

Rapid Access to Thiolactone Derivatives Through Radical-Mediated Acyl-Thiol-Ene and Acyl-Thiol-Yne Cyclisation

Ruairí O. Mc Court,^[a] Fabrice Dénès,^[b] Goar Sanchez-Sanz^[c] and Eoin M. Scanlan^[a]

[a]: Trinity Biomedical Sciences Institute, Trinity College, 152-160 Pearse Street, Dublin 2, Ireland

[b]: CEISAM UMR 6230 - UFR des Sciences et des Techniques, Université de Nantes, 2 rue de la Houssinière - BP 92208, 44322 Nantes Cedex 3 (France)

[c]: Irish Centre for High-End Computing, 7th Floor, Tower Building, Trinity Technology & Enterprise Campus, Grand Canal Quay, Dublin 2, Ireland

E-mail: scanlae@tcd.ie

Contents

1. Instrumental and General Considerations.....	2
2. General Procedures	2
3. Preparation of DMTrtSH	4
4. Preparation of Unsaturated Carboxylic Acids.....	5
5. Synthesis of Protected Thioacids	25
6. Acyl-Thiol-Ene Cyclisation	36
7. Acyl-Thiol-Yne Cyclisation	43
8. Acyl-Thiol-Ene Cyclisation on Large Scale	45
9. Computational Studies.....	46
10. NMR Spectra	58
11. References	118

1. Instrumental and General Considerations

Unless otherwise stated; all commercial chemicals were obtained from Sigma-Aldrich, Fluka, Fluorochem, Alfa-Aesar, or Fischer Scientific, without further purification. Deuterated solvents for NMR were purchased from Apollo. Dry solvents were distilled under argon and dried over 4 Å molecular sieves prior to use. Solvents for synthesis purposes were used at GPR grade. A Bruker Advance 400 spectrometer, ^1H (400.13 MHz) and ^{13}C (100.6 MHz) and a Bruker Ultrashield 600, ^1H (600.13 MHz) and ^{13}C (150.6 MHz), were employed for NMR spectra. Resonances δ , from the centre point, are in ppm units downfield from an internal reference.¹ NMR data was processed using TopSpin software. Infrared spectra (IR) were recorded on a Perkin Elmer spectrometer. Mass spectrometry analysis was performed with a Q-ToF Premier Waters Maldi-quadrupole time-of-flight (Q-ToF) mass spectrometer equipped with a with Z-spray electrospray ionisation (ESI) and matrix assisted laser desorption ionisation (MALDI) sources. LRMS values are reported for DMTrt-thioesters due to their instability in solution. Silica gel Florisil (200 mesh; Aldrich) was used for column chromatography. Thin-layer chromatography (TLC) was performed using Merck 60 F254 silica gel (pre-coated, 0.2 mm thick, 20 x 20 cm) and visualised by UV light (254 nm), iodine, or molybdenum staining. All UV reactions were carried out in a Luzchem photoreactor, LZC-EDU (110 V/ 60 Hz) containing 10 UV lamps irradiating at 350 nm. All compounds prepared *via* general procedures were done with the amount reported, unless otherwise stated.

2. General Procedures

General Procedure A: Synthesis of γ -Unsaturated Ethyl Esters from Allyl/Propargyl Bromides:

To a solution of EtOAc (2.0 equiv.) and CuI (4.0 equiv.) in anhydrous THF (6.5 mL/mmol), under an atmosphere of argon at -78 °C was added 2.0 M LDA in hexane (2.2 equiv.). The mixture was stirred for 30 min and the allylic/propargylic bromide (1.0 equiv.) in anhydrous THF (2 mL/mmol), under argon, was added and the mixture stirred at this temperature for 1 h before being warmed to -30 °C. When full consumption was observed by TLC (10% EtOAc/Hexane (v/v)), the mixture was poured into a separating funnel, diluted with CH_2Cl_2 , and quenched with saturated aqueous solution of NaHCO_3 . After phase separation, the aqueous phase was washed twice with CH_2Cl_2 . The combined organic phases were washed with water, then brine, dried over MgSO_4 , filtered, and the solvent

evaporated *in vacuo*. Purification of the crude product was achieved by column chromatography on silica gel.

General Procedure B: Ester Hydrolysis:

To a stirred solution of the ester (1.0 equiv.) in 10% H₂O/MeOH (10 mL/mmol) was added NaOH (20 equiv.). The mixture was heated at 100 °C for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution, and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂, and the organic phases were discarded. The aqueous phase was acidified with aqueous 4 M HCl solution and extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the carboxylic acids, without requiring further purification.

General Procedure C: Steglich-Coupling of γ -Unsaturated Carboxylic Acids and DMTrtSH:

To a solution of the γ -unsaturated carboxylic acid (1.0 mmol, 1.0 equiv.) in anhydrous THF (12 mL/mmol), under argon was added *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC) (1.2mmol, 1.2 equiv.). The mixture was stirred for 15 min and DMTrtSH (1.0 mmol, 1.0 equiv.) and DMAP (0.25 mmol, 0.25 equiv.) in anhydrous THF (5mL/mmol of DMTrtSH) were added simultaneously. The mixture was stirred at rt for 16–24 h. The solution was diluted with CH₂Cl₂ (150 mL) and filtered through a plug of silica gel. The solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel.

General Procedure D: Deprotection and Cyclisation of Thioacids

To a stirred solution of γ -unsaturated DMTrt-thioester (0.5 mmol, 1.0 equiv.) in CH₂Cl₂ (3.0 mL, 6.0 mL/mmol) was added TFA (1 mL, 2.0 mL/mmol), followed immediately by the addition of Me₂EtSiH (1.5 mmol, 3.0 equiv). The reaction was stirred for 25 min, and the solvent, TFA and Me₂EtSiH were removed *in vacuo*, maintaining the temperature below 30 °C. To the crude thioacid was added 2,2-dimethoxy-2-phenyl-acetophenone (DPAP) (0.1 mmol, 0.2 equiv.) and 4-methoxyacetophenone (MAP) (0.1 mmol, 0.2 equiv.), and the mixture was dried under vacuum for 90 seconds, before the transfer of anhydrous, degassed EtOAc (30 mL, 60 mL/mmol) *via* cannula. The reaction mixture was placed in the UV oven for 2 h at 25 °C. The solvent was removed *in vacuo* and the crude product was purified by column chromatography on silica gel.

