S-Allyl Thiocarbamates from Allylic Alcohols by in situ [3,3]-Sigmatropic Rearrangement of a Thiocarbonyldiimidazole Adduct

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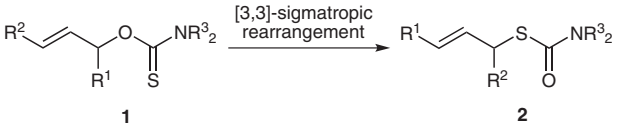
Abstract: Treatment of allylic alcohols with thiocarbonyldiimidazole generates an unstable *O*-allyl imidazolyl thione ester, which rearranges spontaneously and in high yield to the corresponding *S*-allyl imidazolyl thiol ester. Displacement of the imidazole by *N*-alkylanilines in the presence of a nucleophilic catalyst (HOBt or ECHIA) gives *S*-allyl *N*-aryl thiocarbamates in excellent yields (up to 97%) over two steps.

Key words: sigmatropic rearrangement, thiocarbamates, alcohols, stereospecificity, sulfur

Thiocarbamates are valuable as precursors of important sulfur-containing compounds[1] and strategic intermediates in the synthesis of natural products.[2] They also display biological activities as analgesics[3] and anaesthetics,[1,4] fungicides[1,3–5] and bactericides[3,4,6] or antiviral[1,4] and dermatological agents.[5,7] They have been reported to have hypnotic[3] and tuberculostatic activity[3] and can be employed in flavour and fragrance chemistry.[8] *S*-Alkyl thiocarbamates are most known for their use as commercial herbicides.[1,4,9] Allylic thiocarbamates have been used as terminators in radical-based cyclisation reactions.[10] Hoppe made extensive use of *S*-alkyl-, *S*-benzyl-, and *S*-allylthiocarbamates in his seminal work on lithiation and his studies of the configurational stability of the resulting sulfur-stabilised organolithium compounds.[11]

The most straightforward methods for the preparation of thiocarbamates are nucleophilic substitutions of carbamoyl chlorides with thiols or thiolates,[12,13] alkyl chlorothioformates with amines,[13] or sequential attack on trichloroacetyl chloride by a thiol and an amine.[4] Less practical methods employ carbon monoxide and elemental sulfur,[4,14] reactions of unstable *N*,*N*-dialkylcarbamoyl lithiums with sulfur compounds,[9a] or the condensation of gaseous carbonyl sulfide and an amine followed by treatment with a base and alkyl halide.[12] Condensation of a thiol with an isocyanate[6] or hydration of an organic thiocyanate[1,15] also affords a thiocarbamate.

S-Allyl thiocarbamates **2** are readily prepared by rearrangement of their *O*-allyl counterparts **1** (Scheme 1),[4] driven by the thermodynamically favoured formation of a C=O bond from a C=S bond.[16] The rearrangement can be promoted thermally[17] or photochemically,[18] and metal-catalysed processes[17c,19] have also been reported. The thermal reaction seems to be a standard [3,3]-sigmatropic rearrangement, with a broad range of substituents tolerated[16,17] although the rate of the reaction strongly depends on the allylic substitution pattern.[16,17,20]



1 **2**

Scheme 1 [3,3]-Sigmatropic rearrangement of *O*-allyl thiocarbamates

Starting from enantioenriched *O*-allyl thiocarbamates **1**, the [3,3]-sigmatropic rearrangement proceeds with excellent transfer of chirality (up to 97% ee conservation).[11c,e] Enantioselectivity can furthermore be achieved in the rearrangement of achiral or racemic *O*-allyl thiocarbamates.[19] Using a chiral bisphosphine ligand, Gais prepared cyclic and acyclic symmetrical *S*-allylic thiocarbamates with ee values ranging from 85% to ≥99% via a palladium-catalysed reaction.[19a,b] Overman obtained good to excellent ee values (76–88%) in the palladium-catalysed [3,3]-sigmatropic rearrangement of unsymmetrical acyclic substrates using (*R*)-(–)-COP-Cl as the chiral catalyst,[19c] providing the first catalytic asymmetric method for the preparation of secondary allylic thiocarbamates.

We have recently reported that benzyllithiums stabilised by urea,[21] carbamate,[22] or thiocarbamate[23] functions may undergo arylation by intramolecluar migration of an aromatic ring to the carbanionic centre. As part of a programme of research extending this anion arylation methodology to the related allyllithiums,[24] we required a straightforward and efficient general synthesis of a range of allyl thiocarbamate substrates.

Initially, we chose the route to thiocarbamates **7** shown in Scheme 2. Successive substitutions of chloride from thiophosgene gave the *O*-allyl-substituted thiocarbamate **6a** via thiocarbamoyl chloride **4a**. The [3,3]-sigmatropic rearrangement of **6a** to give **7a** took place on refluxing in toluene for 2 to 3 days, or more conveniently on heating for 45 minutes in a microwave at 135 °C.

Replacing thiophosgene with thiocarbonyldiimidazole (TCDI; **8**)[25] resulted in a complex mixture of several unidentified products. Changing the order of the substitutions, with the aim of first converting **5a** to the imidazole

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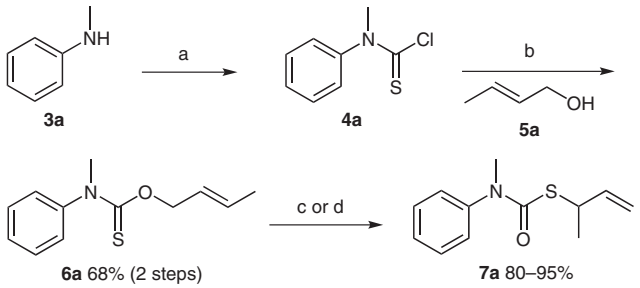
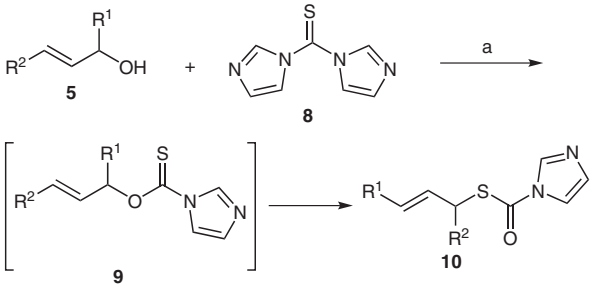


Scheme 2 Synthesis of *S*-allyl thiocarbamates from chlorothioformates. *Reagents and conditions*: a) $CSCl_2$, Et_3N, THF, 0 °C to r.t.; b) NaH, NaI, THF, 0 °C, then **5a**; c) K_2CO_3, toluene, 72 h; d) 0.4 M, μW, 135 °C, 45 min.

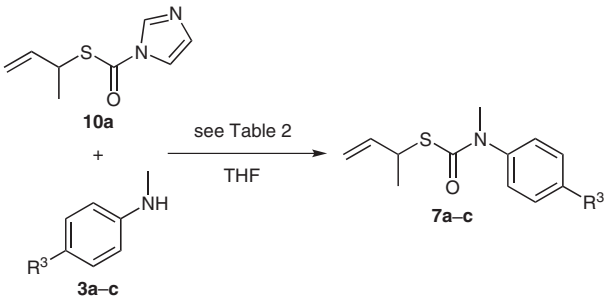
derivative **9**, revealed that under the conditions required to displace imidazole from TCDI the *O*-allyl thiocarbamate product **9** rearranged spontaneously to the *S*-allyl imidazolthiocarboxylate **10**, as previously reported by other groups[26] (Scheme 3). The reaction proved to be reproducible with various alcohols (Table 1).



Scheme 3 [3,3]-Sigmatropic rearrangement of the thiocarbonyl imidazole adduct. *Reagents and conditions*: a) DMAP, CH_2Cl_2, r.t., 18 h.

The unstable *O*-allyl intermediate **9a** (R^1 = Me, R^2 = H) could be isolated by using THF as the solvent and lowering the temperature to –20 °C for six hours. Replacing DMAP with HOBt led to a marked increase in the rate of substitution of imidazole from **8**, affording the imidazole adduct **9a** after one hour in CH_2Cl_2 without rearrangement (as indicated by ^{1}H NMR analysis). However **9a** is too unstable to isolate as a pure compound, undergoing rapid [3,3]-sigmatropic rearrangement during workup and purification via filtration through silica gel. It decomposes over a matter of days in a freezer.

Nonetheless, the rearranged thiocarbonyl imidazoles **10** are themselves valuable intermediates for the synthesis of thiocarbamates. Such acylimidazole intermediates are rather unreactive towards nucleophiles, and displacement of the imidazole is typically achieved[25] by activation using N-methylation. In the case of **10**, however, a range of different methylating conditions led only to decomposition. Substitution of an acylimidazole has alternatively been achieved in the presence of various nucleophilic catalysts,[27] and Table 2 shows the results of treating **10a** with a series of *N*-methylanilines **3**[28] in the presence of DBU, HOBt, or ethyl 2-cyano-2-(hydroxyimino)acetate (ECHIA) (Scheme 4).



Scheme 4 Catalysed formation of the thiocarbamates **7**

HOBt generally gave better yields than ECHIA (Table 2, entries 3, 5, 7, 10, 14, and 16). Although 0.5 equivalent of additive gave satisfying yields in most cases, a higher amount led to improved yields for some substrates (entries 10–12). Reactions run in the microwave always gave poorer yields than under thermal conditions (entries 4, 6, 8, 13, and 15).

The optimised conditions were then applied to various substrates **10** and *N*-methylanilines **3** (Scheme 5), and turned out to be general for a range of substitution patterns in both the acylimidazole and aniline reactants. Remarkably, even the very hindered *N*,2,4,6-tetramethylaniline gave a very high yield (96%). Electron-deficient anilines performed less well: while 4-fluoro- and the 4-chloro-*N*-methylaniline gave good yields (65% and 86%), the 4-trifluoromethyl-*N*-methylaniline afforded thiocarbamate **5g** in only moderate yield (33%) while no product at all was obtained from 4-(methylamino)benzonitrile.

