, *J* = 8.5 Hz, 2 H, aromatic CH), 2.76 (m, 2 H, (C=O)CCH_2), 2.38 (m, 5 H, CH_2CN and SMe), 2.07 (s, 3 H, SMe), 1.81 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.3 (Cq, C=O), 143.9, 139.8, 137.6 and 135.0 (Cq), 130.3 and 129.1 (aromatic CH), 32.8 ((C=O)C*C*H$_2$), 24.2 (*C*H$_2$CH$_2$CN), 17.1 and 16.4 (SMe), 16.8 (*C*H$_2$CN). HRMS Calcd for $C_{15}H_{16}NOS_2Cl$ [M+H]$^+$: 326.0440; Found: 326.0435.

5-(4-Bromobenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (3i): 93.2 mg, 83% yield, yellow solid, m.p.: 64-65 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 2 H, aromatic CH), 7.60 (d, *J* = 8.4 Hz, 2 H, aromatic CH),2.77 (m, 2 H, (C=O)CCH_2), 2.39 (m, 5 H, CH_2CN and SMe), 2.07 (s, 3 H, SMe), 1.82 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.5 (Cq, C=O), 143.9, 137.7, 135.4 and 128.5 (Cq), 132.1 and 130.4 (aromatic CH), 119.3 (CN), 32.8 ((C=O)C*C*H$_2$), 24.3 (*C*H$_2$CH$_2$CN), 17.2 and 16.4 (SMe), 16.8 (*C*H$_2$CN). HRMS Calcd for $C_{15}H_{16}NOS_2Br$ [M+H]$^+$: 369.9935; Found: 369.9939.

5-(Furan-2-carbonyl)-6,6-bis(methylthio)hex-5-enenitrile (3j): 36 mg, 42% yield, yellow solid, m.p.: 55-56 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 0.9 Hz, 1 H, aromatic CH), 7.09 (d, *J* = 3.4 Hz, 1 H, aromatic CH), 6.55 (dd, *J* = 3.5 and 1.7 Hz, 1 H, aromatic CH), 2.78 (m, 2 H, (C=O)CCH_2), 2.40 (m, 5 H, CH_2CN and SMe), 2.16 (s, 3 H, SMe), 1.83 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 184.5 (Cq), 152.6, 143.6 and 138.8 (Cq), 119.4 (CN), 147.2, 118.5 and 112.7 (aromatic CH), 32.7 ((C=O)C*C*H$_2$), 24.3 (*C*H$_2$CH$_2$CN), 17.5 and 16.4 (SMe), 16.7 (*C*H$_2$CN). HRMS Calcd for $C_{13}H_{15}NO_2S_2$ [M+H]$^+$: 282.0622; Found: 282.0619.

6,6-Bis(methylthio)-5-(thiophene-2-carbonyl)hex-5-enenitrile (3k): 41.2 mg, 46% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 4.9 and 1.1 Hz, 1 H, aromatic CH), 7.56 (dd, *J* = 3.8 and 1.1 Hz, 1 H, aromatic CH), 7.13 (dd, *J* = 4.9 and 3.8 Hz, 1 H, aromatic CH), 2.80 (m, 2 H, (C=O)CCH_2), 2.38 (m, 5 H, CH_2CN and SMe), 2.15 (s, 3 H, SMe), 1.85 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.1 (Cq, C=O), 144.6, 143.9 and 137.3 (Cq), 134.6, 133.2 and 128.4 (aromatic CH), 32.8 ((C=O)C*C*H$_2$), 24.3 (*C*H$_2$CH$_2$CN), 17.5 and 16.4 (SMe), 16.8 (*C*H$_2$CN). HRMS Calcd for $C_{13}H_{15}NOS_3$ [M+H]$^+$: 298.0394; Found: 298.0394.

5-(Bis(methylthio)methylene)-6-oxoheptanenitrile (3l): 51.8 mg, 75% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.67 (m, 2 H, (C=O)CCH_2), 2.40 (s, 3 H, Me), 2.35 (m, 5 H, CH_2CN and SMe), 2.29 (s, 3 H, SMe), 1.78 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 203.7 (Cq, C=O), 146.9 and 137.9 (Cq), 119.4 (CN), 32.3 ((C=O)C*C*H$_2$), 30.5 (Me), 24.4 (*C*H$_2$CH$_2$CN), 17.5 and 16.7 (SMe), 16.8 (*C*H$_2$CN). HRMS Calcd for $C_{10}H_{15}NOS_2$ [M+H]$^+$: 230.0673; Found: 230.0677.

5-(Bis(methylthio)methylene)-7,7-dimethyl-6-oxooctanenitrile (3m): 57.5 mg, 70% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (t, *J* = 7.4 Hz, 2 H, (C=O)CCH_2), 2.38 (t, *J* = 7.1 Hz, 2 H, CH_2CN), 2.28 and 2.22 (s each, 3:3 H, SMe), 1.76 (m, 2 H, C*H*$_2$CH$_2$CN), 1.21 (s, 9 H, *t*Bu). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 213.9 (Cq, C=O), 147.6, 131.9 and 119.4 (Cq), 43.8 (*C*(CH$_3$)), 31.9 ((C=O)C*C*H$_2$), 27.9 (C(*C*H$_3$)), 24.0 (*C*H$_2$CH$_2$CN), 17.1 and 16.3 (SMe), 16.4 (*C*H$_2$CN). HRMS Calcd for $C_{13}H_{21}NOS_2$ [M+H]$^+$: 272.1143; Found: 272.1145.

