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Nucleophilic α-addition to β-nitroacrylates: application to the synthesis of α-thioacrylates

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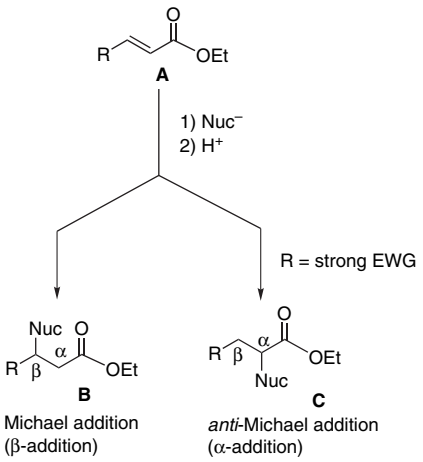
Abstract—The α-addition of alkyl or aryl thionucleophiles to β-nitro-α,β-unsaturated alkenoates in THF in the presence of TEA or DBU gave access to the α-thio-α,β-unsaturated alkenoates. The reaction occurred via formation of β-nitro-α-thioalkanoates and concomitant elimination of nitrous acid from the α-adducts.

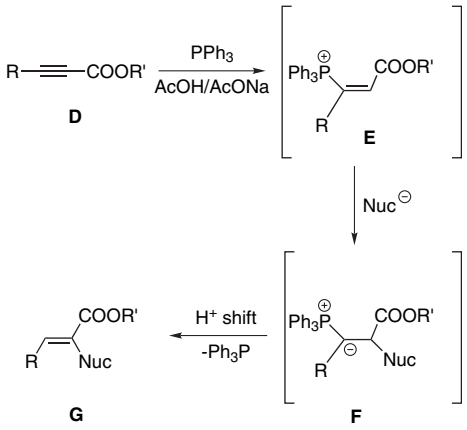
1. Introduction

The Michael reaction is one of the most versatile methods in organic synthesis for the construction of new carbon–carbon or carbon–heteroatom bonds.[1] The Michael addition between various nucleophiles and α,β-unsaturated alkenoates **A** (Scheme 1) in most cases occurs regioselectively at the β-position to give products of type **B** (β-adduct). The regioselectivity of the Michael reaction can be inverted by attaching groups with strongly electron-withdrawing properties at the β carbon, which leads to the formation of the α-substituted products[2–4] of type **C** (α-adduct).



Scheme 1. The α- vs β-addition of the nucleophiles to Michael acceptors.

Recently, Trost and Dake[5] showed that the regioselectivity of Michael additions can be redirected from the classical β-addition to the abnormal α-addition when triphenylphosphine is used as a catalyst. They have shown that PPh_3-catalyzed addition of amines to 2-alkynoates esters **D** occurs at the α-carbon to give 2-amino alkenoates **G**. The overall α-addition resulted from β-addition of PPh_3 to alkynoates **D**, which led to the formation of the vinyl phosphonium intermediate **E**. The latter serves as an α-Michael acceptor (relative to the carbonyl group) and reacts with the nucleophile to give intermediate **F**, which furnishes, after elimination of triphenylphosphine, product **G** with a net result being overall α-substitution (Scheme 2).



Scheme 2. The α-addition of nucleophiles to 2-alkynoates in the presence of PPh_3.

Our recent theoretical studies of the Michael reaction reveal that the reaction barriers to α- vs β-addition decrease as the strength of the electron-withdrawing group on the β carbon increases. For those with sufficiently strong electron-withdrawing groups, α-addition becomes favoured.[6] For instance, it was predicted that methyl 3-nitropropenoate should react with nucleophiles to give an α-substituted

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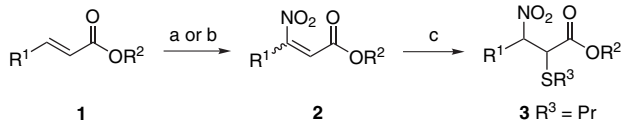
adduct.[6a] On the basis of the theoretical calculations we rationalized that 3-nitro-2-alkenoates would serve as a convenient substrate leading to the formation of *anti*-Michael adducts. After in situ elimination of nitrous acid, such an adduct would be expected to provide access to α-substituted α,β-unsaturated alkenoates, which can serve as precursors for further chemical transformations. Herein, we report application of β-nitroacrylates as α-Michael acceptors in a new approach for the synthesis of α-thioacrylates through an in situ elimination of nitrous acid from the α-adducts.