Table 1 Scope of the Nucleophilic Substitution of Thiocarbonyldiimidazole by Allylic Alcohol

Entry	**5**	R^1	R^2	Conditions	Product, yield (%)
1	**5a**	H	Me	CH_2Cl_2, r.t., 3 days	**10a**, 98
3	**5b**	H	*n*-Pr	DCE, reflux, 24 h	**10b**, 100
5	**5c**	H	CH=CHMe	CH_2Cl_2, r.t., 2.5 d	**10c**, 65
6	**5d**	H	*i*-Pr	DCE, r.t. 6 h, then 40 °C, 20 h	**10d**, 88
7	**5e**	Me	Me	DCE, r.t. 2 h, then 40 °C, 24 h	**10e**, 98
8	**5f**	*c*-C_6H_{11}	Me	DCE, 40 °C, 26 h	**10f**, 90

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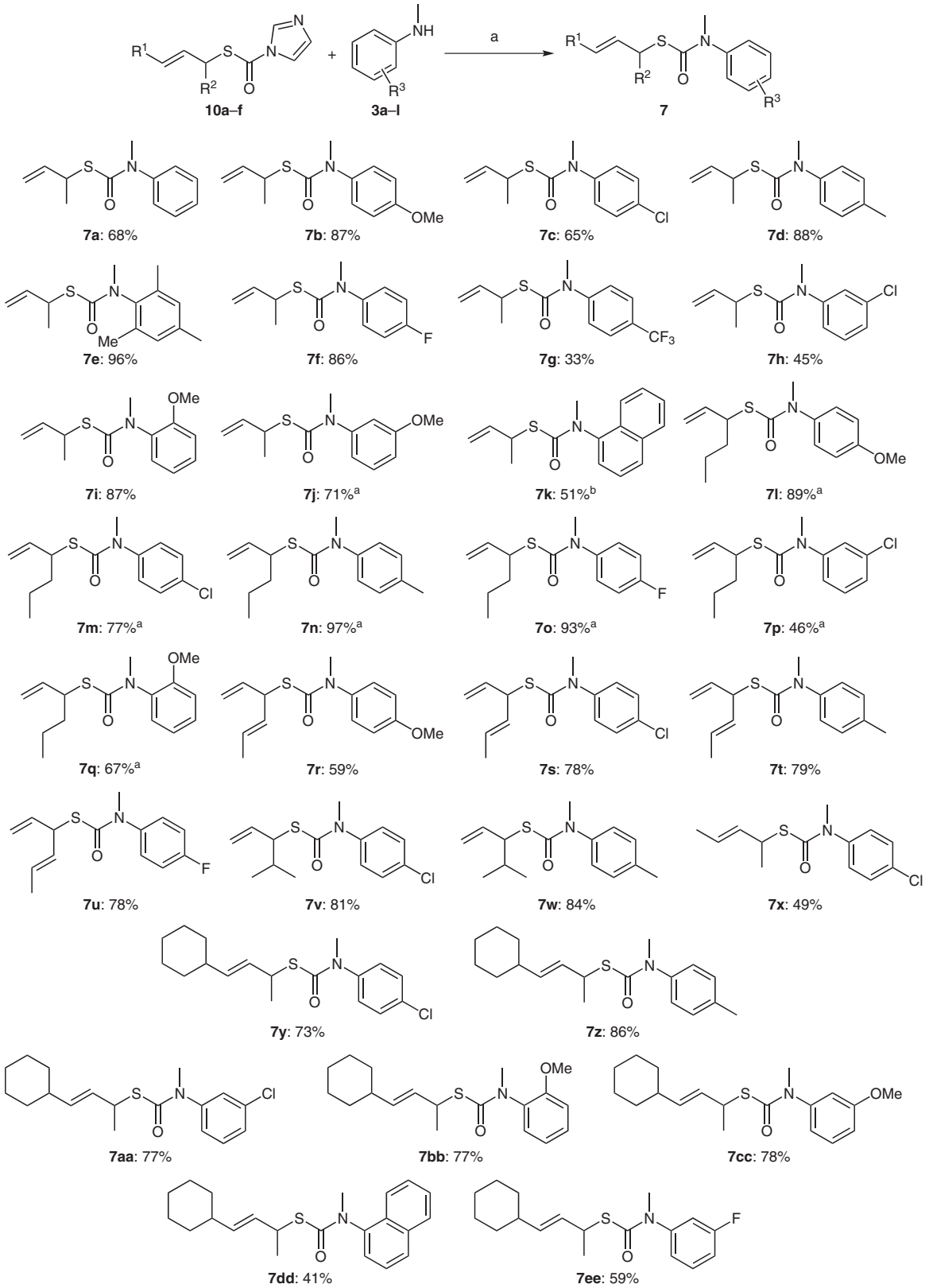
Because of the reported stereospecificity[26a–d,g,h] of related sigmatropic rearrangements,[11c,e] we expected the method to be equally effective for the synthesis of enantiomerically enriched thiocarbamates. Thus, treatment of (*R*)-**5f**, produced in 94:6 er using Sharpless' kinetic resolution,[29] with TCDI under the conditions of Table 1, entry 8, gen-



Scheme 5 Imidazoles derivatives **10** as precursors to *S*-allyl thiocarbamates **7**. *Reagents and conditions*: a) HOBt (0.5 or 1.0 equiv), THF, heat, 24 h. [a] Using ECHIA (0.5 or 1.0 equiv); [b] Using HOBt (1.2 equiv).

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Table 2 Optimisation of the Nucleophilic Displacement of Imidazole from **10a** by *N*-Methylanilines **3**

Entry	**3**	R^3	Additive	Equiv	Conditions	Product, yield (%)
1	**3b**	OMe	DBU	0.5	reflux, 24 h	0
2	**3c**	Cl	DBU	0.5	reflux, 24 h	0
3	**3c**	Cl	HOBt	0.5	reflux, 24 h	**7c**, 65
4	**3c**	Cl	HOBt	0.5	μw, 100 °C, 2 h	0
5	**3c**	Cl	ECHIA	1.0	reflux, 24 h	**7c**, 56
6	**3c**	Cl	ECHIA	1.0	μw, 100 °C, 2 h	**7c**, 21
7	**3b**	OMe	HOBt	0.5	reflux, 24 h	**7b**, 87
8	**3b**	OMe	HOBt	0.5	μw, 100 °C, 2 h	**7b**, 72
9	**3b**	OMe	ECHIA[a]	0.5	reflux, 24 h	**7b**, 68
10	**3b**	OMe	ECHIA	0.5	reflux, 24 h	**7b**, 64
11	**3b**	OMe	ECHIA	1.0	reflux, 24 h	**7b**, 76
12	**3b**	OMe	ECHIA	1.5	reflux, 24 h	**7b**, 81
13	**3b**	OMe	ECHIA	0.5	μw, 100 °C, 1 h	**7b**, 51
14	**3a**	H	HOBt	0.5	reflux, 24 h	**7a**, 68
15	**3a**	H	HOBt	0.5	μw, 100 °C, 2 h	**7a**, 38
16	**3a**	H	ECHIA	0.5	reflux, 24 h	**7a**, 60

[a] Solvent: CH_2Cl_2.

erated (*S*)-**10f** in 94:6 er. This enantioenriched material gave, on reaction with 3-methoxy-*N*-methylaniline, a thiocarbamate **7cc** of undiminished enantiomeric enrichment.

In summary, we have shown that simple acylation of allylic alcohols with thiocarbonyldiimidazole (TCDI, **8**) initiates a rapid stereospecific [3,3]-sigmatropic rearrangement to give an *S*-allyl thiocarbonylimidazole derivative. HOBt-promoted substitution of imidazle from this product provides a general two-step synthesis of *S*-allyl *N*-arylthiocarbamates. The method tolerates a wide range of substituents, either in the alcohol or the aniline component, and gives the thiocarbamate products in generally good to excellent yields.

NMR spectra were recorded on a Bruker Ultrashield 300 or 400 spectrometer. The chemical shifts (δ) are reported in ppm downfield of TMS and coupling constants (*J*) are reported in hertz and rounded to 0.5 Hz. Standard abbreviations were used for denoting the splitting patterns. Solvents were used as internal standards when assigning NMR spectra (δ_H: $CDCl_3$ 7.26; δ_C $CDCl_3$ 77.0; δ_H: DMSO 2.50; δ_C DMSO 39.43). Coupling constants were calculated manually using the chemical shifts given by ChemDraw Ultra 11.0 software.

Low- and high-resolution mass spectra were recorded by staff at the University of Manchester. Electrospray spectra were recorded on a Micromass Platform II and high-resolution mass spectra were recorded either on a Waters QTOF or a Thermo Finnigan MAT95XP mass spectrometer, and are accurate to ± 0.001 Da. IR spectra were recorded on a PerkinElmer FT-IR Spectrum BX spectrometer. Absorptions reported are the most intense. Melting points (mp) were determined on a Bibby Stuart Scientific Melting Point SMP10 apparatus and are uncorrected. Optical rotation measurements were taken on a AA-100 polarimeter or a PerkinElmer 241 polarimeter using a cell with a path length of 0.25 dm, with the solvent, concentration (in g/mL) and sample temperature as stated.

TLC was performed using commercially available precoated plates (Macherey-Nagel Polygram® Sil G/UV_{254} for TLC, 0.20 mm) and visualised with UV light at 254 nm, phosphomolybdic acid dip, Seebach's dip (2.5 g of phosphomolybdic acid hydrate, 1.0 g of cerium(IV) sulfate tetrahydrate, 3.2 mL of concd H_2SO_4 and 90.5 mL of H_2O) or $KMnO_4$ dip. Flash chromatography was carried out using Fluorochem Davisil 40–63 μm 60 Å silica gel, under a positive pressure by means of compressed air.

All reactions were conducted under an N_2 atmosphere unless otherwise stated. Glassware was oven or flame dried. THF was distilled under N_2 from Na, using benzophenone indicator. CH_2Cl_2, cumene, *i*-Pr_2NH, and DMPU were purified by distillation from CaH_2 under N_2. Anhyd Et_2O and toluene were provided by the SPS (Solvent Purification System) Pure Solv model PS-MD-5, serial PS-08-150 apparatus from Innovative Technology Inc. PE refers to the fraction of light petroleum ether (PE) boiling between 40 and 65 °C. All other solvents and commercially available reagents were used as received.

Chiral HPLC measurements were carried out using a Hewlett Packard Series 1050 instrument fitted with a Daicel Chiralcel OD-H, a Daicel Chiralcel AD-H, or a (*R*,*R*)-Whelk-01 stationary phase with a mixture of hexane and *i*-PrOH as eluent. Absorption was measured at 214 or 254 nm.