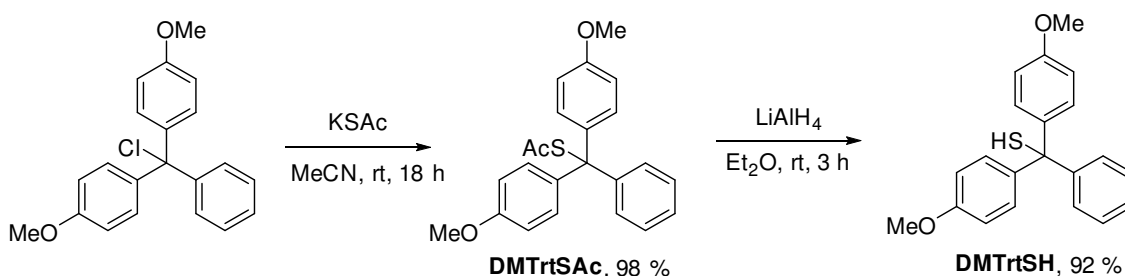
General Procedure E: Bromination with PBr₃:

To a solution of alcohol (1.0 equiv.) in anhydrous CH₂Cl₂ (3.0 mL/mmol), under an atmosphere of argon at 0 °C was slowly added PBr₃ (0.7 equiv.). The mixture was stirred for 10 min before being

allowed to warm to rt. When full conversion was observed by TLC (10% EtOAc/Hexane (v/v)), the mixture was poured into a separating funnel, diluted with CH₂Cl₂, and quenched with saturated aqueous solution of NaHCO₃. After phase separation, the aqueous phase was washed twice with CH₂Cl₂. The combined organic phases were washed with water, then brine, dried over MgSO₄, filtered, and the solvent evaporated *in vacuo*. Purification of the crude product was achieved by column chromatography on silica gel.

3. Preparation of DMTrtSH

DMTrtSH was prepared according to the following sequence:



S-dimethoxytrityl ethanethioate (DMTrtSAc):

To a solution of 4,4'-dimethoxytrityl chloride (4.00 g, 11.8 mmol, 1.0 equiv.) in MeCN (85 mL) at room temperature was added KSAc (5.00 g, 43.9 mmol, 3.7 equiv.), and the suspension was stirred vigorously for 18 h. The mixture was diluted with CH₂Cl₂ (200 mL) and filtered through a plug of silica gel. The solvent was removed *in vacuo* to yield the pure thioester as a red wax (4.37 g, 11.6 mmol, 98%) without the requirement for further purification. **R_f** = 0.19 (40 % EtOAc/Hexane (v/v)). **δ_H** (400 MHz, CDCl₃): 7.32–7.24 (m, 5H, Ar-H), 7.16 (d, *J*_{o-m} = 8.9 Hz, 4H, Ar-H), 6.82 (d, *J*_{m-o} = 8.9 Hz, 4H, Ar-H), 3.82 (s, 6H, OMe), 2.28 (s, 3H, SAc). **δ_C** (100 MHz, CDCl₃): 198.4 (C=O), 158.4 (Ar-OMe), 144.3, 136.2 (q, Ar-C) 130.9, 129.7, 127.8, 127.0, 113.0 (Ar-C), 69.7 (q-C), 55.1 (OMe), 30.6 (SAc). **v_{max}** (ATR)/cm⁻¹: 1033 (C-S), 1260 (C-O), 1692 (C=O). **HRMS**: (EI⁺) *m/z* calcd for C₂₁H₁₉O₂ = 303.1388 ([M-SAc]⁺). Found 381.1385.

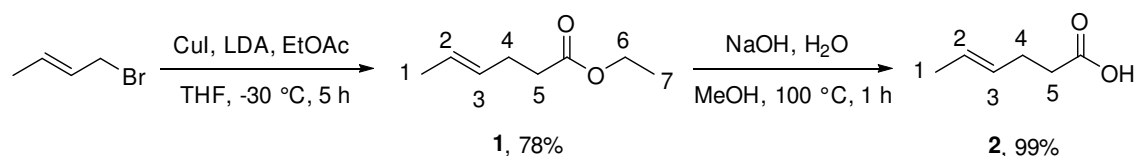
Dimethoxytritylthiol (DMTrtSH):

To a solution of the **DMTrtSAc** (3.78 g, 10.0 mmol, 1.0 equiv.) in anhydrous Et₂O (150 mL) at 0 °C, under an atmosphere of argon was added LiAlH₄ (700 mg, 18.4 mmol, 1.84 equiv.) and the

suspension was stirred at this temperature for 15 min before being warmed to rt and stirred for a further 5 h. The mixture was diluted with Et₂O (100 mL), poured into a separating funnel and quenched with a saturated aqueous solution of NaHCO₃ (100 mL). After phase separation, the aqueous phase was extracted twice more with Et₂O (2 x 60 mL). The combined organic phases were washed with water (50 mL), then brine (50 mL), dried over MgSO₄ and then filtered through a plug of silica gel. The solvent was removed *in vacuo* to yield the pure thiol as a red wax (3.10 g, 9.21 mmol, 92%) without requirement for further purification. **R_f** = 0.25 (40 % EtOAc/Hexane (v/v)). **δ_H** (400 MHz, CDCl₃): 7.33–7.24 (m, 5H, Ar-H), 7.19 (d, *J*_{o-m} = 8.8 Hz, 4H, Ar-H), 6.82 (d, *J*_{m-o} = 8.8 Hz, 4H, Ar-H), 3.83 (s, 6H, OMe), 3.09 (s, 1H, SH). **δ_C** (100 MHz, CDCl₃): 158.2 (Ar-OMe), 139.6, 130.5 (q, Ar-C), 129.2, 129.1, 127.8, 126.8, 113.0 (Ar-C), 77.2 (q-C), 55.3 (OMe). **v_{max}** (ATR)/cm⁻¹: 1087 (C-S), 1247 (C-O), 2578 (S-H). **HRMS**: (ESI) *m/z* calcd for C₂₁H₂₀O₂S ([M-H]⁻): 336.1184; found: 336.1136.