Very recently, Ballini and his group[7] utilized reactions of β-nitroacrylic esters with C-nucleophiles for the synthesis of polyfunctionalized α,β-unsaturated esters prepared via an α-substitution and elimination process. The α-addition of organozinc cuprates, dialkylzinc reagents or trimethylaluminium to β-nitroacrylate esters has been used in the synthesis of optically active β-amino acids.[8] Addition of indoles to the α-carbon of β-nitroacrylates has also been reported.[9]

The α-thioacrylates have been used as Michael acceptors[10] and as dienophiles in Diels–Alder reactions.[11] They have been synthesized by procedures that involve multistep reactions such as: (i) condensation of α-phenylthio acetate carbanions with aldehydes and ketones,[12] (ii) Pummerer-style dehydration of sulfoxides,[13] (iii) *ipso*-substitution of the bromine in α-bromo Michael acceptors,[14] or (iv) nucleophilic substitution—Wittig reaction of α-hypervalent iodine functionalized phosphonium ylide.[15] The above procedures often require harsh conditions and frequently give products with low selectivity.

2. Results and discussion

The starting 3-nitroacrylates **2a–b** were prepared in 70–75% yield by reactions of the corresponding acrylic esters **1a–b** with $NaNO_2$–ceric ammonium nitrate (CAN) followed by dehydration ($MsCl/Et_3N/CH_2Cl_2/-20\ ^\circ C$) as reported recently (Scheme 3).[16] The β-nitrocinnamate derivatives **2c–d** were obtained directly from the corresponding cinnamates **1c–d** with $NaNO_2$–CAN in 57–65% yields. Attempts to prepare the 4-nitrocinnamate analogue using this method were unsuccessful. The 3-nitroacrylic esters **2a** and **2b** were obtained as single *E* isomers while **2c** and **2d** were obtained as a mixture of *E* and *Z* isomers in ratios of 2:1 and 5:1, respectively.



Scheme 3. α-Addition of thiolate nucleophiles to β-nitroacrylates. Reagents and condition: (a) $CAN/NaNO_2/CH_3CN$; (b) (i) $CAN/NaNO_2/CH_3CN$, (ii) $MsCl/Et_3N/CH_2Cl_2/20\ ^\circ C$; (c) R^3SH/Et_3N (cat)/THF rt.

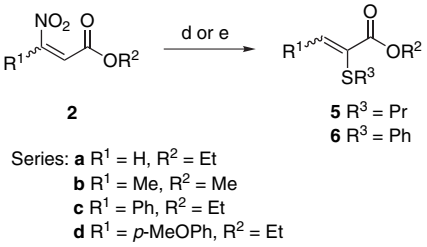
Treatment of 3-nitroacrylates **2a**(*E*) (Scheme 3) with propanethiol in the presence of a catalytic amount of triethylamine (TEA) in tetrahydrofuran (THF) at ambient temperature provided the α-substituted product **3a** in 78% yield (Table 1, entry 1). Analogous treatment of 3-nitrocrotonate **2b**(*E*) and 3-nitrocinnamate **2c–d**(*E*/*Z*) afforded α-adducts **3b–d** as a 1:1 mixture of diastereomers (Table 1, entries 2–4). In the case of **3b**, the diastereomers were separated by column chromatography. The ^1H NMR spectrum for **3b** verified that the adduct was derived from an α-addition since the presence of two sets of signals corresponding to the hydrogens at C2 (d, J=10.5 Hz) and C3 (dq, J=10.5, 7,0 Hz) instead of signals for two hydrogens at C2 was observed.

Table 1. Reaction parameters for the α-addition of thiolate nucleophiles to β-nitroacrylates

Entry	Product	Yield (%)[a]	Condition[b]
1	**3a**	78	c
2	**3b**	84	c
3	**3c**	79	c
4	**3d**	78	c
5	**4c**	86	c
6	**4d**	72	c

[a] Isolated yield.
[b] See Scheme 3.

Contrary to the reactions with propanethiol, treatment of β-nitroacrylates with thiophenol produced the stable α-adducts **4c** and **4d** only in the case of β-nitrocinnamic substrates **2c–d** (Table 1, entries 5 and 6). Treatment of aliphatic **2a** and **2b** with thiophenol initially produced the *anti*-Michael addition products **4a** and **4b** (TLC) as well, but these adducts underwent subsequent in situ elimination of HNO_2 to produce α-thioacrylates **6a** and **6b** even in the absence of TEA (Scheme 4).