1*H*-Imidazole-1-carbothioates 10a–f;[25] General Procedure A

To a stirred solution of alcohol **5** (1.0 equiv) in CH_2Cl_2 or DCE at r.t. were added TCDI (**8**; 2.0 equiv) and DMAP (0.1 equiv). The reaction mixture was stirred at r.t. or heated until completion. Once at

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r.t., EtOAc was added and the crude mixture was washed with brine (2 ×). The organic layer was separated, dried ($MgSO_4$), filtered, and concentrated down. Further purification by column chromatography afforded the pure 1*H*-Imidazole-1-carbothioates **10**.

Phenyl(methyl)carbamothioates 7a–z,aa–ee;[26] General Procedure B

To a solution of 1*H*-imidazole-1-carbamathioate **10** (1.0 equiv) in THF at r.t. were added either HOBt or ECHIA (either 0.5 or 1.0 equiv) and *N*-methylaniline **3** (1.2 equiv). The reaction mixture was heated to reflux for 24 h, and cooled to r.t. EtOAc was added and the organic mixture was washed with aq HCl for the indicated time. The organic layer was separated, dried ($MgSO_4$), filtered, and concentrated. Further purification by column chromatography afforded the pure phenyl(methyl)carbamothioates **7**.

(*E*)-*O*-But-2-enyl Methyl(phenyl)carbamothioate (6a)

To a solution of crotyl alcohol (**5a**; 1.11 g, 15.6 mmol, 1.0 equiv) in THF (12 mL) at 0 °C was added a suspension of NaH (60% in mineral oil, 1.87 g, 46.8 mmol, 3.0 equiv) in THF (60 mL). The reaction mixture was stirred at 0 °C for 30 min and NaI (280 mg, 1.87 mmol, 0.1 equiv) followed by methyl(phenyl)carbamic chloride (**4a**; 3.47 g, 18.7 mmol, 1.2 equiv) were added. The reaction mixture was warmed to r.t., stirred at r.t. for 45 min, warmed to 30 °C, and stirred at 30 °C for 45 min. Sat. aq NH_4Cl (60 mL) was added and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic fractions were washed with H_2O (20 mL) and brine (20 mL), dried ($MgSO_4$), filtered, and concentrated down. Further purification by column chromatography (PE–Et_2O, 95:5 to 7:3) afforded the title compound as a pale yellow fluffy powder (2.80 g, 81%); mp 60–62 °C; R_f = 0.70 (PE–EtOAc, 8:2).

IR (neat): 1490, 1445, 1382, 1273, 1199 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6, 90 °C): δ = 7.42 (t, *J* = 7.5 Hz, 2 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 7.24 (d, *J* = 7.5 Hz, 2 H), 5.67 (m, 1 H), 5.55 (m, 1 H), 4.85 (d, *J* = 6.0 Hz, 2 H), 3.52 (s, 3 H), 1.64 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.7, 143.5, 130.4, 129.1, 127.3, 125.9, 125.8, 124.9, 72.1, 44.2, 17.8.

MS (ES+): *m*/*z* = 244 ($[M + Na]^+$, 100%).

HRMS: *m*/*z* [M + Na] calcd for $C_{12}H_{15}NOS$: 244.0767; found: 244.0765.

***S*-But-3-en-2-yl Methyl(phenyl)carbamothioate (7a)[26]**

Method A: To a solution of **6a** (100 mg, 0.46 mmol, 1.0 equiv) in toluene (1 mL) was added K_2CO_3 (6 mg, 0.046 mmol, 0.1 equiv). The reaction mixture was heated to 135 °C for 45 min in a microwave oven. K_2CO_3 was filtered through a cotton plug and the organic layer was concentrated down. ^1H NMR of the crude showed 95% conversion. Further purification by column chromatography (PE–Et_2O, 95:5 to 85:15) afforded the title compound as a colourless oil.

Method B: General procedure B was followed using *S*-but-3-en-2-yl 1*H*-imidazole-1-carbothioate (**10a**; 300 mg, 1.65 mmol) in THF (3 mL), HOBt (111 mg, 0.82 mmol, 0.5 equiv), and *N*-methylaniline (0.21 mL, 1.94 mmol). The crude mixture was washed with aq 1 M HCl (3 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–Et_2O, 9:1) to afford the title compound as a yellow-orange oil (250 mg, 68%); R_f = 0.32 (PE–Et_2O, 9:1); $[\alpha]_D^{20}$ +16.1 (*c* 2.0, $CHCl_3$).

HPLC: OD-H, hexane–*i*-PrOH (99:1), 1 mL/min, t_R: minor 30.02 min, t_R: major 32.76 min.

IR (film): 1651, 1594, 1494, 1341, 1268 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.39 (m, 3 H), 7.27 (m, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.18 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.02 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H, H-4), 4.12 (quint, *J* = 7.0, 1.0 Hz, 1 H), 3.32 (s, 3 H), 1.37 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 142.2, 139.7, 129.6, 128.5, 114.7, 42.9, 38.3, 20.1.

MS (ES+): *m*/*z* (%) = 222 ($[M + H]^+$, 50), 244 ($[M + Na]^+$, 100), 276 ($[M + Na + MeOH]^+$, 40).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{15}NOS$: 222.0948; found: 222.0945.

***S*-But-3-en-2-yl 4-Methoxyphenyl(methyl)carbamothioate (7b)[26]**

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (18 mg, 0.133 mmol, 0.5 equiv), and 4-methoxy-*N*-methylaniline (45 mg, 0.33 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by column chromatography (PE–EtOAc, 95:5) to afford the title compound as a yellow oil (59 mg, 87%); R_f = 0.41 (PE–EtOAc, 8:2).

IR (film): 1652, 1511, 1246 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 9.0 Hz, 2 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.17 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.01 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.09 (quint, *J* = 7.0 Hz, 1 H), 3.82 (s, 3 H), 3.28 (s, 3 H), 1.36 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 159.4, 139.6, 134.5, 129.7, 114.6, 114.5, 55.4, 42.7, 38.3, 19.9.

MS (ES+): *m*/*z* (%) = 274 ($[M + Na]^+$, 100), 306 ($[M + Na + MeOH]^+$, 50).

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{17}NO_2S$: 274.0873; found: 274.0876.

***S*-But-3-en-2-yl 4-Chlorophenyl(methyl)carbamothioate (7c)[26]**

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (18 mg, 0.133 mmol, 0.5 equiv) and 4-chloro-*N*-methylaniline (0.04 mL, 0.32 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by column chromatography (PE–EtOAc, 98:2 to 85:15) to afford the title compound as a yellow oil (45 mg, 65%); R_f = 0.48 (PE–EtOAc, 8:2).

IR (film): 1653, 1488, 1277 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 9.0 Hz, 2 H), 7.21 (d, *J* = 9.0 Hz, 2 H), 5.86 (ddd, *J* = 17.0, 10.5, 7.0 Hz, 1 H), 5.18 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.03 (ddd, *J* = 10.5, 1.0, 1.0 Hz, 1 H), 4.11 (quint, *J* = 7.0 Hz, 1 H), 3.29 (s, 3 H), 1.37 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 140.5, 139.3, 134.1, 129.7, 129.6, 114.7, 42.8, 38.1, 19.9.

MS (ES+): *m*/*z* (%) = 278 ($[M + Na]^+$, 100), 310 ($[M + Na + MeOH]^+$, 80).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{14}ClNOS$: 274.0558; found: 256.0561.

***S*-But-3-en-2-yl Methyl(*p*-tolyl)carbamothioate (7d)[26]**

General procedure B was followed using **10a** (250 mg, 1.37 mmol) in THF (5 mL), HOBt (93 mg, 0.685 mmol, 0.5 equiv), and 4-methyl-*N*-methylaniline (0.21 mL, 1.64 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 30 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (280 mg, 88%); R_f = 0.71 (PE–EtOAc, 8:2).

IR (film): 1652, 1513, 1342, 1258 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.5 Hz, 2 H), 7.14 (d, *J* = 8.5 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.17 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.01 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.10 (quint, *J* = 7.0, 1.0 Hz, 1 H), 3.29 (s, 3 H), 2.24 (s, 3 H), 1.36 (d, *J* = 7.0 Hz, 3 H).

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^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 139.6, 139.3, 138.5, 130.1, 128.1, 114.5, 42.7, 38.2, 21.2, 19.9.

MS (ES+): *m*/*z* (%) = 258 ([M + Na]$^+$, 100), 290 ([M + Na + MeOH]$^+$, 50).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{17}NOS$: 258.0924; found: 258.0918.

S-But-3-en-2-yl Mesityl(methyl)carbamothioate (7e)[26]

General procedure B was followed using **10a** (51 mg, 0.28 mmol) in THF (1 mL), HOBt (18 mg, 0.133 mmol, 0.5 equiv), and 2,4,6-trimethyl-*N*-methylaniline (0.05 mL, 0.34 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 8:2) to afford the title compound as a yellow oil (71 mg, 96%); R_f = 0.80 (PE–EtOAc, 8:2).

IR (film): 1655, 1300, 1270 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.92 (br s, 2 H), 5.85 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.17 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 4.99 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.08 (quint, *J* = 7.0, 1.0 Hz, 1 H), 3.16 (s, 3 H), 2.30 (s, 3 H), 2.18 (d, *J* = 4.5 Hz, 6 H), 1.34 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 139.7, 138.8, 136.9, 136.2, 129.5, 114.3, 42.1, 35.2, 21.1, 19.9, 17.6.

MS (ES+): *m*/*z* (%) = 286 ([M + Na]$^+$, 100%), 318 ([M + Na + MeOH]$^+$, 40).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{21}NOS$: 286.1237; found: 286.1228.

S-But-3-en-2-yl 4-Fluorophenyl(methyl)carbamothioate (7f)[26]

General procedure B was followed using **10a** (250 mg, 1.37 mmol) in THF (5 mL), HOBt (93 mg, 0.685 mmol, 0.5 equiv) and 4-fluoro-*N*-methylaniline (0.20 mL, 1.64 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 25 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (281 mg, 86%); R_f = 0.73 (PE–EtOAc, 8:2).