4. Preparation of Unsaturated Carboxylic Acids

2 was prepared according to the following sequence:



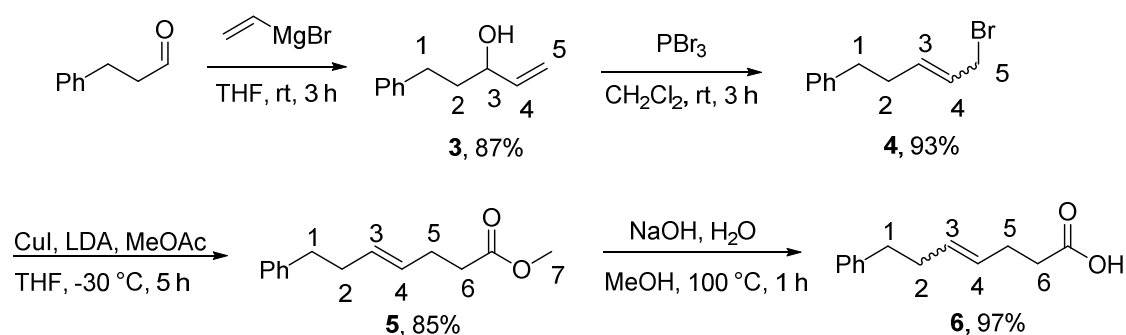
(E)-hex-4-enoate (**1**)

General procedure A to yield the title compound as sweetly fragrant brown oil (775 mg, 5.46 mmol, 78%) from crotyl bromide (0.77 mL, 7.50 mmol). Purification was achieved using 5% EtOAc/Hexane (v/v). **δ_H** (400 MHz, CDCl₃): 5.51–5.35 (m, 2H, H-2, H-3), 4.11 (q, *J*_{6,7} = 7.0 Hz, 2H, H-6), 2.37–2.24 (m, 4H, H-4, H-5), 1.62 (d, *J*_{1,2} = 5.8 Hz, 3H, H-1), 1.23 (t, *J*_{7,6} = 7.0 Hz, 3H, H-7). **LRMS**: (ESI) *m/z* calcd for C₁₆H₂₇O₄ ([2M-H]⁻): 283.2; found: 283.2. The spectral data were in accordance with those reported in the literature.²

(E)-Hex-4-enoic acid (**2**)

General procedure B to yield the title compound as a yellow oil (211 mg, 1.85 mmol, 99%) from **1** (264 mg, 1.86 mmol). **δ_H** (400 MHz, CDCl₃): 11.4 (bs, 1H, CO₂H), 5.54–5.35 (m, 2H, H-2, H-3), 2.40 (t, *J*_{5,4} = 6.9 Hz, 2H, H-5), 2.29 (app-q, 2H, H-4), 1.63 (dd, *J*_{1,2} = 6.0 Hz, *J*_{1,3} = 1.1 Hz, 3H, H-1). **LRMS**: (ESI) *m/z* calcd for C₆H₉O₂ ([M-H]⁻): 113.1; found: 113.2. The spectral data were in accordance with those reported in the literature.³

6 was prepared according to the following sequence:



5-Phenylpent-1-en-3-ol (3)

To a solution of hydrocinnamaldehyde (0.60 mL, 5.0 mmol, 1.0 equiv.) in anhydrous THF (10 mL) under an atmosphere of argon at 0 °C was added 0.7 M vinyl magnesium bromide (8.6 mL, 6.0 mmol, 1.2 equiv.). The reaction was stirred at this temperature for 30 min and then allowed to react at rt for 3 h. The solution was diluted with Et₂O (50 mL), poured into a separating funnel and quenched with a saturated aqueous solution of NH₄Cl (30 mL). After phase separation, the aqueous phase was extracted with Et₂O (3 x 30 mL). The combined organic layers were washed with brine, dried over MgSO₄ and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 10→25% EtOAc/Hexane (v/v) to furnish the product as a colourless oil (705 mg, 4.35 mmol, 87%). δ_{H} (400 MHz, CDCl₃): 7.36–7.26 (m, 3H, Ar-H), 7.23–7.18 (m, 2H, Ar-H), 5.96–5.85 (m, 1H, H-4), 5.39–5.11 (m, 2H, H-5), 4.13 (app-q, 1 H, H-3), 2.82–2.65 (m, 2H, H-1), 1.94–1.81 (m, 2H, H-2). **LRMS**: (ESI⁺) *m/z* calcd for C₁₁H₁₄ONa ([M+Na]⁺): 185.1; found: 185.1. The spectral data were in accordance with those reported in the literature.⁴

(5-Bromopent-3-en-1-yl)benzene (4)

General procedure E to yield the title compound (473 mg, 2.11 mmol, 93%) as a colourless wax from **3** (500 mg, 2.27 mmol). Purification was achieved using 4% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl₃): 7.30–7.25 (m, 2H, Ar-H), 7.20–7.14 (m, 3H, Ar-H), 5.84–5.65 (m, 2H, H-3, H-4), 3.92 (d, *J*_{5,4} = 7.3 Hz, 2H, H-5), 2.69 (t, *J*_{1,2} = 7.3 Hz, 2H, H-1), 2.38 (app-q, 2H, H-2). **LRMS**: (ESI⁺) *m/z* calcd

for $C_{11}H_{13}BrNa$ ($[M+H]^+$): 247.0; found: 247.0. The spectral data were in accordance with those reported in the literature.⁵

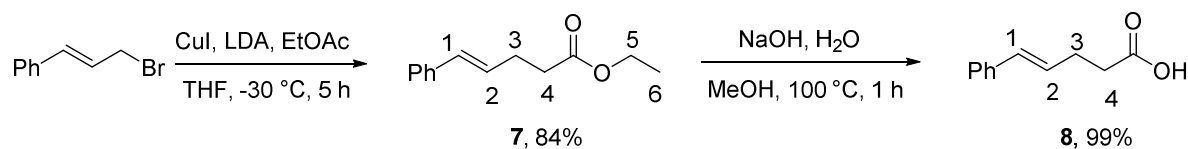
Methyl 7-phenylhept-4-enoate (5)

General procedure A (using MeOAc instead of EtOAc) to yield the title compound as pleasant, fragrant colourless oil (329 mg, 1.51 mmol, 85%) from **4** (400 mg, 1.77 mmol), with no further purification required. δ_H (400 MHz, $CDCl_3$): 7.29–7.23 (m, 2H, Ar-H), 7.20–7.12 (m, 3H, Ar-H), 5.48–5.37 (m, 2H, H-3, H-4), 3.64 (s, 2H, H-7), 2.64 (t, $J_{1-2} = 7.3$ Hz, 2H, H-1), 2.37–2.25 (m, 6H, H-2, H-5, H-6). **LRMS**: (ESI⁺) m/z calcd for $C_{14}H_{18}O_2Na$ ($[M+Na]^+$): 240.9; found: 240.9. The spectral data were in accordance with those reported in the literature.⁶