Scheme 4. Synthesis of α-thioacrylates. Reagents and condition: (d) R^3SH/Et_3N/THF rt; (e) R^3SH/DBU/THF (60 °C oil bath).

In order to optimalize the formation of α-thio-α,β-unsaturated alkanoates **5** and **6** we tested different reaction conditions, such as various ratios of the substrates to nucleophiles and base, as well as different solvents and temperature. We found that for the reaction of aliphatic alkenoates **2a** and **2b** with propanethiol, the highest yields of **5a** and **5b** were obtained with a 1:1.2:1 ratio of **2a** or **2b**/propanethiol/TEA in THF at ambient temperature (Table 2, entries 1 and 2). Using the same reaction conditions the α-phenylthioalkenoates **6a** and **6b** were also obtained (Table 2, entries 5 and 6) in high yield. The α-thiocrotonates **5b** and **6b** were isolated as *Z* isomers. The *Z*-stereochemistry of **6b** was established by comparison of the chemical shift of β-vinyl proton signal, which occurs at a lower field (δ 7.48) than of the corresponding *E* isomer (δ 6.54) with the literature values.[13d,15a]

Table 2. Reaction parameters for the synthesis of α-thioacrylates

Entry	Product	Yield (%)[a]	Condition[b]	Ratio[c] of *E*/*Z*
1	**5a**	82	d	—
2	**5b**	88	d	0:1
3	**5c**	79	e	1:0
4	**5d**	40	e	1:0
5	**6a**	78	d	—
6	**6b**	84	d	0:1
7	**6c**	78	e	0:1
8	**6d**	44	e	0.6:1

[a] Isolated yield.
[b] See Scheme 4.
[c] Estimated by ^{1}H NMR.

In the reaction of cinnamates **2c–d**, the propylthio-**3c–d** as well as phenylthio α-adducts **4c–d** were stable, so stronger base (DBU) and longer reaction times and/or higher temperatures were necessary for the conversion to α-thioacrylates **5** and **6** (Scheme 4). Thus, treatment of **2c** (*E*/*Z*, 1.0:0.5) with propanethiol in the presence of 1.2 equiv DBU in THF at 60 °C for 24 h led to the formation of α-(propanethiol)cinnamate **5c** as a single *E* isomer in 79% yield. Analogous treatment of **2c** with thiophenol (4 h) afforded **6c** in 82% yield as a mixture of isomers (*E*/*Z*, 0.2:1.0).[13d,15a] Prolonged heating led to conversion of the isomers resulting in formation of the more stable *Z* isomer, which was isolated in 78% yield (Table 2, entries 3 and 7). In both the cases the intermediary α-addition products **3c** or **4c** were also isolated in low yields from the reaction mixture (<10%). Interestingly, even treatment of 3-nitro-*p*-methoxycinnamate **2d** with propanethiol as well as with thiophenol led to the formation of quite stable α-adducts **3d** and **4d**, which required heating to convert them to the α-thiocinnamates **5d**(*E*) or **6d** (*E*/*Z*; 0.6:1.0) isomers (Table 2, entries 4 and 8).

It was found that addition of thionucleophiles to β-nitroacrylic esters **2a–d** in THF with an equivalent amount of base affords α-thioacrylates **5** or **6** in a one pot process via *anti*-Michael addition with the formation of β-nitro-α-thio intermediates **3** or **4** and subsequent elimination of nitrous acid. These results indicate that the kind of substituents at the β-position (alkyl or aryl) in β-nitroacrylates and the pK_a of the thionucleophiles are two important factors contributing to the stabilization of α-addition products **3** and **4**.

3. Conclusion

In summary, we have developed an efficient method for the synthesis of α-alkyl(or aryl)thio-α,β-unsaturated alkenoates via α-addition of nucleophiles to β-nitroalkenoates, followed by in situ elimination of nitrous acid from the resulting α-adducts in basic conditions.

4. Experimental

4.1. General

THF was distilled from sodium benzophenone under nitrogen. ^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were determined in $CHCl_3$ on a Bruker Avance-400 instrument. When the spectra were recorded for the mixture of isomers the signals for the respective isomers were assigned based on the COSY and HETCOR experiments. Mass spectra (MS) and HRMS were obtained with electron impact (EI, 20 eV) technique. Merck kieselgel 60-F_{254} sheets were used for TLC and products were detected with 254 nm light. Merck kieselgel 60 (230–400 mesh) was used for column chromatography.