IR (film): 1652, 1508, 1220 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (dd, *J* = 9.5, 5.5 Hz, 2 H), 7.12 (t, *J* = 9.5 Hz, 2 H), 5.90 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.22 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.06 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.14 (quint, *J* = 7.0, 1.0 Hz, 1 H), 3.33 (s, 3 H), 1.40 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 163.4, 139.4, 138.0, 130.3, 130.2, 116.6, 116.3, 114.7, 42.9, 38.2, 20.0.

MS (ES+): *m*/*z* (%) = 262 ([M + Na]$^+$, 100), 294 ([M + Na + MeOH]$^+$, 40).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{14}FNOS$: 262.0673; found: 262.0668.

S-But-3-en-2-yl Methyl[4-(trifluoromethyl)phenyl]carbamothioate (7g)[26]

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (18 mg, 0.133 mmol, 0.5 equiv), and 4-trifluoromethyl-*N*-methylaniline (0.05 mL, 0.32 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 30 min and concentrated down. The crude product was purified by column chromatography (PE–EtOAc, 95:5 to 9:1) to afford the title compound as a yellow oil (26 mg, 33%); R_f = 0.48 (PE–EtOAc, 8:2).

IR (film): 1650, 1608, 1321, 1107 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.0 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 2 H), 5.88 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.20 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.05 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.14 (quint, *J* = 7.0, 1.0 Hz, 1 H), 3.34 (s, 3 H), 1.39 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 145.3, 139.2, 128.2, 126.6, 126.5, 125.1, 122.4, 115.0, 43.0, 37.9, 19.9.

MS (ES+): *m*/*z* (%) = 290 ([M + H]$^+$, 20), 312 ([M + Na]$^+$, 60).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{14}F_3NOS$: 290.0821; found: 290.0816.

S-But-3-en-2-yl 3-Chlorophenyl(methyl)carbamothioate (7h)[26]

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (37 mg, 0.27 mmol, 1.0 equiv) or ECHIA (38 mg, 0.27 mmol, 1.0 equiv), and 3-chloro-*N*-methylaniline (0.04 mL, 0.32 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (31 mg, 45%); R_f = 0.41 (PE–Et_2O, 8:2).

IR (film): 1656, 1589, 1337, 1278 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (m, 2 H), 7.28 (m, 1 H), 7.18 (m, 1 H), 5.88 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.19 (ddd, *J* = 17.0, 1.5, 1.5 Hz, 1 H), 5.04 (ddd, *J* = 10.0, 1.5, 1.5 Hz, 1 H), 4.12 (quint, *J* = 7.0, 1.5 Hz, 1 H), 3.30 (s, 3 H), 1.38 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.0, 143.2, 139.3, 134.7, 130.3, 128.4, 126.4, 114.8, 42.9, 38.0, 19.9.

MS (ES+): *m*/*z* (%) = 256 ([M + H]$^+$, 50), 278 ([M + Na]$^+$, 100), 310 ([M + Na + MeOH]$^+$, 50).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}ClNOS$: 256.0557; found: 256.0561.

S-But-3-en-2-yl 2-Methoxyphenyl(methyl)carbamothioate (7i)[26]

General procedure B was followed using **10a** (280 mg, 1.54 mmol) in THF (6 mL), HOBt (208 mg, 1.54 mmol, 1.0 equiv), and 2-methoxy-*N*-methylaniline (254 mg, 1.85 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 20 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 95:5) to afford the title compound as a yellow oil (336 mg, 87%); R_f = 0.38 (PE–Et_2O 8:2).

IR (film): 1652, 1499, 1271 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (td, *J* = 8.0, 1.5 Hz, 1 H), 7.21 (dd, *J* = 8.0, 1.5 Hz, 1 H), 6.96 (d, *J* = 8.0 Hz, 2 H), 5.86 (2 ddd, rotamers, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.16 (2 d, rotamers, *J* = 17.0 Hz, 1 H), 5.00 (2 d, rotamers, *J* = 10.0 Hz, 1 H), 4.09 (quint, *J* = 7.0 Hz, 1 H), 3.85 (2 s, rotamers, 3 H), 3.22 (s, 3 H), 1.35 (2 d, rotamers, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.8, 156.1, 139.8/139.7 (rotamers), 130.8/130.7 (rotamers), 130.3, 129.9, 120.8/120.7 (rotamers), 114.3/114.2 (rotamers), 112.2, 55.6, 42.5/42.4 (rotamers), 36.7, 20.0/19.9 (rotamers).

MS (ES+): *m*/*z* = 274 ([M + Na]$^+$, 100%).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{17}NO_2S$: 274.0873; found: 274.0875.

S-But-3-en-2-yl 3-Methoxyphenyl(methyl)carbamothioate (7j)[26]

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (37 mg, 0.27 mmol, 1.0 equiv), and 3-methoxy-*N*-methylaniline (0.04 mL, 0.32 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 7:3) to afford the title compound as a yellow oil (48 mg, 71%); R_f = 0.42 (PE–Et_2O, 8:2).

IR (film): 1651, 1599, 1587, 1486, 1282, 1216 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31 (t, *J* = 8.0 Hz, 1 H), 6.90 (ddd, *J* = 8.0, 2.5, 1.5 Hz, 1 H), 6.86 (ddd, *J* = 8.0, 2.5, 1.5 Hz, 1 H), 6.80 (t, *J* = 1.6 Hz, 1 H), 5.88 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.18 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.02 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1

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H), 4.11 (quint, J = 7.0, 1.0 Hz, 1 H), 3.82 (s, 3 H), 3.31 (s, 3 H), 1.37 (d, J = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 160.2, 143.1, 139.6, 130.1, 120.4, 114.5, 114.0, 113.9, 55.4, 42.7, 38.1, 19.9.

MS (ES+): *m*/*z* (%) = 274 ([M + Na]$^+$, 100), 306 ([M + Na + MeOH]$^+$, 15).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{17}NO_2S$: 274.0873; found: 274.0869.

_S_-But-3-en-2-yl Methyl(naphthalen-1-yl)carbamothioate (7k)[26]

General procedure B was followed using **10a** (50 mg, 0.27 mmol) in THF (1 mL), HOBt (44 mg, 0.32 mmol, 1.2 equiv), and *N*-methylnaphthalen-1-amine (50 mg, 0.32 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 30 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 95:5 to 9:1) to afford the title compound as a yellow oil (37 mg, 51%); R_f = 0.61 (PE–EtOAc, 8:2).

IR (film): 1651, 1276, 774 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, J = 7.0, 2.5 Hz, 2 H), 7.81 (d, J = 8.0 Hz, 1 H), 7.56 (m, 2 H), 7.50 (td, J = 8.5, 1.0 Hz, 1 H), 7.45 (d, J = 7.0 Hz, 1 H), 5.81 (2 ddd, rotamers, J = 17.0, 10.5, 7.0 Hz, 1 H), 5.14 (dd, J = 16.0, 16.0 Hz, 1 H), 4.98 (dd, J = 19.5, 10.0 Hz, 1 H), 4.12 (m, 1 H), 3.42 (2 s, rotamers, 3 H), 1.30 (2 d, rotamers, J = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.1/169.0 (rotamers), 139.5, 137.9, 134.6, 130.5, 129.4, 128.6, 127.6/127.5 (rotamers), 127.3, 126.7, 125.7/125.6 (rotamers), 122.5/122.4 (rotamers), 114.5/114.3 (rotamers), 42.6, 38.0, 19.8.

MS (ES+): *m*/*z* (%) = 272 ([M + H]$^+$, 100), 294 ([M + Na]$^+$, 100).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}NOS$: 272.1104; found: 272.1109.

_S_-Hex-1-en-3-yl 4-Methoxyphenyl(methyl)carbamothioate (7l)[26]

General procedure B was followed using *S*-hex-1-en-3-yl 1*H*-imidazole-1-carbothioate **(10b**; 50 mg, 0.24 mmol) in THF (1 mL), ECHIA (17 mg, 0.12 mmol, 0.5 equiv), and 4-methoxy-*N*-methylaniline (40 mg, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (60 mg, 89%); R_f = 0.53 (PE–EtOAc, 8:2).

IR (film): 1652, 1510, 1244 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, J = 9.5 Hz, 2 H), 6.90 (d, J = 9.5 Hz, 2 H), 5.72 (ddd, J = 17.0, 10.0, 8.0 Hz, 1 H), 5.20 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 5.03 (d, J = 10.0 Hz, 1 H), 3.97 (q, J = 8.0 Hz, 1 H), 3.82 (s, 3 H), 3.27 (s, 3 H), 1.58 (m, 2 H), 1.37 (sext, J = 8.0 Hz, 2 H), 0.88 (t, J = 8.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.5, 159.4, 138.8, 134.6, 129.7, 115.3, 114.6, 55.4, 48.2, 38.4, 36.4, 20.3, 13.7.

MS (ES+): *m*/*z* (%) = 302 ([M + Na]$^+$, 100), 334 ([M + Na + MeOH]$^+$, 60).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{21}NO_2S$: 302.1186; found: 302.1190.

_S_-Hex-1-en-3-yl 4-Chlorophenyl(methyl)carbamothioate (7m)[26]

General procedure B was followed using **10b** (50 mg, 0.24 mmol) in THF (1 mL), ECHIA (34 mg, 0.24 mmol, 1.0 equiv), and 4-chloro-*N*-methylaniline (0.04 mL, 0.29 mmol). The crude mixture was washed with aq 2 M HCl (2 mL) for 30 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (52 mg, 77%); R_f = 0.70 (PE–EtOAc, 8:2).

IR (film): 1648, 1485, 1261 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, J = 8.5 Hz, 2 H), 7.21 (d, J = 8.5 Hz, 2 H), 5.73 (ddd, J = 17.0, 10.0, 7.5 Hz, 1 H), 5.21 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 5.05 (ddd, J = 10.0, 1.0, 1.0 Hz, 1 H), 3.99 (q, J = 7.5 Hz, 1 H), 3.29 (s, 3 H), 1.60 (m, 2 H), 1.36 (2 sext, J = 7.5 Hz, 2 H), 0.89 (t, J = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 140.6, 138.6, 134.1, 129.7, 129.6, 115.6, 48.3, 38.1, 36.4, 20.3, 13.7.

MS (ES+): *m*/*z* (%) = 284 ([M + H]$^+$, 100), 306 ([M + Na]$^+$, 55).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}ClNOS$: 284.0871; found: 284.0872.