5-(Cyclopropanecarbonyl)-6,6-bis(methylthio)hex-5-enenitrile (3n): 62.1 mg, 81% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 (dd, *J* = 8.3 and 6.9 Hz, 2 H, (C=O)CCH_2), 2.35 (m, 5 H, SMe and CH_2CN), 2.29 (s, 3 H, SMe), 2.20 (m, 1 H, cyclopropyl CH), 1.79 (m, 2 H, C*H*$_2$CH$_2$CN), 1.14 and 0.97 (m each, 2:2 H, cyclopropyl CH). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 206.3 (Cq), 147.5 and 138.0 (Cq), 119.4 (CN), 32.7 ((C=O)C*C*H$_2$), 24.5 (*C*H$_2$CH$_2$CN), 22.1, 17.5, 16.7 and 16.6 (cyclopropyl CH and *C*H$_2$CN), 12.8 (SMe). HRMS Calcd for $C_{12}H_{17}NOS_2$ [M+H]$^+$: 256.0830; Found: 256.0830.

5-Benzoyl-6,6-bis(ethylthio)hex-5-enenitrile (3o): 73.5 mg, 76% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84, 7.57 and 7.45 (m each, 2:1:2 H, aromatic CH), 2.82 (m, 4 H, SCH_2 and (C=O)CCH_2), 2.62 (q, *J* = 7.4 Hz, 2 H, SCH_2), 2.38 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 1.84 (m, 2 H, C*H*$_2$CH$_2$CN), 1.30 (t, *J* = 7.3 Hz, 3 H, CH_2CH_3), 1.02 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.8 (Cq, C=O), 147.2, 136.2 and 133.6 (Cq), 133.5, 129.1 and 128.8 (aromatic CH), 119.4 (CN), 32.7 ((C=O)C*C*H$_2$), 28.1, 27.3, 24.4, 16.7, 15.4 and 14.3 (CH_2 and CH_3). HRMS Calcd for $C_{17}H_{21}NOS_2$ [M+H]$^+$: 320.1143; Found: 320.1141.

5-(1,3-Dithiolan-2-ylidene)-6-oxo-6-phenylhexanenitrile (3p): 66.2 mg, 76% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (m, 5 H, aromatic CH), 3.38 (m, 4 H, SCH_2CH_2S), 2.73 (dd, *J* = 8.6 and 6.9 Hz, 2 H, (C=O)CCH_2), 2.21 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 1.75 (m, 2 H, C*H*$_2$CH$_2$CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6 (Cq, C=O), 162.3, 139.4 and 122.9 (Cq), 130.9, 128.4 and 127.5 (aromatic CH), 119.2 (CN), 39.1, 36.5,

33.8, 24.2 and 16.8 (CH_2). HRMS Calcd for $C_{15}H_{15}NOS_2$ $[M+H]^+$: 290.0673; Found: 290.0672.

5-(1,3-Dithiolan-2-ylidene)-6-oxoheptanenitrile (3q): 52.8 mg, 77% yield, yellow solid, m.p.: 77-78 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (m, 4 H, SCH_2CH_2S), 2.70 (m, 2 H, (C=O)CCH_2), 2.41 (t, *J* = 7.0 Hz, 2 H, CH_2CN), 2.26 (s, 3 H, Me), 1.86 (m, 2 H, C*H*$_2$$CH_2CN$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.6 (Cq, C=O), 162.6 and 122.6 (Cq), 119.3 (CN), 39.4, 35.8, 33.2, 27.2, 24.1 and 17.1 (CH_2 and CH_3). HRMS Calcd for $C_{10}H_{13}NOS_2$ $[M+H]^+$: 228.0517; Found: 228.0516.

5-(1,3-Dithian-2-ylidene)-6-oxo-6-phenylhexanenitrile (3r): 76.5 mg, 84% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78, 7.53 and 7.43 (m each, 2:1:2 H, aromatic CH), 3.01 (m, 2 H, CH_2), 2.76 (t, *J* = 6.7 Hz, 2 H, CH_2), 2.68 (m, 2 H, (C=O)CCH_2), 2.34 (t, *J* = 7.2 Hz, 2 H, CH_2), 2.11 (m, 2 H, CH_2), 1.80 (m, 2 H, CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.1 (Cq, C=O), 139.9, 137.3 and 135.4 (Cq), 132.9, 128.8 and 128.7 (aromatic CH), 119.4 (CN), 31.4, 29.4, 28.9, 24.0, 23.9 and 16.7 (CH_2). HRMS Calcd for $C_{16}H_{17}NOS_2$ $[M+H]^+$: 304.0830; Found: 304.0828.

Ethyl 2-(bis(methylthio)methylene)-5-cyanopentanoate (3s): 56 mg, 71% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.23 (q, *J* = 7.1 Hz, 2 H, OCH_2), 2.73 (m, 2 H, (C=O)CCH_2), 2.32 (m, 8 H, SMe and c), 1.82 (m, 2 H, C*H*$_2$$CH_2CN$), 1.30 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7 (Cq, C=O), 142.2 and 137.0 (Cq), 119.4 (CN), 61.3 (OCH_2), 31.9 ((C=O)C*C*H$_2$), 24.6 (*C*H_2CH_2CN), 17.8, 17.0, 16.6 and 14.2 (SMe, CH_2CH_3 and *C*H_2CN). HRMS Calcd for $C_{11}H_{17}NO_2S_2$ $[M+H]^+$: 260.0779; Found: 260.0776.