7-Phenylhept-4-enoic acid (6)

General procedure B to yield the title compound as a brown wax (356 mg, 1.743 mmol, 97%) from **5** (427 mg, 1.80 mmol). δ_H (400 MHz, $CDCl_3$): 7.29–7.23 (m, 2H, Ar-H), 7.19–7.12 (m, 3H, Ar-H), 5.65–5.40 (m, 2H, H-3, H-4), 2.56 (t, $J_{1-2} = 7.5$ Hz, 2H, H-1), 2.41–2.36 (m, 2H, H-6), 2.34–2.25 (m, 4H, H-2, H-5). **HRMS**: (ESI⁻) m/z calcd for $C_{13}H_{15}O_2$ ($[M-H]^-$): 203.1078; found: 203.1089. The spectral data were in accordance with those reported in the literature.⁷

8 was prepared according to the following sequence:



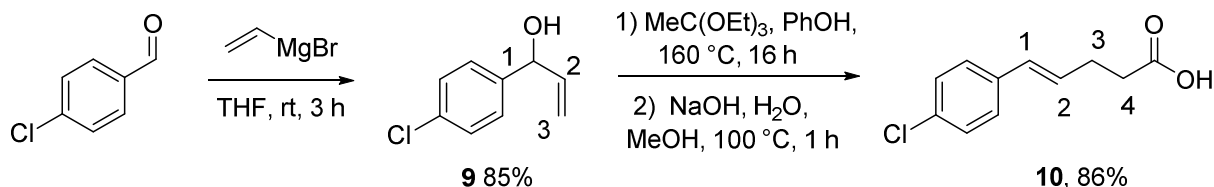
Ethyl (E)-5-phenylpent-4-enoate (7)

General procedure A to yield the title compound as sweetly fragrant yellow oil (513 mg, 2.51 mmol, 84%) from (*E*)-cinnamyl bromide (589 mg, 3.0 mmol). Purification was achieved using 5→7% EtOAc/Hexane (v/v). δ_H (400 MHz, $CDCl_3$): 7.36–7.20 (m, 5H, Ar-H), 6.45 (d, $J_{1-2} = 16.0$ Hz, 1H, H-1), 6.23 (dt, $J_{2-1} = 16.0$ Hz, $J_{2-3} = 6.4$ Hz, 1H, H-2), 4.17 (q, $J_{5-6} = 7.2$ Hz, 2H, H-5), 2.59–2.53 (m, 2H, H-4), 2.52–2.47 (m, 2H, H-3), 1.28 (t, $J_{6-5} = 7.2$ Hz, 3H, H-6). **LRMS**: (ESI⁻) m/z calcd for $C_{13}H_{15}O_2$ ($[M-H]^-$): 203.1; found: 203.0. The spectral data were in accordance with those reported in the literature.⁸

(E)-5-Phenylpent-4-enoic acid (8)

General procedure B to yield the title compound as a white wax (262 mg, 1.50 mmol, 99%) from **7** (306 mg, 1.50 mmol). δ_{H} (400 MHz, CDCl_3): 12.14 (bs, 1H, CO_2H), 7.45–7.29 (m, 5H, Ar-H), 6.54 (d, $J_{1,2} = 15.8$ Hz, 1H, H-1), 6.32–6.26 (m, 1H, H-2), 2.65–2.61 (m, 4H, H-3, H-4). **LRMS**: (ESI) m/z calcd for $\text{C}_{11}\text{H}_{11}\text{O}_2$ ($[\text{M}-\text{H}]^-$): 175.1; found: 175.0. The spectral data were in accordance with those reported in the literature.⁹

10 was prepared according to the following sequence:



1-(4-Chlorophenyl)prop-2-en-1-ol (9)

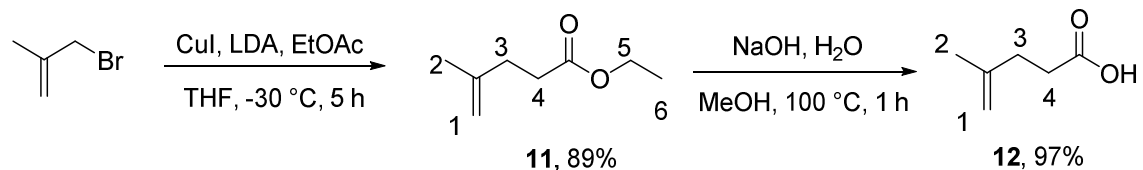
To a solution of 4-chlorobenzaldehyde (1.06 g, 7.5 mmol, 1.0 equiv.) in anhydrous THF (15 mL) under an atmosphere of argon at 0 °C was added 1.0 M vinyl magnesium bromide (8.25 mL, 8.25 mmol, 1.1 equiv.). The reaction was stirred at this temperature for 30 min and then allowed to react at rt for 3 h. The solution was diluted with Et_2O (50 mL), poured into a separating funnel and quenched with a saturated aqueous solution of NH_4Cl (30 mL). After phase separation, the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine, dried over MgSO_4 and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 50% $\text{EtOAc}/\text{Hexane}$ (v/v) to furnish the product as a colourless oil (1.07 g, 6.37 mmol, 85%). δ_{H} (400 MHz, CDCl_3): 7.35–7.29 (m, 4H, Ar-H), 6.06–5.96 (m, 1H, H-2), 5.39–5.20 (m, 2H, H-3), 5.20–5.17 (m, 1H, H-1), 1.97 (d, $J_{\text{OH-1}} = 3.2$ Hz, 1H, OH). **LRMS**: (ESI) m/z calcd for $\text{C}_9\text{H}_8\text{OCl}$ ($[\text{M}-\text{H}]^-$): 167.0; found: 167.0. The spectral data were in accordance with those reported in the literature.¹⁰

(E)-5-(4-Chlorophenyl)pent-4-enoic acid (10)