_S_-Hex-1-en-3-yl Methyl(*p*-tolyl)carbamothioate (7n)[26]

General procedure B was followed using **10b** (50 mg, 0.24 mmol) in THF (1 mL), ECHIA (17 mg, 0.12 mmol, 0.5 equiv), and 4-methyl-*N*-methylaniline (0.04 mL, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (61 mg, 97%); R_f = 0.48 (PE–EtOAc, 9:1).

IR (film): 1654, 1513, 1270 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, J = 8.0 Hz, 2 H), 7.14 (d, J = 8.0 Hz, 2 H), 5.73 (ddd, J = 17.0, 10.0, 7.5 Hz, 1 H), 5.20 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 5.03 (dd, J = 10.0, 1.0 Hz, 1 H), 3.98 (q, J = 7.5 Hz, 1 H), 3.28 (s, 3 H), 2.38 (s, 3 H), 1.58 (2 sept, J = 7.5 Hz, 2 H), 1.36 (2 sext, J = 7.5 Hz, 2 H), 0.88 (t, J = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 139.4, 138.8, 138.4, 130.1, 128.1, 115.4, 48.2, 38.3, 36.4, 21.2, 20.3, 13.7.

MS (ES+): *m*/*z* = 286 ([M +Na]$^+$, 60%).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{21}NOS$: 286.1237; found: 286.1237.

_S_-Hex-1-en-3-yl 4-Fluorophenyl(methyl)carbamothioate (7o)[26]

General procedure B was followed using **10b** (50 mg, 0.24 mmol) in THF (1 mL), ECHIA (17 mg, 0.12 mmol, 0.5 equiv), and 4-fluoro-*N*-methylaniline (0.04 mL, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 25 min and concentrated down to afford the title compound as a yellow oil (60 mg, 93%); R_f = 0.71 (PE–EtOAc, 8:2).

IR (film): 1655, 1508, 1220 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26 (dd, J = 9.0, 5.0 Hz, 2 H), 7.10 (dd, J = 9.0 Hz, 2 H), 5.74 (ddd, J = 17.0, 10.0, 7.0 Hz, 1 H), 5.22 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 5.05 (dd, J = 10.0, 1.0 Hz, 1 H), 3.99 (q, J = 7.0 Hz, 1 H), 3.30 (s, 3 H), 1.61 (m, 2 H), 1.38 (sext, J = 7.5 Hz, 2 H), 0.90 (t, J = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.3, 163.4, 138.7, 138.1, 130.2, 116.5, 116.3, 115.6, 48.3, 38.3, 36.4, 20.3, 13.7.

MS (ES+): *m*/*z* (%) = 268 ([M + H]$^+$, 70), 290 ([M + Na]$^+$, 100), 322 ([M + Na + MeOH]$^+$, 25).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}FNOS$: 268.1166; found: 268.1164.

_S_-Hex-1-en-3-yl 3-Chlorophenyl(methyl)carbamothioate (7p)[26]

General procedure B was followed using **10b** (250 mg, 1.19 mmol) in THF (5 mL), HOBt (161 mg, 1.18 mmol, 1.0 equiv), and 3-chloro-*N*-methylaniline (0.18 mL, 1.43 mmol). The crude mixture was washed with aq 2 M HCl (5 mL) for 15 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 98:2, then 95:5) to afford the title compound as a yellow oil (157 mg, 46%); R_f = 0.67 (PE–EtOAc 8:2).

IR (film): 1656, 1589, 1336, 1277 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.32 (m, 2 H), 7.28 (m, 1 H), 7.18 (ddd, J = 5.5, 3.5, 2.0 Hz, 1 H), 5.74 (ddd, J = 17.0, 10.0, 8.0 Hz, 1 H), 5.22 (ddd, J = 17.0, 1.0, 1.0 Hz, 1 H), 5.05 (ddd, J = 10.0,

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1.5, 1.0 Hz, 1 H), 4.00 (q, *J* = 8.0 Hz, 1 H), 3.30 (s, 3 H), 1.60 (m, 2 H), 1.38 (sext, *J* = 7.5 Hz, 2 H), 0.90 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 143.3, 138.5, 134.7, 130.3, 128.4, 126.4, 115.6, 48.3, 38.1, 36.4, 20.3, 13.7.

MS (ES+): *m*/*z* = 306 ([M + Na]$^+$, 100%).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}ClNOS$: 284.0871; found: 284.0868.

(*S*)-Hex-1-en-3-yl 2-Methoxyphenyl(methyl)carbamothioate (7q)[26]

General procedure B was followed using **10b** (250 mg, 1.19 mmol) in THF (5 mL), HOBt (161 mg, 1.18 mmol, 1.0 equiv), and 2-methoxy-*N*-methylaniline (0.18 mL, 1.43 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 15 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 98:2, then 95:5) to afford the title compound as a yellow oil (223 mg, 67%); R_f = 0.57 (PE–EtOAc, 8:2).

IR (film): 1655, 1499, 1271, 747 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (t, *J* = 7.5 Hz, 1 H), 7.21 (d, *J* = 7.5 Hz, 1 H), 6.97 (d, *J* = 7.5 Hz, 2 H), 5.72 (m, rotamers, 1 H), 5.19 (2 d, rotamers, *J* = 17.0 Hz, 1 H), 5.01 (2 d, rotamers, *J* = 10.0 Hz, 1 H), 3.97 (q, *J* = 7.5 Hz, 1 H), 3.84 (2 s, rotamers, 3 H), 3.21 (s, 3 H), 1.61–1.52 (m, 2 H), 1.36 (sept, *J* = 7.5 Hz, 2 H), 0.88 (2 t, rotamers, *J* = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.9, 156.2, 139.0/138.9 (rotamers), 130.9/130.7 (rotamers), 130.2, 130.2/130.1 (rotamers), 120.8/120.7 (rotamers), 115.2/115.1 (rotamers), 112.2/112.1 (rotamers), 55.6, 47.9/47.8 (rotamers), 36.8, 36.4, 20.4/20.2 (rotamers), 13.7.

MS (ES+): *m*/*z* = 302 ([M + Na]$^+$, 100%).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{21}NO_2S$: 280.1366; found: 280.1353.

(*E*)-*S*-Hexa-1,4-dien-3-yl 4-Methoxyphenyl(methyl)carbamothioate (7r)[26]

General procedure B was followed using (*E*)-*S*-hexa-1,4-dien-3-yl 1*H*-imidazole-1-carbothioate (**10c**; 50 mg, 0.24 mmol) in THF (1 mL), ECHIA (16 mg, 0.12 mmol, 0.5 equiv), and 4-methoxy-*N*-methylaniline (40 mg, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (40 mg, 59%); R_f = 0.65 (PE–EtOAc, 8:2).

IR (film): 1652, 1510, 1245 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (d, *J* = 9.0 Hz, 2 H), 6.90 (d, *J* = 9.0 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.0 Hz, 1 H), 5.65 (m, 1 H), 5.47 (dqd, *J* = 15.0, 7.0, 1.0 Hz, 1 H), 5.20 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.06 (d, *J* = 10.0 Hz, 1 H), 4.60 (t, *J* = 7.0 Hz, 1 H), 3.82 (s, 3 H), 3.27 (s, 3 H), 1.67 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 159.5, 137.4, 134.4, 129.7, 129.0, 127.8, 115.7, 114.6, 55.4, 49.9, 38.4, 17.9.

MS (ES+): *m*/*z* (%) = 300 ([M + Na]$^+$, 100), 332 ([M + Na + MeOH]$^+$, 55).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NO_2S$: 300.1029; found: 300.1023.

(*E*)-*S*-Hexa-1,4-dien-3-yl 4-Chlorophenyl(methyl)carbamothioate (7s)[26]

General procedure B was followed using **10c** (50 mg, 0.24 mmol) in THF (1 mL), HOBt (32 mg, 0.236 mmol, 1.0 equiv), and 4-chloro-*N*-methylaniline (0.04 mL, 0.29 mL). The crude mixture was washed with aq 2 M HCl (2 mL) for 30 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a pale orange oil (53 mg, 78%); R_f = 0.70 (PE–EtOAc, 8:2).

IR (film): 1654, 1488, 1277 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 8.0 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1 H), 5.66 (dqd, *J* = 15.0, 6.5, 1.0 Hz, 1 H), 5.48 (ddq, *J* = 15.0, 7.5, 1.5 Hz, 1 H), 5.21 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.08 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.62 (br t, *J* = 7.5 Hz, 1 H), 3.29 (s, 3 H), 1.67 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6, 137.1, 129.7, 129.6, 128.7, 128.2, 116.0, 50.0, 38.1, 17.9;

MS (ES+): *m*/*z* (%) = 282 ([M + H]$^+$, 100), 304 ([M + Na]$^+$, 60), 336 ([M + Na + MeOH]$^+$, 30).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}ClNOS$: 304.0533; found: 304.0528.

(*E*)-*S*-Hexa-1,4-dien-3-yl Methyl(*p*-tolyl)carbamothioate (7t)[26]

General procedure B was followed using **10c** (50 mg, 0.24 mmol) in THF (1 mL), HOBt (16 mg, 0.118 mmol, 0.5 equiv), and 4-methyl-*N*-methylaniline (0.04 mL, 0.29 mL). The crude mixture was washed with aq 1 M HCl (2 mL) for 15 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (50 mg, 79%); R_f = 0.37 (PE–EtOAc, 9:1).

IR (film): 1653, 1513, 1268 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.5 Hz, 2 H), 7.15 (d, *J* = 9.0 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1 H), 5.65 (dqd, *J* = 15.5, 6.5, 1.0 Hz, 1 H), 5.48 (ddq, *J* = 15.5, 7.5, 1.5 Hz, 1 H), 5.20 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.06 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.62 (br t, *J* = 7.5 Hz, 1 H), 3.29 (s, 3 H), 2.37 (s, 3 H), 1.66 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 139.2, 138.5, 137.4, 130.1, 129.0, 128.2, 127.9, 115.7, 49.9, 38.3, 21.2, 17.9.

MS (ES+) *m*/*z* (%) = 262 ([M + H]$^+$, 100), 284 ([M + Na]$^+$, 60).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{19}NOS$: 284.1080; found: 284.1071.