4.1.1. Ethyl 3-nitro-2-propylthiopropanoate (3a) (procedure A). Propanethiol (0.15 mL, 126 mg, 1.66 mmol) and TEA (24 μL, 17 mg, 0.17 mmol) were added to a stirred solution of **2a** (60 mg, 0.41 mmol) in THF (2 mL) at ambient temperature. After 10 min, the resulting mixture was evaporated to dryness under vacuum and the oily residue was column chromatographed (hexane→5% EtOAc/hexane) to give **3a** (71 mg, 78%) as an oil: IR ($CHCl_3$) 1735 (C=O), 1550 (NO_2) cm^{-1}; ^{1}H NMR δ 1.01 (t, *J*=7.3 Hz, 3H), 1.32 (t, *J*=7.1 Hz, 3H), 1.64 (dq, *J*=2.1, 7.3 Hz, 2H), 2.68 (dt, *J*=2.1, 7.3 Hz, 2H), 3.94 (dd, *J*=10.2, 5.1 Hz, 1H), 4.27 (q, *J*=7.1 Hz, 2H), 4.58 (dd, *J*=14.8, 5.1 Hz, 1H), 4.90 (dd, *J*=14.8, 10.2 Hz, 1H); ^{13}C NMR δ 13.2, 13.4, 22.6, 33.8, 42.1, 62.1, 74.4, 169.5; HRMS (EI) *m*/*z* calcd for $C_8H_{15}NO_4S$ (M^+) 221.0722, found 221.0711.

4.1.2. Methyl 3-nitro-2-propylthiobutanoate (3b). Treatment of **2b** (*E*; 76 mg, 0.52 mmol) with propanethiol (0.19 mL, 158 mg, 2.08 mmol) by procedure A gave **3b** (93 mg, 84%) as a separable mixture (1:1) of two diastereomers: IR ($CHCl_3$) 1736 (C=O), 1550 (NO_2) cm^{-1}. The less polar isomer had: ^{1}H NMR δ 0.97 (t, *J*=7.3 Hz, 3H), 1.61 (qd, *J*=7.3, 3.5 Hz, 2H), 1.78 (d, *J*=7.0 Hz, 3H), 2.64 (td, *J*=7.3, 2.1 Hz, 2H), 3.71 (d, *J*=10.5 Hz, 1H), 3.77 (s, 3H), 4.84 (dq, *J*=10.5, 7.0 Hz, 1H); ^{13}C NMR δ 13.2, 17.8, 22.4, 33.6, 48.5, 52.8, 82.1, 170.2. The more polar isomer had: ^{1}H NMR δ 0.91 (t, *J*=7.3 Hz, 3H), 1.51–1.58 (m collapsed with d, *J*=6.7 Hz, 5H), 1.78 (d, *J*=7.0 Hz, 3H), 2.54–2.61 (m, 2H), 3.65 (d, *J*=10.0 Hz, 1H), 3.72 (s, 3H), 4.79 (dq, *J*=10.0, 6.7 Hz, 1H); ^{13}C NMR δ 13.3, 18.1, 22.6, 34.4, 49.3, 52.8, 83.4, 169.6; HRMS (EI) *m*/*z* calcd for $C_8H_{15}NO_4S$ (M^+) 221.0722, found 221.0710.