To a stirred solution of **9** (600 mg, 3.57 mmol, 1.0 equiv.) in $\text{MeC}(\text{OEt})_3$ (1.37 mL, 7.5 mmol, 2.1 equiv.) was added phenol (34 mg, 0.38 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 15 h in a Dean-Stark apparatus. After this time, the remaining $\text{MeC}(\text{OEt})_3$ was distilled off, and 2.5 M NaOH solution in 10% $\text{H}_2\text{O}/\text{MeOH}$ (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (15 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH_2Cl_2 (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and the solvent removed *in vacuo* to yield the title

compound as a colourless oil (645 mg, 3.07 mmol, 86%), without further purification being required. δ_{H} (400 MHz, CDCl_3): 7.51–7.20 (m, 4H, Ar-H), 6.56–6.12 (m, 2H, H-1, H-2), 2.83–2.37 (m, 4H, H-3, H-4). **LRMS:** (ESI) m/z calcd for $\text{C}_{11}\text{H}_{10}\text{O}_2\text{Cl}$ ([M-H]⁻): 209.0; found: 209.1. The spectral data were in accordance with those reported in the literature.¹¹

12 was prepared according to the following sequence:



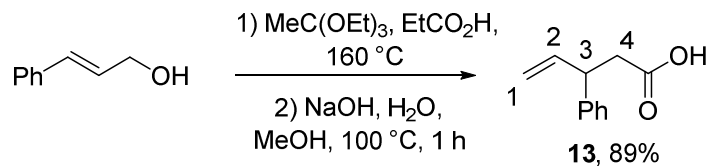
Ethyl 4-methylpent-4-enoate (11)

General procedure A to yield the title compound (506 mg, 3.56 mmol, 89%) as a colourless wax from 3-bromo-2-methylpropene (400 μL , 4.0 mmol). Purification was achieved using 15% EtOAc / Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 4.73 (s, 1H, H-1), 4.67 (s, 1H, H-1'), 4.19 (q, $J_{5-6} = 7.0\text{ Hz}$, 2H, H-5), 2.46–2.40 (t, $J_{4-3} = 7.5\text{ Hz}$, 2H, H-4), 2.32 (t, $J_{3-4} = 7.5\text{ Hz}$, 2H, H-3), 1.73 (s, 3H, H-2), 1.24 (t, $J_{6-5} = 7.0\text{ Hz}$, 3H, H-6). **LRMS:** (ESI) m/z calcd for $\text{C}_{16}\text{H}_{17}\text{O}_2$ ([2M-H]⁻): 283.2; found: 283.2. The spectral data were in accordance with those reported in the literature.¹²

4-Methylpent-4-enoic acid (12)

General procedure B to yield the title compound as a brown wax (221 mg, 1.94 mmol, 97%) from **9** (284 mg, 2.00 mmol). δ_{H} (400 MHz, CDCl_3): 10.08 (bs, 1H, CO_2H), 4.75 (s, 1H, H-1), 4.70 (s, 1H, H-1'), 2.50 (t, $J_{4-3} = 7.5\text{ Hz}$, 2H, H-4), 2.33 (t, $J_{3-4} = 7.5\text{ Hz}$, 2H, H-3), 1.73 (s, 3H, H-2). **LRMS:** (ESI) m/z calcd for $\text{C}_6\text{H}_{10}\text{O}_2$ ([M-H]⁻): 113.1; found: 113.1. The spectral data were in accordance with those reported in the literature.¹³

13 was prepared according to the following sequence:

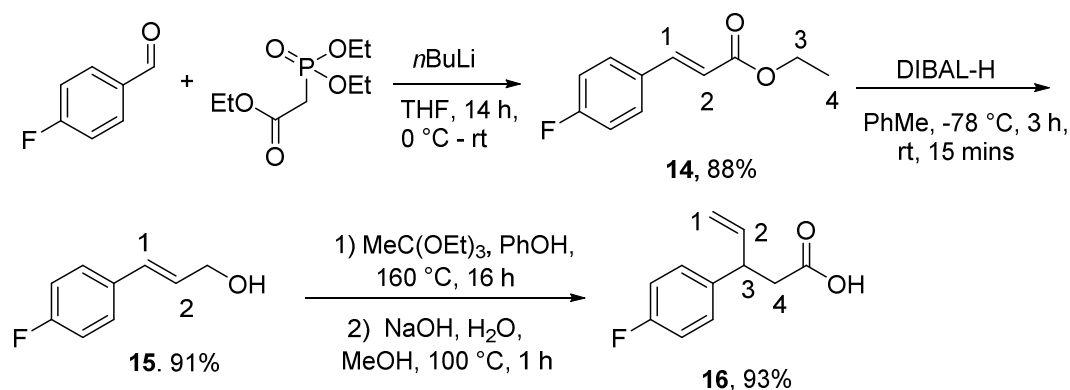


3-Phenylpent-4-enoic acid (13)

To a stirred solution of (*E*)-cinnamyl alcohol (700 mg, 7.46 mmol, 1.0 equiv.) in $\text{MeC}(\text{OEt})_3$ (6.3 mL, 49.3 mmol, 6.6 equiv.) was added EtCO_2H (0.24 mL, 4.48 mmol, 0.6 equiv.) and the mixture was heated at $160\text{ }^\circ\text{C}$ for 16 h in a Dean-Stark apparatus. After this time, the propionic acid and

MeC(OEt)₃ were distilled off, and 2.5 M NaOH solution in 10% H₂O/MeOH (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (10 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 x 10 mL), then acidified with aqueous 4 M HCl solution. The Aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the title compound as a colourless oil (1.117 g, 6.66 mmol, 89%), without further purification being performed. δ_{H} (400 MHz, CDCl₃): 7.40–7.15 (m, 5H, Ar-H), 6.04–5.90 (m, 1H, H-2), 5.12–5.02 (m, 2H, H-1), 3.85 (app-q, 1H, H-3), 2.84–2.70 (m, 2H, H-4). **LRMS:** (ESI) *m/z* calcd for C₁₁H₁₂OBr ([M+Br]⁺): 254.9; found: 254.9. The spectral data were in accordance with those reported in the literature.¹⁴

16 was prepared according to the following sequence:



Ethyl (E)-3-(4-fluorophenyl)acrylate (14)