2-(Bis(methylthio)methylene)hexanedinitrile (3t): 40.4 mg, 63% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (m, 2 H, (C=O)CCH_2), 2.42 (m, 8 H, SMe and (C=O)CCH_2), 1.99 – 1.93 (m, 2 H, c). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.1 and 113.1 (Cq), 118.8 and 117.6 (CN), 31.7 ((C=O)C*C*H$_2$), 23.8 (*C*H_2CH_2CN), 18.2 and 16.5 (SMe), 17.3 (*C*H_2CN). HRMS Calcd for $C_9H_{12}N_2S_2$ $[M+H]^+$: 213.0520; Found: 213.0524.

5-Methyl-6,6-diphenylhex-5-enenitrile (3u): 45.1 mg, 54% yield, yellow solid, m.p.: 35-36 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 and 7.17 (m each, 4:6 H, aromatic CH), 2.28 (m, 2 H, (C=O)CCH_2), 2.18 (m, 4 H, C*H*$_2$$CH_3$ and CH_2CN), 1.78 (m, 2 H, (C=O)CCH_2), 1.02 (t, *J* = 7.5 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 142.9, 139.8 and 138.2 (Cq), 129.1, 129.0, 128.4, 128.2, 126.6 and 126.5 (aromatic CH), 119.7 (CN), 30.5 ((C=O)C*C*H$_2$), 25.0, 24.5, 17.1 and 13.4 (CH_2 and CH_3). HRMS Calcd for $C_{20}H_{21}N$ $[M+H]^+$: 276.1752; Found: 276.1754.

General procedure for the synthesis of cyanoalkylated ketene dithioacetals (4).

Under a nitrogen atmosphere a mixture of α-(*p*-methylbenzoyl) ketene di(methylthio)acetal (**1d**) (72 mg, 0.30 mmol), *O*-benzoyl cyclobutanone oxime ester (**2**) (0.54 mmol), and $FeCl_3$ (4.9 mg, 0.03 mmol) in 1.5 mL $PhCF_3$ was stirred at 110 °C for 24 h. After cooled to ambient temperature, EtOAc and saturated aqueous $NaHCO_3$ (10 mL each) were successively added. The organic phase was separated and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic phase was washed with water (3×10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resultant mixture was subjected to purification by column chromatography on silica gel (eluent: petroleum ether (60-90 °C)/ethyl acetate = 20:1, v/v) to afford the target product **4**.

3-Argio-5-(4-methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (4a): 80.2 mg, 68% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.2 Hz, 2 H, aromatic CH), 7.27 (d, *J* = 8.0 Hz, 2 H, aromatic CH), 2.79 (dd, *J* = 14.1 and 9.1 Hz, 1 H, CH_2CN), 2.66 (dd, *J* = 14.1 and 5.6 Hz, 1 H, CH_2CN), 2.45 (d, *J* = 5.4 Hz, 2 H, (C=O)CCH_2), 2.41 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3), 1.91 (m, 1 H, C*H*CH_2CN), 1.45 and 1.25 (m each, 2:8 H, CH_2 of *n*Hex), 0.85 (t, *J* = 6.8 Hz, 3 H, CH_3 of *n*Hex). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.2 (Cq, C=O), 144.8, 144.5, 136.8 and 133.5 (Cq), 129.5 and 129.2 (aromatic CH), 118.6 (CN), 38.1, 34.5, 33.6, 31.7, 29.2, 26.5, 22.6, 21.8, 21.3, 17.2, 16.4 and 14.1 (CH, CH_2 and CH_3). HRMS Calcd for $C_{22}H_{31}NOS_2$ $[M+H]^+$: 390.1925; Found: 390.1921.

***tert*-Butyl 2-(cyanomethyl)-4-(4-methylbenzoyl)-5,5-bis(methylthio)pent-4-enoate (4b)**: 85.6 mg, 70% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.1 Hz, 2 H, aromatic CH), 7.26 (d, *J* = 8.0 Hz, 2 H, aromatic CH), 3.05 (m, 2 H, CH_2CN), 2.82 (m, 1 H, C*H*CH_2CN), 2.67 (d, *J* = 6.2 Hz, 2 H, (C=O)CCH_2), 2.39 (6 H, Me and SMe), 2.07 (s, 3 H, SMe), 1.42 (s, 9 H, $(CH_3)_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.9 (Cq, C=O), 170.6 (Cq, C=O), 144.5, 142.4, 138.7 and 133.7 (Cq), 129.5 and 129.2 (aromatic CH), 117.8 (CN), 82.5 (Cq, *C*$(CH_3)_3$), 41.4 (CH), 34.7 ((C=O)CCH_2), 27.9 (C(*C*$H_3)_3$), 21.8, 19.2, 17.1 and 16.4 (Me and CH_2CN). HRMS Calcd for $C_{21}H_{27}NO_3S_2$ $[M+H]^+$: 406.1511; Found: 406.1511.