(*E*)-*S*-Hexa-1,4-dien-3-yl 4-Fluorophenyl(methyl)carbamothioate (7u)[26]

General procedure B was followed using **10c** (50 mg, 0.24 mmol) in THF (1 mL), HOBt (32 mg, 0.236 mmol, 1.0 equiv), and 4-fluoro-*N*-methylaniline (0.04 mL, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 25 min and concentrated down to afford the title compound as a yellow oil (50 mg, 78%); R_f = 0.63 (PE–EtOAc, 8:2).

IR (film): 1650, 1503, 1219 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (dd, *J* = 9.0, 5.0 Hz, 2 H), 7.08 (dd, *J* = 9.0 Hz, 2 H), 5.87 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1 H), 5.67 (dqd, *J* = 15.0, 6.5, 1.0 Hz, 1 H), 5.48 (ddq, *J* = 15.0, 7.5, 1.5 Hz, 1 H), 5.22 (ddd, *J* = 17.0, 1.5, 1.5 Hz, 1 H), 5.08 (ddd, *J* = 10.0, 1.5, 1.5 Hz, 1 H), 4.62 (br t, *J* = 7.5 Hz, 1 H), 3.29 (s, 3 H), 1.67 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 161.5, 137.9, 137.2, 130.3, 128.8, 128.1, 116.5, 116.3, 115.9, 50.0, 38.3, 17.9.

MS (ES+): *m*/*z* (%) = 266 ([M + H]$^+$, 30), 388 ([M + Na]$^+$, 70).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}FNOS$: 288.0829; found: 288.0835.

(*S*)-4-Methylpent-1-en-3-yl 4-Chlorophenyl(methyl)carbamothioate (7v)[26]

General procedure B was followed using (*S*)-4-methylpent-1-en-3-yl 1*H*-imidazole-1-carbothioate **(10d**; 200 mg, 0.95 mmol) in THF (4.5 mL), HOBt (128 mg, 0.95 mmol, 1.0 equiv), and 4-chloro-*N*-methylaniline (0.14 mL, 1.14 mmol). The crude mixture was washed with aq 1 M HCl (3 mL) for 15 min and concentrated down. The crude product was purified by column chromatography (100%

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PE, then PE–EtOAc, 95:5) to afford the title compound as a pale yellow oil (219 mg, 81%); R_f = 0.53 (PE–EtOAc, 8:2).

IR (film): 1657, 1488, 1277 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 9.0 Hz, 2 H), 7.21 (d, *J* = 9.0 Hz, 2 H), 5.73 (ddd, *J* = 17.0, 10.0, 9.0 Hz, 1 H), 5.22 (ddd, *J* = 17.0, 1.5, 1.0 Hz, 1 H), 5.07 (dd, *J* = 10.0, 1.0 Hz, 1 H), 3.93 (dd, *J* = 9.0, 6.0 Hz, 1 H), 3.28 (s, 3 H), 1.91 (oct, *J* = 6.0 Hz, 1 H), 0.93 (d, *J* = 6.0 Hz, 3 H), 0.91 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 140.7, 136.7, 136.3, 129.6, 129.5, 116.4, 55.8, 38.2, 32.2, 20.2, 19.6;

MS (ES+): *m*/*z* (%) = 284 ([M + H]$^+$, 70), 306 ([M + Na]$^+$, 100), 338 ([M + Na + MeOH]$^+$, 54).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{18}ClNOS$: 284.0871; found: 284.0871.

(*S*)-4-Methylpent-1-en-3-yl Methyl(*p*-tolyl)carbamothioate (7w)[26]

General procedure B was followed using **10d** (50 mg, 0.24 mmol) in THF (1 mL), HOBt (16 mg, 0.12 mmol, 0.5 equiv), and 4-methyl-*N*-methylaniline (0.04 mL, 0.29 mmol). The crude mixture was washed with aq 1 M HCl (2 mL) for 40 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (353 mg, 84%); R_f = 0.75 (PE–EtOAc, 8:2).

IR (film): 1654, 1513, 1266 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 5.73 (ddd, *J* = 17.5, 10.5 Hz, 9.0, 1 H), 5.22 (dd, *J* = 17.5, 1.5 Hz, 1 H), 5.06 (dd, *J* = 10.5, 1.5 Hz, 1 H), 3.93 (dd, *J* = 9.0, 6.0 Hz, 1 H), 3.28 (s, 3 H), 2.38 (s, 3 H), 1.89 (oct, *J* = 6.0 Hz, 1 H), 0.92 (d, *J* = 6.0 Hz, 3 H), 0.91 (d, *J* = 6.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 139.6, 138.3, 137.0, 130.1, 128.1, 116.2, 55.6, 38.4, 32.2, 21.2, 20.3, 19.6.

MS (ES+): *m*/*z* (%) = 264 ([M + H]$^+$, 30), 286 ([M + Na]$^+$, 50).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{21}NOS$: 264.1417; found: 264.1413.

(*E*)-*S*-Pent-3-en-2-yl 4-Chlorophenyl(methyl)carbamothioate (7x)[26]

General procedure B was followed using (*E*)-*S*-pent-3-en-2-yl 1*H*-imidazole-1-carbothioate (**10e**; 50 mg, 0.25 mmol) in THF (2.5 mL), HOBt (18 mg, 0.13 mmol, 0.5 equiv), and 4-chloro-*N*-methylaniline (0.04 mL, 0.30 mmol). The crude mixture was washed with aq 3 M HCl (3 mL) for 50 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 95:5, then 9:1) to afford the title compound as a colourless oil (33 mg, 49%), R_f = 0.36 (PE–EtOAc, 8:2).

IR (film): 1651, 1487, 1013 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 9.0 Hz, 2 H), 7.20 (d, *J* = 9.0 Hz, 2 H), 5.62 (dqd, *J* = 15.0, 6.5, 1.0 Hz, 1 H), 5.47 (ddq, *J* = 15.0, 7.0, 1.5 Hz, 1 H), 4.07 (quint, *J* = 7.0 Hz, 1 H), 3.29 (s, 3 H), 1.64 (d, *J* = 6.5 Hz, 3 H), 1.36 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 140.7, 134.0, 132.1, 129.6, 129.5, 126.1, 42.7, 38.0, 21.0, 17.8.

MS (ES+): *m*/*z* (%) = 270 ([M + H]$^+$, 40), 292 ([M + Na]$^+$, 100).

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{16}ClNOS$: 292.0534; found: 292.0525.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 4-Chlorophenyl(methyl)carbamothioate (7y)[26]

General procedure B was followed using (*E*)-*S*-4-cyclohexylbut-3-en-2-yl 1*H*-imidazole-1-carbothioate (**10f**; 180 mg, 0.68 mmol) in THF (2.5 mL), HOBt (46 mg, 0.34 mmol, 0.5 equiv), and 4-chloro-*N*-methylaniline (0.10 mL, 0.82 mmol). The crude mixture was washed with aq 2 M HCl (3 mL) for 30 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (169 mg, 73%); R_f = 0.77 (PE–EtOAc, 8:2).

IR (film): 2921, 1651, 1486, 1280, 964 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 9.0 Hz, 2 H), 7.20 (d, *J* = 9.0 Hz, 2 H), 5.54 (dd, *J* = 15.5, 6.5 Hz, 1 H), 5.41 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.08 (quint, *J* = 7.0 Hz, 1 H), 3.28 (s, 3 H), 1.93–1.84 (m, 1 H), 1.71–1.58 (m, 4 H), 1.37 (d, *J* = 7.0 Hz, 3 H), 1.28–0.96 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 140.7, 137.2, 133.9, 129.6, 129.5, 128.1, 42.7, 40.3, 38.1, 32.8/32.7, 26.1/26.0, 21.1.

MS (ES+): *m*/*z* (%) = 338 [M + H]$^+$, 70), 360 ([M + Na]$^+$, 100).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{24}ClNOS$: 338.1340; found: 338.1346.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl Methyl(*p*-tolyl)carbamothioate (7z)[26]

General procedure B was followed using **10f** (180 mg, 0.68 mmol) in THF (2.5 mL), HOBt (46 mg, 0.34 mmol, 0.5 equiv), and 4-methyl-*N*-methylaniline (0.11 mL, 0.82 mmol). The crude mixture was washed with aq 1 M HCl (3 mL) for 20 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (185 mg, 86%); R_f = 0.76 (PE–EtOAc, 8:2).

IR (film): 2921, 1651, 1513, 1268, 1107 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (d, *J* = 8.0 Hz, 2 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 5.52 (dd, *J* = 15.5, 6.0 Hz, 1 H), 5.40 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.07 (quint, *J* = 7.0 Hz, 1 H), 3.28 (s, 3 H), 2.37 (s, 3 H), 1.91–1.83 (m, 1 H), 1.69–1.60 (m, 4 H), 1.36 (d, *J* = 7.0 Hz, 3 H), 1.27–0.95 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 139.5, 138.3, 136.9, 130.1, 128.3, 128.0, 42.6, 40.3, 38.2, 32.8/32.7, 26.1/26.0, 21.2, 21.1.

MS (ES+): *m*/*z* (%) = 318 ([M + H]$^+$, 100), 340 ([M + Na]$^+$, 60).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{27}NOS$: 338.1887; found: 318.1892.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 3-Chlorophenyl(methyl)carbamothioate (7aa)[26]

General procedure B was followed using **10f** (180 mg, 0.68 mmol) in THF (2.5 mL), HOBt (92 mg, 0.68 mmol, 1.0 equiv), and 3-chloro-*N*-methylaniline (0.10 mL, 0.82 mmol). The crude mixture was washed with aq 2 M HCl (3 mL) for 30 min and concentrated down. The crude product was purified by filtration over silica gel (PE–EtOAc, 9:1) to afford the title compound as a yellow oil (178 mg, 77%); R_f = 0.79 (PE–EtOAc, 8:2).

IR (film): 2922, 1656, 1589, 1277, 965, 694 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.32 (m, 2 H), 7.28–7.27 (m, 1 H), 7.18 (ddd, *J* = 5.5, 3.5, 2.0, 1 H), 5.55 (ddd, *J* = 15.5, 6.5, 1.0 Hz, 1 H), 5.41 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.09 (quint, *J* = 7.0 Hz, 1 H), 3.29 (s, 3 H), 1.93–1.85 (m, 1 H), 1.71–1.60 (m, 4 H), 1.38 (d, *J* = 7.0 Hz, 3 H), 1.27–0.97 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 143.4, 137.2, 134.7, 130.3, 128.3, 128.0, 126.4, 42.7, 40.3, 38.0, 32.8/32.7, 26.1/26.0, 21.1.