To triethyl phosphonoacetate (3.0 mL, 15 mmol, 1.25 equiv.) in anhydrous THF (50 mL) under an atmosphere of argon at 0 °C was added 2.5 M *n*BuLi (7 mL, 17.5 mmol, 1.5 equiv.) and the mixture was stirred for 30 min. 4-Fluorobenzaldehyde (1.3 mL, 12 mmol, 1.0 equiv.) was then added, and after 10 mins the reaction mixture was allowed to warm to rt, and was stirred for a further 14 h. The reaction was diluted CH₂Cl₂ (250 mL) and quenched with 2 M aqueous HCl (40 mL). After phase separation, the aqueous phase was extracted further with CH₂Cl₂ (2 x 50 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 3.0→7.0% EtOAc/Hexane (v/v) to afford the title compound as yellow wax (2.049 g, 10.6 mmol, 88%). δ_{H} (400 MHz, CDCl₃): 7.65 (d, *J*_{1,2} = 16.0 Hz, 1H, H-1), 7.54–7.48 (m, 2H, Ar-H), 7.11–7.04 (m, 2H, Ar-H), 6.36 (d, *J*_{2,1} = 16.0 Hz, 1H, H-2), 4.27 (q, *J*_{3,4} = 7.2 Hz, 2H, H-3), 1.33 (t, *J*_{4,3} = 7.2 Hz, 3H, H-4). **LRMS:** (ESI) *m/z* calcd for C₁₁H₈O₂F ([M-H₂O-H]⁻): 175.1; found: 175.1. The spectral data were in accordance with those reported in the literature.¹⁵

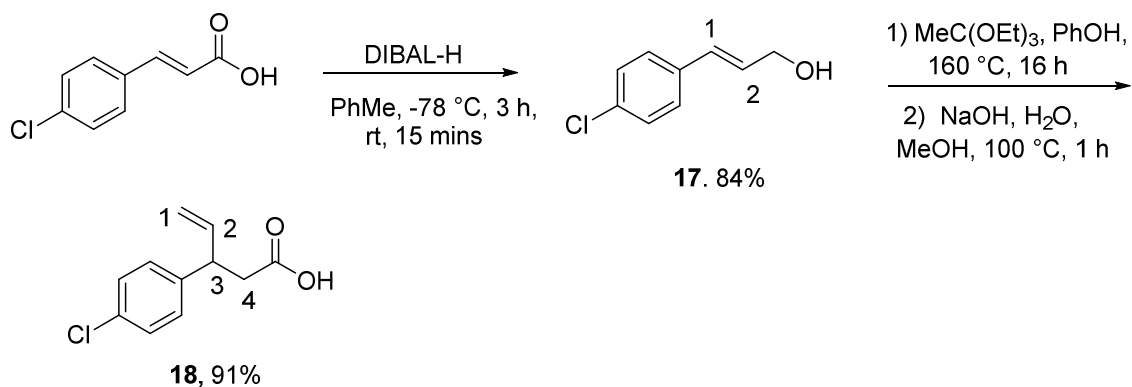
(E)-3-(4-Fluorophenyl)prop-2-en-1-ol (15)

To a solution of **14** (970 mg, 5 mmol, 1.0 equiv.) in anhydrous PhMe (30 mL) under an atmosphere of argon at -78 °C was added 1 M DIBAL-H in PhMe (12.5 mL, 12.5 mmol 2.5 equiv.), and the reaction was stirred at this temperature for 3 h. The reaction was then warmed to rt and H₂O (2 mL), then aqueous 1 M NaOH solution (15 mL), followed again by H₂O (5 mL), were added, with 5 minutes between each addition, maintaining vigorous stirring. The mixture was then poured into a separating funnel, and after phase separation, the aqueous phase was extracted with PhMe (2 x 25 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered through a plug of silica gel, and the solvent removed *in vacuo* to yield the title compound (692 mg, 4.55 mmol, 91%) without the requirement for further purification. δ_{H} (400 MHz, CDCl₃): 7.38–7.32 (m, 2H, Ar-H), 7.04–6.98 (m, 2H, Ar-H), 6.59 (d, $J_{1,2} = 15.9$ Hz, 1H, H-1), 6.29 (dt, $J_{2,1} = 15.9$ Hz, $J_{2,3} = 5.8$ Hz 1H, H-2), 4.32 (app-dt, 2H, H-3), 1.42 (t, $J_{\text{OH-3}} = 5.8$ Hz, 1H, OH). **LRMS**: (ESI) m/z calcd for C₉H₈OF ([M-H]): 151.1; found: 151.1. The spectral data were in accordance with those reported in the literature.¹⁶

3-(4-Fluorophenyl)pent-4-enoic acid (16)

To a stirred solution of **15** (581 mg, 3.0 mmol, 1.0 equiv.) in MeC(OEt)₃ (1.20 mL, 6.3 mmol, 2.1 equiv.) was added phenol (28 mg, 0.3 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 16 h in a Dean-Stark apparatus. After this time, the remaining MeC(OEt)₃ was distilled off, and 2.5 M NaOH solution in 10% H₂O/MeOH (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (15 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered, and the solvent removed *in vacuo* to yield the title compound as a colourless oil (619 mg, 2.79 mmol, 93%), without further purification being required. δ_{H} (400 MHz, CDCl₃): 10.28 (bs, 1H, CO₂H), 7.21–7.15 (m, 2H, Ar-H), 7.04–6.96 (m, 2H, Ar-H), 6.01–5.90 (m, 1H, H-2), 5.13–5.04 (m, 2H, H-1), 3.85 (app-q, 1H, H-3), 2.84–2.67 (m, 2H, H-4). **LRMS**: (ESI) m/z calcd for C₁₁H₁₀O₂F ([M-H]): 193.1; found: 193.1. The spectral data were in accordance with those reported in the literature.¹⁷

18 was prepared according to the following sequence:



(E)-3-(4-Chlorophenyl)prop-2-en-1-ol (17)