4.1.3. Ethyl 3-nitro-3-phenyl-2-propylthiopropanoate (3c). Treatment of **2c** (*E*/*Z*, 1.0:0.5; 47 mg, 0.19 mmol) with propanethiol (0.07 mL, 58 mg, 0.76 mmol) by procedure A gave **3c** (50 mg, 79%) as a mixture (1:1) of two diastereomers as yellow oil: IR ($CHCl_3$) 1752 (C=O), 1568 (NO_2) cm^{-1}. One isomer had: ^{1}H NMR δ 0.80 (t, *J*=7.3 Hz, 3H), 0.90 (t, *J*=7.1 Hz, 3H), 1.62 (sextet, *J*=7.3, 2.8 Hz, 2H), 2.30–2.38 (m, 2H), 3.90 (q, *J*=7.1 Hz, 2H), 4.56 (d, *J*=11.5 Hz, 1H), 5.39 (d, *J*=11.5 Hz, 1H), 7.18–7.27 (m, 5H, Ar); ^{13}C NMR δ 13.2, 13.4, 22.3, 33.9, 48.5, 63.0, 91.3, 128.0, 128.5, 128.8, 136.3, 162.2. Second isomer had: ^{1}H NMR δ 0.80 (t, *J*=7.3 Hz, 3H), 1.29 (t, *J*=7.1 Hz, 3H), 1.62 (sextet, *J*=7.3, 2.8 Hz, 2H), 2.30–2.38 (m, 2H), 4.27 (qd, *J*=7.1, 2.7 Hz, 2H), 4.57 (d, *J*=10.7 Hz, 1H), 5.34 (d, *J*=10.7 Hz, 1H), 7.18–7.27 (m, 5H, Ar); ^{13}C NMR δ 13.2, 13.9, 22.4, 34.4, 49.7, 63.4, 92.0, 128.4, 128.5, 128.9, 136.8, 162.6; HRMS (EI) *m*/*z* calcd for $C_{14}H_{19}NO_4S$ (M^+) 297.1035, found 297.1032.

4.1.4. Ethyl 3-(4-methoxyphenyl)-3-nitro-2-propylthiopropanoate (3d). Treatment of **2d** (*E*/*Z*, 1.0:0.2; 52 mg, 0.21 mmol) with propanethiol (74 μL, 69 mg, 0.83 mmol)

by procedure A gave **3d** (53 mg, 78%) as a mixture (1:1) of two isomers as an oil: IR ($CHCl_3$) 1752 (C=O), 1569 (NO_2) cm^{-1}. One isomer had: ^1H NMR δ 0.91 (t, J=7.3 Hz, 3H), 1.05 (t, J=7.1 Hz, 3H), 1.52–1.55 (m, 2H), 2.36–2.44 (m, 2H), 3.81 (s, 3H), 4.03 (m, 2H), 4.62 (d, J=11.4 Hz, 1H), 5.42 (d, J=11.4 Hz, 1H), 6.86–6.89 (m, 2H, Ar), 7.27–7.30 (m, 2H, Ar); ^{13}C NMR δ 13.3, 13.6, 22.4, 33.8, 48.1, 55.2, 63.0, 91.6, 114.2, 127.9, 129.2, 159.6, 162.3. Second isomer had: ^1H NMR δ 0.91 (t, J=7.3 Hz, 3H), 1.36 (t, J=7.1 Hz, 3H), 1.52–1.55 (m, 2H), 2.36–2.44 (m, 2H), 3.82 (s, 3H), 4.37 (qd, J=7.1, 2.4 Hz, 2H), 4.64 (d, J=10.5 Hz, 1H), 5.39 (d, J=10.3 Hz, 1H), 6.86–6.89 (m, 2H, Ar), 7.27–7.30 (m, 2H, Ar); ^{13}C NMR δ 13.2, 13.9, 22.4, 34.2, 49.1, 55.4, 63.4, 92.2, 114.3, 128.5, 129.7, 159.6, 162.7; HRMS (EI) *m/z* calcd for $C_{15}H_{21}NO_5S$ (M^+) 327.1140, found 327.1138.

4.1.5. Ethyl 3-nitro-3-phenyl-2-phenylthiopropanoate (4c). Treatment of **2c** (*E*/*Z*, 1.0:0.5; 57 mg, 0.26 mmol) with thiophenol (32 μL, 34 mg, 0.31 mmol) by procedure A (without addition of TEA) gave **4c** (73 mg, 86%) as a mixture (1:1) of two isomers as an oil: IR ($CHCl_3$) 1752 (C=O), 1566 (NO_2) cm^{-1}. One isomer had: ^1H NMR δ 0.90 (t, J=7.1 Hz, 3H), 3.89–3.96 (m, 2H), 4.84 (d, J=10.6 Hz, 1H), 5.46 (d, J=10.6 Hz, 1H), 6.99–7.05 (m, 2H, Ar), 7.15–7.21 (m, 8H, Ar); ^{13}C NMR δ 13.4, 52.2, 63.1, 90.5, 127.8, 128.4, 128.6, 128.9, 129.1, 130.6, 134.8, 135.7, 162.1. Second isomer had: ^1H NMR δ 1.29 (t, J=7.1 Hz, 3H), 4.22–4.27 (m, 2H), 4.87 (d, J=11.5 Hz, 1H), 5.49 (d, J=11.5 Hz, 1H), 6.99–7.05 (m, 2H, Ar), 7.15–7.21 (m, 8H, Ar); ^{13}C NMR δ 13.9, 53.7, 63.5, 91.3, 128.4, 128.5, 128.7, 129.0, 129.2, 131.5, 135.1, 135.8, 162.6; HRMS (EI) *m/z* calcd for $C_{17}H_{17}O_4SN$ (M^+) 331.0878, found 331.0889.