3-Benzyl-5-(4-methylbenzoyl)-6,6-bis(methylthio)-hex-5-enenitrile (4c): 93 mg, 78% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.1 Hz, 2 H, aromatic CH), 7.18 and 7.08 (m each, 4:3 H, aromatic CH), 2.73 (m, 3 H, CH_2), 2.55 (dd, *J* = 13.8 and 9.4 Hz, 1 H, CH_2), 2.324 (m, 7 H, Me and CH_2), 2.16 (m, 2 H, CH_2), 2.02 (s, 3 H, Me). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 196.1 (Cq, C=O), 144.5, 144.3, 138.6, 137.2 and 133.5 (Cq), 129.5, 129.2, 129.0, 128.6 and 126.6 (aromatic CH), 118.2 (CN), 39.5, 37.9, 36.6, 21.8, 20.7, 17.2 and 16.4 (CH, CH_2 and CH_3). HRMS Calcd for $C_{23}H_{25}NOS_2$ $[M+H]^+$: 396.1456; Found: 396.1454.

Methyl 4-(cyanomethyl)-3,3-dimethyl-6-(4-methylbenzoyl)-7,7-bis(methylthio)hept-6-enoate (4d): 83.1 mg, 66% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2 H, aromatic CH), 7.27 (d, *J* = 7.9 Hz, 2 H, aromatic CH), 3.49 (s, 3 H, OMe), 3.02, 2.65, 2.53, 2.29 and 1.98 (m each, 1:2:1:2:1 H, CH and CH_2), 2.40, 2.09 and 1.07 (s each, 3:3:3:3:3 H, Me). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 195.9 and 171.7 (Cq, C=O), 144.4, 144.3, 137.2 and 133.6 (Cq), 129.5 and 119.6 (aromatic CH), 51.2, 44.34, 41.9, 36.4, 33.5, 25.2, 24.6, 21.7, 17.0, 16.8 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{22}H_{29}NO_3S_2$ $[M+H]^+$: 420.1667; Found: 420.1667.

5-(4-Methylbenzoyl)-6,6-bis(methylthio)-3-phenyl-hex-5-enenitrile (4e): 85.5 mg, 74% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.2 Hz, 2 H, aromatic CH), 7.19 and 7.12 (m each, 4:3 H, aromatic CH),

3.17 (m, 1 H, CH), 3.06 (d, J = 7.5 Hz, 2 H, CH_2CN), 2.63 (m, 2 H, (C=O)CCH_2), 2.32, 2.18 and 1.95 (s each, 3 H, Me). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.2 (Cq, C=O), 144.2, 143.6, 140.7, 138.0 and 133.7 (Cq), 129.4, 129.2, 128.7, 127.7 and 127.6 (aromatic CH), 118.3 (CN), 40.9, 39.2, 24.3, 21.8, 17.2 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{22}H_{23}NOS_2$ $[M+H]^+$: 382.1299; Found: 382.1296.

3-(4-(*tert*-Butyl)phenyl)-5-(4-methylbenzoyl)-6,6-bis-(methylthio)hex-5-enenitrile (4f): 84 mg, 64% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.2 Hz, 2 H, aromatic CH), 7.14 and 7.04 (m each, 2:4 H, aromatic CH), 3.07 (m, 3 H, CH and CH_2CN), 2.58 (m, 2 H, (C=O)CCH_2), 2.26, 2.14, 1.91 and 1.14 (s each, 3:3:3:9 H, Me). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.2 (Cq, C=O), 150.4, 143.9, 143.8, 138.0, 137.6 and 133.7 (Cq), 129.2, 129.1, 127.2 and 125.5 (aromatic CH), 118.5 (CN), 40.6, 39.3, 34.4, 31.3, 24.4, 21.7, 17.2 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{26}H_{31}NOS_2$ $[M+H]^+$: 438.1925; Found: 438.1925.

5-(4-Methylbenzoyl)-6,6-bis(methylthio)-3-(4-(trifluoromethyl)phenyl)hex-5-enenitrile (4g): 88 mg, 65% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.0 Hz, 2 H, aromatic CH), 7.51 (d, J = 8.1 Hz, aromatic CH), 7.39 (d, J = 8.1 Hz, 2 H, aromatic CH), 7.18 (d, J = 8.0 Hz, 2 H, aromatic CH), 3.32 (m, 1 H, CH), 3.14 (m, 2 H, CH_2CN), 2.73 (m, 2 H, (C=O)CCH_2), 2.38, 2.25 and 2.03 (s each, 3:3:3 H, Me). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.1 (Cq, C=O), 144.6, 144.4, 142.5, 138.7 and 133.5 (Cq), 130.0 (q, J = 32.3 Hz, *i*-C of $CF_3C_6H_4$), 129.4, 129.1 and 128.2 (aromatic CH), 125.7 (q, J = 3.7 Hz, *o*-C of $CF_3C_6H_4$), 124.0 (q, J = 270.4 Hz, CF_3), 117.9 (CN), 40.9, 38.9, 24.2, 21.7, 17.1 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{23}H_{22}NOF_3S_2$ $[M+H]^+$: 450.1173; Found: 450.1170.