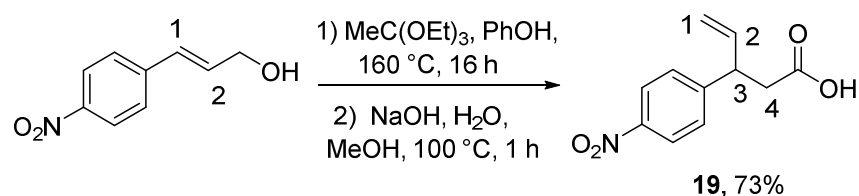
To a solution of cinnamic acid (913 mg, 5 mmol, 1.0 equiv.) in anhydrous PhMe (30 mL) under an atmosphere of argon at $-78\text{ }^{\circ}\text{C}$ was added 1 M DIBAL-H in PhMe (12.5 mL, 12.5 mmol 2.5 equiv.), and the reaction was stirred at this temperature for 3 h. The reaction was then warmed to rt and H₂O (2 mL), then aqueous 1 M NaOH solution (15 mL), followed again by H₂O (5 mL), were added, with 5 minutes between each addition, maintaining vigorous stirring. The mixture was then poured into a separating funnel, and after phase separation, the aqueous phase was extracted with PhMe (2 x 25 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered through a plug of silica gel, and the solvent removed in vacuo to yield the title compound (707 mg, 4.21 mmol, 84%) without the requirement for further purification. δ_{H} (400 MHz, CDCl₃): 7.33–7.24 (m, 5H, Ar-H), 6.59 (d, $J_{1-2} = 15.9$ Hz, 1H, H-1), 6.34 (dt, $J_{2-1} = 15.9$ Hz, $J_{2-3} = 5.6$ Hz 1H, H-2), 4.33 (app-t, 2H, H-3). **LRMS:** (ESI) m/z calcd for C₉H₈ClO ([M-H]⁻): 167.0; found: 167.0. The spectral data were in accordance with those reported in the literature.¹⁸

3-(4-Chlorophenyl)pent-4-enoic acid (18)

To a stirred solution of **17** (371 mg, 2.2 mmol, 1.0 equiv.) in MeC(OEt)₃ (0.85 mL, 4.7 mmol, 2.1 equiv.) was added phenol (21 mg, 0.2 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 15 h in a Dean-Stark apparatus. After this time, the remaining MeC(OEt)₃ was distilled off, and 2.5 M NaOH solution in 10% H₂O/MeOH (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (15 mL), and poured into a

separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the title compound as a colourless oil (422 mg, 2.01 mmol, 91%), without further purification being required. δ_{H} (400 MHz, CDCl₃): 7.31–7.26 (m, 2H, Ar-H), 7.18–7.14 (m, 2H, Ar-H), 6.01–5.90 (m, 1H, H-2), 5.14–5.05 (m, 2H, H-1), 3.85 (app-q, 1H, H-3), 2.85–2.68 (m, 2H, H-4). **LRMS**: (ESI) *m/z* calcd for C₁₁H₁₀O₂Cl ([M-H]⁻): 209.0; found: 209.1. The spectral data were in accordance with those reported in the literature.¹⁷

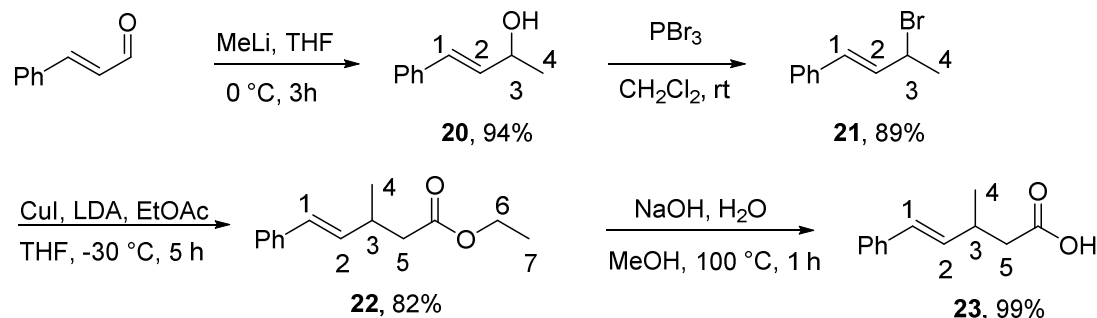
19 was prepared according to the following sequence:



3-(4-Nitrophenyl)pent-4-enoic acid (19)

To a stirred solution of 4-nitrocinnamyl alcohol (716 mg, 4.00 mmol, 1.0 equiv.) in MeC(OEt)₃ (1.54 mL, 8.4 mmol, 2.1 equiv.) was added phenol (38 mg, 0.40 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 12 h in a Dean-Stark apparatus. After this time, the remaining MeC(OEt)₃ was distilled off, and 1.5 M NaOH solution in 10% H₂O/MeOH (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (15 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the title compound as a brown oil (645 mg, 2.92 mmol, 73%), without further purification being required. δ_{H} (400 MHz, CDCl₃): 10.01 (bs, 1H, CO₂H), 8.16 (d, *J*_{*o-m*} = 8.2 Hz, 2H, Ar-H), 7.38 (d, *J*_{*m-o*} = 8.2 Hz, 2H, Ar-H), 6.00–5.88 (m, 1H, H-2), 5.21–5.05 (m, 2H, H-1), 3.97 (app-q, 1H, H-3), 2.91–2.72 (m, 2H, H-4). **LRMS**: (ESI) *m/z* calcd for C₁₁H₁₀NO₄ ([M-H]⁻): 220.1; found: 220.1. The spectral data were in accordance with those reported in the literature.¹⁹

23 was prepared according to the following sequence:



(E)-4-Phenylbut-3-en-2-ol (20)

To a solution of (*E*)-cinnamaldehyde (0.63 mL, 5.0 mmol, 1 equiv.) in anhydrous THF (15 mL) under an atmosphere of argon at 0 °C was added 1.6 M MeLi in Et₂O (3.75 mL, 6 mmol, 1.2 equiv.) and the mixture was stirred at this temperature for 3 h. The mixture was diluted with CH₂Cl₂ (75 mL) and poured into a separating funnel. The solution was quenched with 30 mL of aqueous 2 M HCl. After phase separation, the aqueous phase was extracted a further three times with CH₂Cl₂ (3 x 40 mL). The combined organic layers were washed with brine (50 mL), dried over MgSO₄ and filtered to furnish the title compound as a yellow oil, (697 mg, 0.471 mmol, 94 %) without the requirement for further purification. δ_{H} (400 MHz, CDCl₃): 7.39–7.35 (m, 2H, Ar-H), 7.33–7.28 (m, 2H, Ar-H), 7.24–7.20 (m, 1H, Ar-H), 6.56 (d, $J_{1,2}$ = 16.0 Hz, 1H, H-1), 6.25 (dd, $J_{2,1}$ = 16.0 Hz, $J_{2,3}$ = 6.4 Hz, 1H, H-2), 4.53–4.44 (m, 1H, H-3), 1.54 (d, $J_{\text{OH},3}$ = 4.0 Hz, 1H, OH), 1.36 (d, $J_{4,3}$ = 6.4 Hz, 3H, H-4). **LRMS:** (ESI⁺) m/z calcd for C₁₀H₁₂ONa ([M+Na]⁺): 171.1; found: 171.1. The spectral data were in accordance with those reported in the literature.²⁰