4.1.6. Ethyl 3-(4-methoxyphenyl)-3-nitro-2-phenylthiopropanoate (4d). Treatment of **2d** (*E*/*Z*, 1.0:0.2; 50 mg, 0.2 mmol) with thiophenol (24 μL, 26 mg, 0.22 mmol) by procedure A gave **4d** (52 mg, 72%) as a mixture (1:1) of two isomers as an oil: IR ($CHCl_3$) 1752 (C=O), 1569 (NO_2) cm^{-1}. One isomer had: ^1H NMR δ 1.04 (t, J=7.1 Hz, 3H), 3.78 (s, 3H), 4.03–4.06 (m, 2H), 4.92 (d, J=10.5 Hz, 1H), 5.52 (d, J=10.5 Hz, 1H), 6.77–6.81 (m, 2H, Ar), 7.02–7.07 (m, 2H, Ar), 7.26–7.27 (m, 4H, Ar), 7.29–7.32 (m, 1H, Ar); ^{13}C NMR δ 13.5, 51.9, 55.3, 63.1, 90.7, 114.0, 127.5, 128.9, 129.0, 130.8, 132.2, 134.7, 159.6, 162.1. Second isomer had: ^1H NMR δ 1.38 (t, J=7.1 Hz, 3H), 3.80 (s, 3H), 4.26–4.35 (m, 2H), 4.94 (d, J=11.4 Hz, 1H), 5.53 (d, J=11.4 Hz, 1H), 6.77–6.81 (m, 2H, Ar), 7.02–7.07 (m, 2H, Ar), 7.26–7.27 (m, 4H, Ar), 7.29–7.32 (m, 1H, Ar); ^{13}C NMR δ 13.9, 53.1, 55.5, 63.5, 91.4, 114.1, 127.7, 129.1, 129.6, 131.6, 132.6, 135.1, 159.6, 162.6; HRMS (EI) *m/z* calcd for $C_{18}H_{19}O_5SN$ (M^+) 361.0984, found 361.1004.

4.1.7. Ethyl 2-propylthiopropenoate (5a) (procedure B). Propanethiol (37 μL, 31.4 mg, 0.41 mmol) and TEA (47 μL, 34.3 mg, 0.34 mmol) were added to a stirred solution of **2a** (50 mg, 0.34 mmol) in THF (2 mL) at ambient temperature and stirring was continued for 10 h. The resulting mixture was evaporated to dryness under vacuum and the residue was column chromatographed (hexane→1% EtOAc/hexane) to give **5a** (28 mg, 82%) as an oil: IR ($CHCl_3$) 1712 (C=O), 1614 (C=C) cm^{-1}; ^1H NMR δ 0.97 (t, J=7.3 Hz, 3H), 1.26 (t, J=7.1 Hz, 3H), 1.64 (sextet, J=7.3 Hz, 2H), 2.62 (t, J=7.3 Hz, 2H), 4.20 (q, J=7.1 Hz, 2H), 5.33 (s, 1H), 6.27 (s, 1H); ^{13}C NMR δ 13.6, 14.1, 21.2, 33.5, 61.7, 118.8, 137.9, 164.6; HRMS (EI) *m/z* calcd for $C_8H_{14}O_2S$ (M^+) 174.0714, found 174.0710.

4.1.8. Methyl 2-propylthio-2(*Z*)-butenoate (5b). Treatment of **2b** (*E*; 46 mg, 0.32 mmol) with propanethiol (34 μL, 29 mg, 0.38 mmol) and TEA (44 μL, 32.3 mg, 0.32 mmol) by procedure B gave **5b** (27 mg, 88%) as an oil: IR ($CHCl_3$) 1710 (C=O), 1610 (C=C) cm^{-1}; ^1H NMR δ 0.89 (t, J=7.3 Hz, 3H), 1.46 (sextet, J=7.3 Hz, 2H), 1.95 (d, J=7.0 Hz, 3H), 2.61 (t, J=7.3 Hz, 2H), 3.72 (s, 3H), 7.21 (q, J=7.0 Hz, 1H); ^{13}C NMR δ 13.2, 16.6, 23.0, 35.7, 52.7, 128.3, 146.5, 166.2; HRMS (EI) *m/z* calcd for $C_8H_{14}O_2S$ (M^+) 174.0714, found 174.0708.