3-(4-Chlorophenyl)-5-(4-methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (4h): 83 mg, 66% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.1 Hz, 2 H, aromatic CH), 7.13 (m, 6 H, aromatic CH), 3.15 (m, 1 H, CH), 3.02 and 2.60 (m each, 2:2 H, CH_2), 2.32, 2.18 and 1.95 (s each, 3:3:3 H, Me). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 196.0 (Cq, C=O), 144.3, 142.9, 139.0, 138.3, 133.6 and 133.4 (Cq), 129.4, 129.1 and 128.8 (aromatic CH), 118.1 (CN), 40.4, 39.1, 24.4, 21.8, 17.1 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{22}H_{22}NOS_2Cl$ $[M+H]^+$: 416.0910; Found: 416.0908.

3-(3-Chlorophenyl)-5-(4-methylbenzoyl)-6,6-bis(methylthio)hex-5-enenitrile (4i): 79 mg, 63% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.1 Hz, 2 H, aromatic CH), 7.13 (m, 6H), 3.06 (m, 3 H, CH and CH_2CN), 2.61 (m, 2 H, (C=O)CCH_2), 2.32, 2.18 and 1.95 (s each, 3:3:3 H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.9 (Cq, C=O), 144.4, 142.7, 142.5, 138.4, 134.4 and 133.5 (Cq), 130.0, 129.3, 129.1, 127.9, 127.8 and 126.0 (aromatic CH), 118.0 (CN), 40.7, 38.9, 24.2, 21.8, 17.1 and 16.3 (CH, CH_2 and CH_3). HRMS Calcd for $C_{22}H_{22}NOS_2Cl$ $[M+H]^+$: 416.0910; Found: 416.0914.

4-Methyl-5-(4-methylbenzoyl)-6,6-bis(methylthio)-hex-5-enenitrile (4j): 77.5 mg, 80% yield, yellow solid, m.p.: 69-70 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 and 7.19 (d each, J = 8.1 Hz, 2:2 H, aromatic CH), 3.56 (m, 1 H, CH), 2.41 (m, 2 H, CH_2CN), 2.33 (d, 6 H, CH_3), 2.00 (s, 3 H, CH_3), 1.84 (m, 1 H, CHCH_2), 1.68 (m, 1 H, CHCH_2), 0.95 (d, J = 7.0 Hz, 3 H, CHCH_3). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.6 (Cq, C=O), 148.3, 144.2, 135.5 and 135.0 (Cq), 129.4 and 129.2 (aromatic CH), 119.9 (CN), 37.5, 31.5, 21.8, 18.9, 16.9, 16.4 and 15.4 (CH, CH_2 and CH_3). HRMS Calcd for $C_{17}H_{21}NOS_2$ $[M+H]^+$: 320.1143; Found: 320.1145.

4-Benzyl-5-(4-methylbenzoyl)-6,6-bis(methylthio)-hex-5-enenitrile (4k): 83 mg, 70% yield, yellow solid, m.p.: 110-111 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 and 7.14 (m, 2:7 H, aromatic CH), 3.83 (m, 1 H, CH), 2.83 (dd, J = 13.7 and 6.5 Hz, 1 H, CH_2Bn), 2.37 (m, 6 H, CH_2 and CH_3), 2.20 (s, 3 H, CH_3), 1.97 (s, 3 H, CH_3), 1.70 (m, 2 H, CH_2). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.5 (Cq, C=O), 145.9, 144.2, 138.9, 138.3 and 134.8 (Cq), 129.3, 129.2, 128.5 and 126.5 (aromatic CH), 119.7 (CN), 44.9, 40.0, 28.5, 21.8, 16.9, 16.4 and 15.5 (CH, CH_2 and CH_3). HRMS Calcd for $C_{23}H_{25}NOS_2$ $[M+H]^+$: 396.1456; Found: 396.1452.

General procedure for the synthesis of cyanoalkoxylated ketene dithioacetals (5)

Under an atmospheric dioxygen atmosphere a mixture of ketene dithioacetal (**1**) (0.3 mmol), *O*-benzoyl cyclobutanone oxime ester **2** (0.6 mmol), and $CuCl_2$ (4 mg, 0.03 mmol) in 3 mL $PhCF_3$ was stirred at 100 °C for 5 h. After cooled to ambient temperature, EtOAc and saturated aqueous $NaHCO_3$ (10 mL each) were successively added. The organic phase was separated and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic phase was washed with water (3×10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The resultant mixture was subjected to purification by column chromatography on silica gel (eluent: petroleum ether (60-90 °C)/ethyl acetate = 20:1, v/v) to afford the target product **5**.

4-((1,1-Bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)-oxy)butanenitrile (5a): 46.5 mg, 50% yield, yellow liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (m, 2 H, aromatic CH), 7.59 (t, J = 7.4 Hz, 1 H, aromatic CH), 7.49 (t, J = 7.6 Hz, 2 H, aromatic CH), 3.89 (t, J = 5.6 Hz, 2 H, OCH_2), 2.57 (t, J = 7.2 Hz, 2 H, CH_2CN), 2.39 (s, 3 H, SMe), 2.05 (s, 3 H, SMe), 1.97 (m, 2 H, OCH_2CH_2). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 191.4 (Cq, C=O), 152.5, 136.6 and 121.5 (Cq), 133.9, 129.2 and 128.8 (aromatic CH), 119.2 (CN), 68.7 (OCH_2), 25.9 (OCH_2CH_2), 17.8, 15.7 and 14.1 (SMe and CH_2CN). HRMS Calcd for $C_{15}H_{17}NO_2S_2$ $[M+H]^+$: 308.0779; Found: 308.0779.