MS (ES+): *m*/*z* (%) = 338 ([M + H]$^+$, 50), 360 ([M + Na]$^+$, 100).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{24}ClNOS$: 338.1340; found: 338.1349.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 2-Methoxyphenyl(methyl)carbamothioate (7bb)[26]

General procedure B was followed using (200 mg, 0.76 mmol) in THF (4.0 mL), HOBt (154 mg, 1.14 mmol, 1.5 equiv), and 2-methoxy-*N*-methylaniline (125 mg, 0.91 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 25 min and concentrated down. The crude product was purified by column chromatography (100%

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PE, then PE–EtOAc, 98:2, then 96:4, then 95:5) to afford the title compound as a colourless sticky oil (196 mg, 77%); R_f = 0.48 (PE–EtOAc, 8:2).

IR (film): 2921, 1651, 1499, 1271, 747 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (ddd, *J* = 8.0, 8.0, 1.5 Hz, 1 H), 7.21 (br d, *J* = 8.0 Hz, 1 H), 6.96 (m, 2 H), 5.50 (m, 1 H), 5.40 (m, 1 H), 4.07 (m, 1 H), 3.85 (s, 3 H), 3.21 (s, 3 H), 1.91–1.84 (m, 1 H), 1.69–1.60 (m, 4 H), 1.34 (2 d, rotamers, *J* = 7.0 Hz, 3 H), 1.25–0.95 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2/156.1 (rotamers), 136.7/136.6 (rotamers), 130.8, 130.2, 128.6/128.5, 120.8, 112.2/112.1 (rotamers), 55.6, 42.3/42.2 (rotamers), 40.4, 36.7, 32.8/32.7, 26.1/26.0, 21.1.

MS (ES+): *m*/*z* = 334 ($[M + H]^+$, 100%).

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{27}NO_2S$: 356.1655; found: 356.1659.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 3-Methoxyphenyl(methyl)carbamothioate (7cc)[26]

General procedure B was followed using **10f** (200 mg, 0.76 mmol) in THF (4.0 mL), HOBt (154 mg, 1.14 mmol, 1.5 equiv), and 3-methoxy-*N*-methylaniline (0.12 mL, 0.91 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 25 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 98:2, then 96:4, then 95:5) to afford the title compound as a yellow oil (197 mg, 78%); R_f = 0.48 (PE–EtOAc, 8:2); $[\alpha]_D^{20}$ –10.75 (*c* 0.16, $CHCl_3$).

HPLC: er 94:6; (*R*,*R*)-Whelk-01, hexane–*i*-PrOH (95:5), 1 mL/min, 254.4 nm; *S*-enantiomer (major), t_R = 8.9 min, *R*-enantiomer (minor), t_R = 11.2 min.

IR (film): 2921, 1651, 1599, 1283, 1217, 1042 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.30 (dd, *J* = 8.0, 8.0 Hz, 1 H), 6.89 (ddd, *J* = 8.5, 2.5, 1.0 Hz, 1 H), 6.86 (ddd, *J* = 8.0, 2.5, 1.0 Hz, 1 H), 6.80 (dd, *J* = 2.5, 2.5 Hz, 1 H), 5.53 (ddd, *J* = 15.5, 6.5, 1.0 Hz, 1 H), 5.41 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.08 (quint, *J* = 7.0 Hz, 1 H), 3.82 (s, 3 H), 3.30 (s, 3 H), 1.93–1.84 (m, 1 H), 1.71–1.58 (m, 4 H), 1.37 (d, *J* = 7.0 Hz, 3 H), 1.28–0.96 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 160.2, 143.3, 137.0, 130.0, 128.3, 120.3, 113.9, 113.7, 55.4, 42.6, 40.4, 38.1, 32.8/32.7, 26.1/26.0, 21.1.

MS (ES+): *m*/*z* (%) = 334 ($[M + H]^+$,100), 356 ($[M + Na]^+$, 40).

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{27}NO_2S$: 356.1655; found: 356.1649.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl Methyl(naphthalen-1-yl)carbamothioate (7dd)[26]

General procedure B was followed using **10f** (200 mg, 0.76 mmol) in THF (4.0 mL), HOBt (153 mg, 1.14 mmol, 1.5 equiv), and *N*-methylnaphthalen-1-amine (143 mg, 0.91 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 25 min and concentrated down. The crude product was purified by column chromatography (PE–EtOAc, 95:5, then 9:1) to afford the title compound as a brown solid (110 mg, 41%); mp 83–85 °C; R_f = 0.36 (PE–EtOAc 8:2).

IR (neat): 2927, 1643, 1338, 1279, 777 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.76 (m, 2 H), 7.70–7.67 (m, 1 H), 7.47–7.31 (m, 4 H), 5.41–5.34 (m, 1 H), 5.21 (2 dd, rotamers, *J* = 15.5, 7.0 Hz, 1 H), 4.01–3.96 (m, 1 H), 3.30/3.29 (2 s, rotamers, 3 H), 1.75–1.68 (m, 1 H), 1.57–1.48 (m, 4 H), 1.19 (2 d, *J* = 7.0 Hz, 3 H), 1.12–0.81 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4/169.3 (rotamers), 138.1/138.0, 136.9/136.6, 134.6, 130.5, 129.3, 128.5, 128.4, 128.2, 127.5/127.4 (rotamers), 127.2/127.2 (rotamers), 126.5, 125.6/125.6 (rotamers), 122.6 /122.4 (rotamers), 42.4, 40.3/40.2 (rotamers), 40.0, 32.8/32.6, 26.0/25.9, 20.9/20.7 (rotamers).

MS (ES+): *m*/*z* (%) = 354 ($[M + H]^+$, 100), 376 ($[M + Na]^+$, 80).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{27}NOS$: 354.1887; found: 354.1889.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 3-Fluorophenyl(methyl)carbamothioate (7ee)[26]

General procedure B was followed using **10f** (200 mg, 0.76 mmol) in THF (4.0 mL), HOBt (154 mg, 1.14 mmol, 1.5 equiv), and 3-fluoro-*N*-methylaniline (0.10 mL, 0.91 mmol). The crude mixture was washed with aq 1 M HCl (5 mL) for 25 min and concentrated down. The crude product was purified by column chromatography (100% PE, then PE–EtOAc, 98:2, then 96:4) to afford the title compound as a yellow oil (145 mg, 59%); R_f = 0.68 (PE–EtOAc, 8:2).

IR (film): 2922, 1656, 1485, 1282, 1194, 966, 696 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (ddd, *J* = 8.0, 8.0, 6.5 Hz, 1 H), 7.08–7.05 (m, 2 H), 7.03–6.99 (m, 1 H), 5.55 (ddd, *J* = 15.5, 6.5 Hz, 1 H), 5.41 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.09 (quint, *J* = 7.0 Hz, 1 H), 3.30 (s, 3 H), 1.94–1.85 (m, 1 H), 1.71–1.60 (m, 4 H), 1.37 (d, *J* = 7.0 Hz, 3 H), 1.28–0.97 (m, 6 H)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.4, 164.0, 143.7/143.6 (rotamers), 137.2, 130.4/130.4 (rotamers), 128.1, 123.8, 115.6/115.4/115.3/115.2, 42.7, 40.3, 38.0, 32.8/32.7, 26.1/26.0, 21.0.

MS (ES+): *m*/*z* = 344 $[M + Na]^+$; 100%).

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{24}FNOS$: 344.1455; found: 344.1445.

***S*-But-3-en-2-yl 1*H*-Imidazole-1-carbothioate (10a)[25]**

General procedure A was followed using crotyl alcohol (**5a**; 500 mg, 6.9 mmol), TCDI (2.5 g, 13.8 mmol), DMAP (86 mg, 0.70 mmol), and CH_2Cl_2 (70 mL). The crude product was purified by column chromatography (PE–EtOAc, 8:2) to afford the title compound as a yellow oil (1.24 g, 98%); R_f = 0.44 (PE–EtOAc, 1:1).

IR (film): 1687, 1468, 1210 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.17 (br s, 1 H), 7.44 (t, *J* = 1.0 Hz, 1 H), 7.08 (m, 1 H), 5.94 (ddd, *J* = 17.0, 10.5, 7.0 Hz, 1 H), 5.36 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.20 (ddd, *J* = 10.5, 1.0, 1.0 Hz, 1 H), 4.38 (quint, *J* = 7.0, 1.0 Hz, 1 H), 1.55 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 136.9, 135.2, 130.7, 116.8, 115.6, 43.2, 19.4.

MS (ES+): *m*/*z* (%) = 183 ($[M + H]^+$, 30), 205 ($[M + Na]^+$, 70), 237 ($[M + Na + MeOH]^+$, 100).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_8H_{10}N_2OS$: 183.0587; found: 183.0586.

***S*-Hex-1-en-3-yl 1*H*-Imidazole-1-carbothioate (10b)[25]**

General procedure A was followed using hex-2-en-1-ol (500 mg, 5.0 mmol), TCDI (1.8 g, 10.1 mmol), DMAP (60 mg, 0.49 mmol), and CH_2Cl_2 (50 mL). The crude product was purified by filtration over silica gel (PE–EtOAc, 1:1) to afford the title compound as a yellow oil (1.05 g, 100%); R_f = 0.16 (PE–EtOAc, 8:2).

IR (film): 1689, 1467, 1211 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (br s, 1 H), 7.43 (br s, 1 H), 7.06 (br s, 1 H), 5.81 (ddd, *J* = 17.0, 10.0, 7.5 Hz, 1 H), 5.34 (d, *J* = 17.0 Hz, 1 H), 5.17 (d, *J* = 10.0 Hz, 1 H), 4.24 (q, *J* = 7.5 Hz, 1 H), 1.76 (q, *J* = 7.5 Hz, 2 H), 1.50–1.40 (m, 2 H), 0.94 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.2, 136.4, 135.4, 130.8, 117.6, 115.8, 48.7, 35.8, 20.2, 13.5.

MS (ES+) *m*/*z* (%) = 233 ($[M + Na]^+$, 50), 265 ($[M + Na + MeOH]^+$, 100).

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HRMS: *m/z* [M + Na]$^+$ calcd for $C_{10}H_{14}N_2OS$: 233.0719; found: 233.0722.