4.1.9. Ethyl 3-phenyl-2-propylthio-2(*E*)-propenoate (5c). Treatment of **2c** (*E*/*Z*, 1.0:0.5; 47 mg, 0.21 mmol) with propanethiol (23 μL, 19 mg, 0.25 mmol) and DBU (31 μL, 32 mg, 0.21 mmol) by procedure B (stirring was continued for 24 h at 60 °C) gave separable mixture of **5c** (42 mg, 79%) and **4c** (5 mg, 8%; as a mixture of two isomers). Compound **5c** had: IR ($CHCl_3$) 1693 (C=O), 1602 (C=C) cm^{-1}; ^1H NMR δ 0.83 (t, J=7.2 Hz, 3H), 1.32 (t, J=7.1 Hz, 3H), 1.46 (sextet, J=7.2 Hz, 2H), 2.37 (t, J=7.2 Hz, 2H), 4.25 (q, J=7.1 Hz, 2H), 5.93 (s, 1H), 7.33–7.35 (m, 2H, Ar), 7.39–7.41 (m, 3H, Ar); ^{13}C NMR δ 13.2, 14.4, 23.0, 34.7, 60.0, 115.9, 128.0, 128.4, 128.7, 138.8, 160.6, 165.9; HRMS (EI) *m/z* calcd for $C_{14}H_{18}O_2S$ (M^+) 250.1027, found 250.1029.

4.1.10. Ethyl 3-(4-methoxyphenyl)-2-propylthio-2(*E*)-propenoate (5d). Treatment of **2d** (*E*/*Z*, 1.0:0.2; 70 mg, 0.21 mmol) with propanethiol (30 μL, 25 mg, 0.33 mmol) and DBU (50 μL, 51 mg, 0.33 mmol) by procedure B (stirring was continued for 24 h at 60 °C) gave separable mixture of **5d** (31 mg, 40%) and **4d** (28 mg, 30%; as a mixture of two isomers). Compound **5d** had: IR ($CHCl_3$) 1693 (C=O), 1607 (C=C) cm^{-1}; ^1H NMR δ 0.85 (t, J=7.2 Hz, 3H), 1.32 (t, J=7.1 Hz, 3H), 1.46 (sextet, J=7.2 Hz, 2H), 2.41 (t, J=7.2 Hz, 2H), 3.85 (s, 3H), 4.23 (q, J=7.1 Hz, 2H), 5.92 (s, 1H), 6.91–6.93 (m, 2H, Ar), 7.29–7.31 (m, 2H, Ar); ^{13}C NMR δ 13.3, 14.4, 23.0, 29.7, 34.8, 55.3, 59.9, 113.8, 115.7, 129.4, 131.2, 160.1, 165.9; HRMS (EI) *m/z* calcd for $C_{15}H_{20}O_3S$ (M^+) 280.1133, found 280.1128.

4.1.11. Ethyl 2-phenylthiopropenoate (6a) (procedure C). Thiophenol (25 μL, 27.3 mg, 0.25 mmol) and TEA (3 μL, 2.5 mg, 0.025 mmol) were added to a stirred solution of **2a** (30 mg, 0.21 mmol) in THF (2 mL) at ambient temperature and stirring was continued for 2 h. The resulting mixture was evaporated to dryness under vacuum and the residue was column chromatographed (hexane→1% EtOAc/hexane) to give **6a**[13b] (33 mg, 78%) as an oil: IR ($CHCl_3$) 1720 (C=O), 1610 (C=C) cm^{-1}; ^1H NMR δ 1.24 (t, J=7.1 Hz, 3H), 4.26 (q, J=7.1 Hz, 2H), 5.26 (s, 1H), 6.32 (s, 1H),

7.34–7.42 (m, 3H, Ar), 7.48–7.51 (m, 2H, Ar); ^{13}C NMR δ 14.1, 61.8, 122.6, 128.7, 129.5, 134.1, 139.1, 143.4, 164.7.