4-((1,1-Bis(methylthio)-3-oxo-3-(p-tolyl)prop-1-en-2-yl)-oxy)butanenitrile (5b): 43.2 mg, 44% yield, yellow solid, m.p.: 43-44 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.1 Hz, 2 H, aromatic CH), 7.32 (d, J = 8.0 Hz, 2 H aromatic CH), 3.91 (t, J = 5.6 Hz, 2 H, OCH_2), 2.59 (t, J = 7.2 Hz, 2 H, CH_2CN), 2.45 and 2.42 (s each, 3:3 H, SMe and Me), 2.10 (s, 3 H, SMe), 1.98 (m, 2 H, OCH_2CH_2). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.9 (Cq, C=O), 152.8, 145.0, 133.9 and 120.0 (Cq), 129.5 and 129.3 (aromatic CH), 119.1 (CN), 68.5 (OCH_2), 25.9, 21.8, 17.8, 15.5 and 14.0 (CH_2 and CH_3). HRMS Calcd for $C_{16}H_{19}NO_2S_2$ $[M+H]^+$: 322.0935; Found: 322.0935.

CCDC-1873200 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge

Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

4-((3-(4-Methoxyphenyl)-1,1-bis(methylthio)-3-oxo-prop-1-en-2-yl)oxy)butanenitrile (5c): 48.2 mg, 47% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 and 6.96 (m each, 2:2 H, aromatic CH), 3.88 (m, 5 H, OMe and OCH_2), 2.57 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.38 and 2.08 (s each, 3:3 H, SMe), 1.96 (m, 2 H, OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.0 (Cq, C=O), 164.4, 153.1, 129.3 and 119.3 (Cq), 131.8 and 114.2 (aromatic CH), 119.2 (CN), 68.6 (OCH_2), 55.7 (OMe), 25.9, 17.9, 15.6 and 14.1 (CH_2 and CH_3). HRMS Calcd for $C_{16}H_{19}NO_3S_2$ $[M+H]^+$: 338.0885; Found: 338.0888.

4-((1,1-Bis(methylthio)-3-oxo-3-(4-(trifluoromethyl)-phenyl)prop-1-en-2-yl)oxy)butanenitrile (5d): 57 mg, 50% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 7.9 Hz, 2 H, aromatic CH), 7.74 (d, *J* = 7.9 Hz, 2 H, aromatic CH), 3.91 (t, *J* = 5.6 Hz, 2 H, OCH_2), 2.59 (t, *J* = 7.1 Hz, 2 H, CH_2CN), 2.41 (s, 3 H, SMe), 2.00 (m, 5 H, SMe and OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.2 (Cq, C=O), 151.5, 139.8 and 125.3 (Cq), 134.7 (q, *J* = 32.4 Hz, *i*-C of $CF_3C_6H_4$), 129.3 (aromatic CH), 125.8 (q, *J* = 3.7 Hz, *o*-C of $CF_3C_6H_4$), 123.6 (q, *J* = 271.0 Hz, CF_3), 119.1 (CN), 69.1 (OCH_2), 25.9, 17.8, 15.8 and 14.1 (CH_2 and CH_3). HRMS Calcd for $C_{16}H_{16}NO_2F_3S_2$ $[M+H]^+$: 376.0653; Found: 376.0655.

4-((3-(2-Bromophenyl)-1,1-bis(methylthio)-3-oxo-prop-1-en-2-yl)oxy)butanenitrile (5e): 48.2 mg, 41% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.9 and 0.8 Hz, 1 H, aromatic CH), 7.47 (dd, *J* = 7.6 and 1.6 Hz, 1 H, aromatic CH), 7.37 (td, *J* = 7.5 and 1.0 Hz, 1 H, aromati CH), 7.29 (td, *J* = 7.7 and 1.7 Hz, 1 H, aromatic CH), 3.96 (t, *J* = 5.6 Hz, 2 H, OCH_2), 2.50 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.43 (s, 3 H, SMe), 2.04 (s, 3 H, SMe), 1.96 (m, 2 H, OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.1 (Cq, C=O), 151.1, 140.8, 136.3 and 120.5 (Cq), 119.5 (CN), 133.7, 131.8, 130.1 and 127.2 (aromatic CH), 69.1 (OCH_2), 26.2, 17.9, 16.4 and 14.1 (CH_2 and CH_3). HRMS Calcd for $C_{15}H_{16}NO_2S_2Br$ $[M+H]^+$: 385.9884; Found: 385.9881.

4-((3-(3-Bromophenyl)-1,1-bis(methylthio)-3-oxo-prop-1-en-2-yl)oxy)butanenitrile (5f): 56.2 mg, 48% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (t, *J* = 1.7 Hz, 1 H, aromatic CH), 7.82 (d, *J* = 7.8 Hz, 1 H, aromatic CH), 7.71 (m, 1 H, aromatic CH), 7.37 (t, *J* = 7.9 Hz, 1 H, aromatic CH), 3.89 (t, *J* = 5.6 Hz, 2 H, OCH_2), 2.59 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.41 (s, 3 H, SMe), 2.07 (s, 3 H, SMe), 1.98 (m, 2 H, OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 189.9 (Cq, C=O), 151.5, 138.6, 124.4 and 123.1 (Cq), 136.5, 131.8, 130.4 and 127.6 (aromatic CH), 69.1 (OCH_2), 25.9, 17.8, 15.8 and 14.2 (CH_2 and CH_3). HRMS Calcd for $C_{15}H_{16}NO_2S_2Br$ $[M+H]^+$: 385.9884; Found: 385.9886.