(*E*)-*S*-Hexa-1,4-dien-3-yl 1*H*-Imidazole-1-carbothioate (10c)[25]
General procedure A was followed using hexa-2,4-dien-1-ol (500 mg, 5.1 mmol), TCDI (1.8 g, 10.1 mmol), DMAP (62 mg, 0.51 mmol), and CH_2Cl_2 (50 mL). The crude product was purified by filtration over silica gel (PE–EtOAc, 1:1) to afford the title compound as a yellow oil (689 mg, 65%); R_f = 0.64 (PE–EtOAc, 1:1).

IR (film): 1690, 1468, 1212 cm^{-1}.

^{1}H NMR (400 MHz; $CDCl_3$): δ = 8.17 (br s, 1 H), 7.43 (t, *J* = 1.5 Hz, 1 H), 7.08 (m, 1 H), 5.96 (ddd, *J* = 17.20, 10.0, 7.0 Hz, 1 H), 5.84 (dqd, *J* = 15.0, 6.5, 1.0 Hz, 1 H), 5.59 (ddq, *J* = 15.0, 7.0, 1.5 Hz, 1 H), 5.36 (ddd, *J* = 17.0, 1.0, 1.0 Hz, 1 H), 5.24 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.87 (br t, *J* = 7.0 Hz, 1 H), 1.74 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.9, 135.4, 134.9, 130.9, 130.5, 126.8, 118.0, 115.8, 50.5, 17.9.

MS (ES+): *m/z* = 209 ([M + H]$^+$, 90), 231 ([M + Na]$^+$, 40), 263 ([M + Na + MeOH]$^+$, 100).

HRMS: *m/z* [M + H]$^+$ calcd for $C_{10}H_{12}N_2OS$: 209.0743; found: 209.0726.

***S*-4-Methylpent-1-en-3-yl 1*H*-Imidazole-1-carbothioate (10d)[25]**
General procedure A was followed using 4-methylpent-2-en-1-ol (25 mg, 0.25 mmol), TCDI (89 mg, 0.50 mmol), DMAP (3 mg, 0.025 mmol), and CH_2Cl_2 (52.5 mL). The crude product was purified by filtration over silica gel (PE–EtOAc, 8:2) to afford the title compound as a pale yellow oil (47 mg, 88%); R_f = 0.27 (PE–EtOAc, 8:2).

IR (film): 1689, 1467, 1211 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (br s, 1 H), 7.46 (t, *J* = 1.5 Hz, 1 H), 7.08 (dd, *J* = 1.5, 1.0 Hz, 1 H), 5.85 (ddd, *J* = 17.0, 10.0, 9.0 Hz, 1 H), 5.35 (d, *J* = 17.0 Hz, 1 H), 5.21 (ddd, *J* = 10.0, 1.0, 1.0 Hz, 1 H), 4.18 (dd, *J* = 9.0, 6.5 Hz, 1 H), 2.08 (oct, *J* = 6.5 Hz, 1 H), 1.04 (2 dd, *J* = 6.5, 1.0 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3, 135.5, 134.8, 130.8, 118.4, 115.9, 56.2, 32.0, 20.0, 19.7.

MS (ES+) *m/z* (%) = 211 ([M + H]$^+$, 20), 233 ([M + Na]$^+$, 100), 265 ([M + Na + MeOH]$^+$, 50).

HRMS: *m/z* [M + Na]$^+$ calcd for $C_{10}H_{14}N_2OS$: 233.0719; found: 233.0729.

(*E*)-*S*-Pent-3-en-2-yl 1*H*-Imidazole-1-carbothioate (10e)[25]
General procedure A was followed using pent-3-en-2-ol (50 mg, 0.58 mmol), TCDI (206 mg, 1.16 mmol), DMAP (7 mg, 0.06 mmol), and DCE (6 mL). The reaction mixture was stirred at r.t. for 2 h, then heated to 40 °C, and stirred at 40 °C for 24 h. The crude product was purified by filtration over silica gel (PE–EtOAc, 8:2) to afford the title compound as a yellow oil (112 mg, 98%); R_f = 0.30 (PE–EtOAc, 8:2).

IR (film): 1686, 1211, 880 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H), 7.42 (d, *J* = 1.5 Hz, 1 H), 7.07 (s, 1 H), 5.80 (dqd, *J* = 15.0, 6.45, 1.0 Hz, 1 H), 5.54 (ddq, *J* = 15.0, 7.5, 1.5 Hz, 1 H), 4.34 (quint, *J* = 7.5 Hz, 1 H), 1.70 (d, *J* = 6.5 Hz, 3 H), 1.52 (d, *J* = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 135.4, 130.8, 130.1, 128.5, 115.8, 43.4, 20.5, 17.7.

MS (ES+): *m/z* (%) = 197 ([M + H]$^+$, 100), 219 ([M + Na]$^+$, 70), 251 ([M + Na + MeOH]$^+$, 70).

HRMS: *m/z* [M + Na]$^+$ calcd for $C_9H_{12}N_2OS$: 219.0563; found: 219.0567.

(*E*)-*S*-4-Cyclohexylbut-3-en-2-yl 1*H*-Imidazole-1-carbothioate (10f)[25]
General procedure A was followed using (*E*)-1-cyclohexylbut-2-en-1-ol (1.0 g, 6.48 mmol), TCDI (2.31 g, 12.97 mmol), DMAP (79 mg, 0.65 mmol), and CH_2Cl_2 (40 mL). The crude product was purified by column chromatography (PE–EtOAc, 9:1, then, 85:15, then 8:2) to afford the title compound as a yellow oil (1.55 g, 90%); R_f = 0.51 (PE–EtOAc, 8:2); $[\alpha]_D^{20}$ –48.0 (*c* 0.07, $CHCl_3$).

HPLC: er 6:94; Chiralpak AD-H, hexane–*i*-PrOH (97:3), 214.4 and 254.4 nm, 1 mL/min; *R*-enantiomer (minor), t_R = 15.3 min; *S*-enantiomer (major), t_R = 20.3 min.

IR (film): 1689, 1212, 882 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H), 7.43 (d, *J* = 1.0 Hz, 1 H), 7.07 (s, 1 H), 5.73 (dd, *J* = 15.5, 7.0 Hz, 1 H), 5.47 (ddd, *J* = 15.5, 7.0, 1.0 Hz, 1 H), 4.34 (quint, *J* = 7.0 Hz, 1 H), 1.99–1.91 (m, 1 H), 1.74–1.62 (m, 4 H), 1.52 (d, *J* = 7.0 Hz, 3 H), 1.31–1.01 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 139.6, 135.4, 130.7, 126.2, 115.8, 43.6, 40.3, 32.6/32.6, 26.0/25.9, 20.6.

MS (ES+): *m/z* (%) = 265 ([M + H]$^+$, 100), 287 ([M + Na]$^+$, 55).

HRMS: *m/z* [M + H]$^+$ calcd for $C_{14}H_{20}N2OS$: 265.1370; found: 265.1369.

Kinetic Resolution of 1-Cyclohexylbut-2-en-1-ol via Sharpless Asymmetric Epoxidation[27]
To a solution of 1-cyclohexylbut-2-en-1-ol (1.00 g, 6.48 mmol) in CH_2Cl_2 (25 mL) at r.t. was added (+)-diisopropyl tartrate [(+)-DIPT, 0.20 mL, 228 mg, 0.97 mmol, 0.15 equiv], followed by powdered 4 Å molecular sieves (250 mg, 20–30 wt% based on allylic alcohol, previously dried under reduced pressure at 160 °C overnight). The reaction mixture was cooled to –20 °C (internal temperature monitored). Ti(O*i*-Pr)$_4$ (0.19 mL, 184 mg, 0.65 mmol, 0.10 equiv) was added and the mixture was stirred at –20 °C for 20–30 min. Anhyd *tert*-butyl hydroperoxide (TBHP) (0.71 mL, 5.5 M in decane, 3.89 mmol, 0.6 equiv) was added dropwise, maintaining the internal temperature between –21 and –19 °C. The reaction mixture was stirred at –20 °C for 15 h before an aliquot (0.1 mL) was removed and quenched with 2 mL of an aq solution of $FeSO_4 \cdot 7H_2O$ and citric acid monohydrate (33 g of $FeSO_4 \cdot 7H_2O$, 11 g of citric acid monohydrate, 100 mL of distilled H_2O). ^{1}H NMR of the concentrated organic fraction of the aliquot showed an allylic alcohol/epoxide ratio of 1:1.3. The reaction was quenched at –20 °C by adding the aforementioned ferrous aqueous solution (20 mL) and warming the reaction to r.t. and vigorously stirring until two clear phases appeared (30 min). The mixture was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic layers concentrated to the original volume, washed with 30% NaOH in brine (6.5 mL, 1 mL/1.0 mmol of substrate). The mixture was extracted with CH_2Cl_2 (3 × 30 mL) and the combined organic layers were washed with brine (2 × 50 mL), dried ($MgSO_4$), filtered, and concentrated down. The crude was purified by column chromatography (100% PE, then PE–EtOAc, 95:5, then, 9:1, then, 85:15) to afford the *R*-allylic alcohol as a colourless oil (296 mg, 30%).

The enantiomeric ratio was determined by chiral GC [chiral column G-TA, method: 3 min at 50 °C, up to 80 °C by 5 °C/min, up to 102 °C by 1 °C/min, 5 min hold at 102 °C, up to 110 °C by 1 °C/min, up to 180 °C by 10 °C/min; *R*-enantiomer (major), t_R = 29.3 min, *S*-enantiomer (minor), t_R = 31.1 min, er 93:7].

R_f = 0.58 (PE–EtOAc, 8:2); $[\alpha]_D^{20}$ –1.0 (*c* 0.12, $CHCl_3$) {Lit[27] $[\alpha]_D^{25}$ –13.33 (*c* 2.76, EtOH).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.62 (dq, *J* = 15.0, 6.5 Hz, 1 H), 5.47 (ddq, *J* = 15.0, 7.0, 1.5 Hz, 1 H), 3.75 (t, *J* = 7.0 Hz, 1 H), 1.87–1.83 (m, 1 H), 1.77–1.63 (m, 4 H), 1.70 (dd, *J* = 6.5, 1.5 Hz, 3 H), 1.43–0.86 (m, 8 H).

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