4.1.12. Methyl 2-phenylthio-2(*Z*)-butenoate (6b). Treatment of **2b** (*E*; 50 mg, 0.34 mmol) with thiophenol or benzenethiol (42 μL, 45.5 mg, 0.41 mmol) by procedure C gave **6b**[13d] (61 mg, 84%) as an oil: IR ($CHCl_3$) 1715 (C=O), 1607 (C=C) cm^{-1}; ^{1}H NMR δ 2.02 (d, J=7.0 Hz, 3H), 3.61 (s, 3H), 7.07–7.10 (m, 1H, Ar), 7.12–7.19 (m, 4H, Ar), 7.48 (q, J=7.0 Hz, 1H); ^{13}C NMR δ 16.7, 52.5, 125.9, 127.3, 127.9, 128.9, 135.7, 149.3, 165.9.

4.1.13. Ethyl 3-phenyl-2-phenylthio-2(*Z*)-propenoate (6c). DBU (33 μL, 33 mg, 0.22 mmol) was added to a stirred solution of **2c** (*E*/*Z*, 1.0:0.5; 48 mg, 0.22 mmol) in THF (2 mL) containing thiophenol (27 μL, 29 mg, 0.26 mmol), and stirring was continued for 24 h at 60 °C. After cooling to ambient temperature, CH_2Cl_2 (5 mL) and 5% HCl (4 mL) were added. The organic layer was separated and was washed (H_2O, brine), dried ($MgSO_4$) and column chromatographed (hexane→1% EtOAc/hexane) to give **6c**[15a] (48 mg, 78%) and **4c** (5 mg, 7%; as a mixture of two isomers). Compound **6c** had: IR ($CHCl_3$) 1706 (C=O), 1602 (C=C) cm^{-1}; ^{1}H NMR δ 0.97 (t, J=7.1 Hz, 3H), 4.03 (q, J=7.1 Hz, 2H), 7.07–7.12 (m, 1H, Ar), 7.14–7.23 (m, 4H, Ar), 7.28–7.35 (m, 3H, Ar), 7.73–7.77 (m, 2H, Ar), 8.00 (s, 1H); ^{13}C NMR δ 13.6, 61.8, 125.8, 126.4, 127.8, 128.3, 128.4, 128.7, 128.9, 129.9, 130.8, 134.4, 135.7, 145.1, 166.1.

4.1.14. Ethyl 3-(4-methoxyphenyl)-2-phenylthio-2(*E*/*Z*)-propenoate (6d). Treatment of **2d** (*E*/*Z*, 1.0:0.2; 40 mg, 0.16 mmol) with thiophenol (20 μL, 21 mg, 0.19 mmol) and DBU (31 μL, 22 mg, 0.22 mmol) as described for **6c** gave **6d** (*E*/*Z*, 0.6:1.0; 22 mg, 44%): IR ($CHCl_3$) 1706 (C=O), 1601 (C=C) cm^{-1}. *Z*-Isomer had: ^{1}H NMR δ 1.09 (t, J=7.1 Hz, 3H), 3.86 (s, 3H), 4.13 (q, J=7.1 Hz, 2H), 6.92–6.94 (m, 2H, Ar), 7.23–7.31 (m, 5H, Ar), 7.91–7.93 (m, 2H, Ar), 8.12 (s, 1H); ^{13}C NMR δ 13.9, 55.2, 61.7, 113.8, 116.0, 126.0, 128.1, 128.9, 130.2, 133.0, 145.9, 161.1, 166.5. *E* Isomer had: ^{1}H NMR δ 1.36 (t, J=7.1 Hz, 3H), 3.72 (s, 3H), 4.28 (q, J=7.1 Hz, 2H), 6.09 (s, 1H), 6.64–6.66 (m, 2H, Ar), 7.06–7.11 (m, 2H, Ar), 7.14–7.19 (m, 5H, Ar); ^{13}C NMR δ 14.3, 55.4, 60.2, 113.2, 122.0, 127.0, 127.5, 128.4, 130.7, 133.5, 136.0, 158.2, 159.8, 165.9; HRMS (EI) *m*/*z* calcd for $C_{18}H_{18}O_3S$ (M^+) 314.0977, found 314.0988.

Notes: The 4-methoxybenzaldehyde and **4d** were also detected in the reaction mixture.

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