4-((3-(4-Bromophenyl)-1,1-bis(methylthio)-3-oxo-prop-1-en-2-yl)oxy)butanenitrile (5g): 61 mg, 52% yield, yellow solid, m.p.: 61-62 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.5 Hz, 2 H, aromatic CH), 7.62 (d, *J* = 8.5 Hz, 2 H, aromatic CH), 3.88 (t, *J* = 5.6 Hz, 2 H, OCH_2), 2.58 (t, *J* = 7.2 Hz, 2 H, CH_2CN), 2.39 (s, 3 H, SMe), 2.06 (s, 3 H, SMe), 1.95 (m, 2 H, OCH_2CH_2). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 190.3 (Cq, C=O), 151.8, 135.5, 129.0 and 123.1 (Cq), 132.2 and 130.6 (aromatic CH), 119.2 (CN), 68.9 (OCH_2), 25.9, 17.8, 15.7 and 14.1 (CH_2 and CH_3). HRMS Calcd for $C_{15}H_{16}NO_2S_2Br$ $[M+H]^+$: 385.9884; Found: 385.9880.

4-((1,1-Bis(ethylthio)-3-oxo-3-phenylprop-1-en-2-yl)-oxy)butanenitrile (5h): 44 mg, 43% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 2 H, aromatic CH), 7.59 (t, *J* = 7.4 Hz, 1 H, aromatic CH), 7.48 (t, *J* = 7.6 Hz, 2 H, aromatic CH), 3.87 (t, *J* = 5.6 Hz, 2 H, OCH_2), 2.88 (q, *J* = 7.3 Hz, 2 H, SCH_2), 2.58 (m, 4 H, SCH_2 and CH_2CN), 1.95 (m, 2 H, OCH_2CH_2), 1.31 (t, *J* = 7.3 Hz, 3 H, CH_2CH_3), 1.04 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 191.6 (Cq, C=O), 154.3, 136.4 and 118.5 (Cq), 133.9, 129.3 and 128.8 (aromatic CH), 119.2 (CN), 68.9 (OCH_2), 28.4, 26.6, 25.9, 15.55, 14.2 and 14.0 (CH_2 and CH_3). HRMS Calcd for $C_{17}H_{21}NO_2S_2$ $[M+H]^+$: 336.1092; Found: 336.1090.

4-((1,1-Bis(methylthio)-3-oxo-3-phenylprop-1-en-2-yl)oxy)pentanenitrile (5i): 49 mg, 50% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2 H, aromatic CH), 7.59 (t, *J* = 7.0 Hz, 1 H, aromatic CH), 7.48 (t, *J* = 7.7 Hz, 2 H, aromatic CH), 4.00 (m, 1 H, OCH), 2.42 (m, 5 H, SMe and CH_2), 2.05 (s, 3 H, SMe), 1.88 (m, 2 H, CH_2), 1.22 (d, *J* = 6.2 Hz, 3 H, $CHCH_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 191.6 (Cq, C=O), 151.9, 136.4 and 122.1 (Cq), 133.9, 129.2 and 128.8 (aromatic CH), 119.5 (CN), 75.6 (OCH), 32.3, 20.1, 18.0, 15.5 and 13.2 (CH_2 and CH_3). HRMS Calcd for $C_{16}H_{19}NO_2S_2$ $[M+H]^+$: 322.0935; Found: 322.0934.

Condensation of cyanoalkylation product 3a with hydrazine hydrate

A mixture of **3a** (58 mg, 0.20 mmol), hydrazine hydrate (118 mg, 2.0 mmol, aq 85%) in toluene (2 mL) was stirred in a 10 mL sealed tube at 110 °C. When TLC monitoring on silica gel indicated complete consumption of the substrate over a period of 72 h, the reaction mixture was cooled to ambient temperature, and all the volatiles were removed under reduced pressure. The resultant residue was purified by silica gel column chromatography (eluent: petroleum ether (60-90 °C)/ethyl acetate = 10:1, v/v) to afford the target product **6**.

4-(5-(Methylthio)-3-phenyl-1H-pyrazol-4-yl)butane-nitrile (6): 42 mg, 81% yield, white solid, m.p.: 102-103 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (brs, 1 H, NH), 7.42 (m, 5 H, aromatic CH), 2.75 (m, 2 H, CH_2CN), 2.42 (s, 3 H, SMe), 2.25 (t, *J* = 7.2 Hz, 2 H, CCH_2), 1.83 (m, 2 H, CH_2CH_2CN). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.4 and 143.8 (Cq), 130.6 and 116.6 (Cq), 129.1, 128.7 and 127.5 (aromatic CH), 119.5 (CN), 25.9, 22.6, 17.2 and 16.7 (CH_2 and CH_3). HRMS Calcd for $C_{14}H_{15}N_3S$ $[M+H]^+$: 258.1065; Found: 258.1062.

General procedure for the synthesis of *α*-cinnamyl ketene dithioacetal (7)

A mixture of 5-(bis(methylthio)methylene)-6-oxoheptanenitrile (**3l**) (460 mg, 2.0 mmol), benzaldehyde (233 mg, 2.2 mmol) and NaOH (160 mg, 4.0 mmol) in EtOH (5 mL) was stirred at ambient temperature for 2 h. After **3l** was completely consumed as indicated by TLC monitoring after 2 h, 20 mL of water was added, extracted with

CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with saturated aqueous NaCl (3×15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure to yield the crude product, which was purified by silica gel chromatography (eluent, petroleum ether/ethyl acetate: 5/1, v/v) to afford the target product **7**.

(*E*)-5-(Bis(methylthio)methylene)-6-oxo-8-phenyloct-7-enenitrile (7): 572 mg, 90% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 and 7.37 (m each, 2:3 H, aromatic CH), 7.45 and 6.90 (d each, *J* = 16.1 Hz, 1:1 H, CH), 2.84–2.69 (m, 2 H, CCH_2), 2.42–2.32 (m, 5 H, SMe and CH_2), 2.26 (s, 3 H, SMe), 1.89–1.74 (m, 2 H, CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 195.4 (Cq, C=O), 145.7, 138.6 and 134.5 (Cq), 143.0 and 126.6 (CH), 130.5, 129.0 and 128.3 (aromatic CH), 119.3 (CN), 32.8, 24.3, 17.5, 16.7 and 16.5 (CH_3 and CH_2). HRMS Calcd for $C_{17}H_{19}NOS_2$ $[M+H]^+$: 318.0986; Found: 318.0983.

General procedure for the synthesis of 2,3-dihydrothiopyran-4-one (8)

A mixture of (*E*)-5-(bis(methylthio)methylene)-6-oxo-8-phenyloct-7-enenitrile (7) (64 mg, 0.2 mmol) and $Na_2S·9H_2O$ (53 mg, 0.22 mmol) in DMF (2 mL) was stirred at 80 °C for 1 h. After cooled to ambient temperature, the reaction was quenched with saturated aqueous Na_2CO_3 (10 mL) and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with brine (3×20 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to give a yellow residue. Purification was carried out by flash silica gel chromatography (eluent, petroleum ether/ethyl acetate: 20/1, v/v) to afford the target product **8**.

4-(6-(Methylthio)-4-oxo-2-phenyl-3,4-dihydro-2H-thiopyran-5-yl)butanenitrile (8): 46 mg, 75% yield, yellow solid, m.p.: 97-98 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.30 (m, 5 H, aromatic CH), 4.61 (dd, *J* = 14.1 and 2.9 Hz, 1 H, CH), 3.14 (dd, *J* = 16.3 and 14.2 Hz, 1 H, $CHCH_2$), 2.97 (dd, *J* = 16.4 and 3.0 Hz, 1 H, $CHCH_2$), 2.79–2.63 (m, 2 H, CCH_2), 2.52 (s, 3 H, CH_3), 2.36 (t, *J* = 7.3 Hz, 2 H, CH_2CN), 1.82 (m, 2 H, CH_2CH_2CN). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.4 (Cq, C=O), 158.5, 137.3 and 128.3 (Cq), 129.2, 128.9 and 127.7 (aromatic CH), 120.0 (CN), 46.8, 44.5, 27.0, 23.9, 17.1 and 15.5 (CH, CH_2 and CH_3). HRMS Calcd for $C_{16}H_{17}NOS_2$ $[M+H]^+$: 304.0830; Found: 304.0829.

General procedure for the synthesis of 4-cyanoalkyl-5-hydroxy-*α*,*β*-unsaturated *γ*-lactam (9)

Under a nitrogen atmosphere, a mixture of compound **3l** (46 mg, 0.2 mmol), triphenylsilane (62 mg, 0.24 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.01 mmol), ethyl 2-isocyanoacetate (66 μL, 0.6 mmol) in DMSO (2.0 mL)/H_2O (0.5 mL) was stirred at 70 °C for 5 h. After **1l** was completely consumed by TLC monitoring on silica gel, the reaction was continued for 1h in air. The reaction mixture was then poured into ice water (30 mL), extracted with CH_2Cl_2 (3×15 mL). The combined organic extracts were washed with brine (3×15 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography (eluent, petroleum ether/ethyl acetate: 12/1, v/v) to afford the target product **9**.

Ethyl 2-(3-(3-cyanopropyl)-2-hydroxy-2-methyl-4-(me-thylthio)-5-oxo-2,5-dihydro -1H-pyrrol-1-yl)acetate (9): 46 mg, 73% yield, yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 and 3.89 (d each, J = 17.8 Hz, 1:1 H, NCH_2), 4.18 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 3.63 (s, 1 H, OH), 2.69 (m, 1 H, CH2), 2.54–2.38 (m, 6 H, SMe and CH2), 2.12–1.93 (m, 2 H, CH2), 1.43 (s, 3 H, CH3), 1.27 (t, *J* = 7.1 Hz, 3 H, CH_2CH_3). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.7 and 167.3 (Cq, C=O), 158.4 and 128.7 (Cq), 119.3 (CN), 89.3 (COH), 62.1 (OCH_2), 40.2 (NCH_2), 25.4, 23.9, 21.8, 17.3, 15.1 and 14.2 (CH_3 and CH_2). HRMS Calcd for $C_{14}H_{20}N_2O_4S$ $[M+Na]^+$: 335.1041; Found: 335.1037.

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FULL PAPER

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