(E)-(3-Bromobut-1-en-1-yl)benzene (21)

General procedure E to yield the title compound (467 mg, 2.225 mmol, 89%) as an orange oil from **20** (370 mg, 2.50 mmol), without further purification being performed. δ_{H} (400 MHz, CDCl₃): 7.40–7.22 (m, 5H, Ar-H), 6.56 (d, $J_{1,2}$ = 16.0 Hz, 1H, H-1), 6.41 (dd, $J_{2,1}$ = 16.0 Hz, $J_{2,3}$ = 8.6 Hz, 1H, H-2), 4.93–4.85 (m, 1H, H-3), 1.88 (d, $J_{4,3}$ = 6.6 Hz, 3H, H-4). **LRMS:** (ESI⁺) m/z calcd for C₁₀H₁₁Br₂ ([M+Br]⁺): 288.9; found: 288.9. The spectral data were in accordance with those reported in the literature.²¹

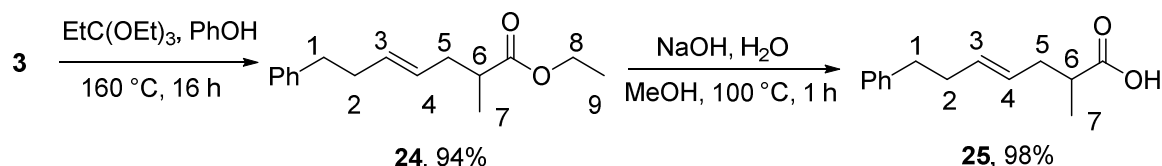
Ethyl (E)-3-methyl-5-phenylpent-4-enoate (22)

General procedure A to yield the title compound as pleasantly fragrant yellow oil (297 mg, 1.361 mmol, 82%) from **21** (349 mg, 1.66 mmol). Purification was achieved using 3% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 7.34–7.30 (m, 2H, Ar-H), 7.29–7.25 (m, 2H, Ar-H), 7.21–7.16 (m, 1H, Ar-H), 6.39 (d, $J_{1,2} = 16.0$ Hz, 1H, H-1), 6.13 (dd, $J_{2,1} = 16.0$ Hz, $J_{2,3} = 7.5$ Hz, 1H, H-2), 4.11 (q, $J_{6,7} = 7.1$ Hz, 2H, H-6), 2.91–2.79 (m, 1H, H-3), 2.45–2.30 (m, 2H, H-5), 1.22 (t, $J_{7,6} = 7.1$ Hz, 3H, H-7), 1.14 (d, $J_{5,4} = 6.8$ Hz, 3H, H-4). **LRMS**: (ESI^+) m/z calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2\text{K}$ ($[\text{M}+\text{K}]^+$): 257.1; found: 257.0. The spectral data were in accordance with those reported in the literature.²²

(E)-3-Methyl-5-phenylpent-4-enoic acid (23)

General procedure B to yield the title compound as an orange wax (184 mg, 0.976 mmol, 99%) from **22** (213 mg, 0.967 mmol). δ_{H} (400 MHz, CDCl_3): 9.96 (bs, 1H, CO_2H), 7.36–7.25 (m, 4H, Ar-H), 7.21–7.16 (m, 1H, Ar-H), 6.40 (d, $J_{1,2} = 16.0$ Hz, 1H, H-1), 6.13 (dd, $J_{2,1} = 16.0$ Hz, $J_{2,3} = 7.5$ Hz, 1H, H-2), 2.89–2.77 (m, 1H, H-3), 2.50–2.32 (m, 2H, H-5), 1.15 (d, $J_{5,3} = 6.9$ Hz, 3H, H-4). **LRMS**: (ESI^+) m/z calcd for $\text{C}_{12}\text{H}_{14}\text{O}_2\text{Na}$ ($[\text{M}+\text{Na}]^+$): 213.1; found: 213.0. The spectral data were in accordance with those reported in the literature.²³

25 was prepared according to the following sequence:



Ethyl (E)-2-methyl-7-phenylhept-4-enoate (24)

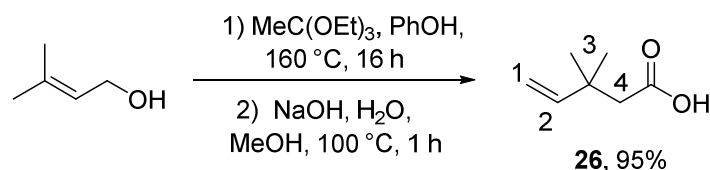
To a stirred solution of **3** (1.62 g, 10.0 mmol, 1.0 equiv.) in $\text{EtC}(\text{OEt})_3$ (4.2 mL, 21.0 mmol, 2.1 equiv.) was added PhOH (94 mg, 1.0 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 16 h in a Dean-Stark apparatus. After this time, the apparatus was rearranged for distillation at 165 °C. After distilling for 2 h, the crude oil was dissolved in Et_2O (80 mL), poured into a separating funnel and washed with 2.0 M aqueous NaOH solution (3 x 30 mL). The combined organic layers were then washed with brine (40 mL), dried over MgSO_4 , filtered, and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 3.0 % $\text{EtOAc}/\text{Hexane}$ (v/v) to yield the title compound (2.31 g, 9.37 mmol, 94%) as a sweet-smelling, colourless oil. $R_f = 0.42$ (10 % $\text{EtOAc}/\text{Hexane}$ (v/v)). δ_{H} (400 MHz, CDCl_3): 7.32–7.27 (m, 2H, Ar-H), 7.22–7.17 (m, 3H, Ar-H), 5.53 (dt, $J_{3,4} = 15.3$ Hz, $J_{3,2} = 6.4$ Hz, 1H, H-3), 5.40 (dt, $J_{4,3} = 15.3$ Hz, $J_{4,5} = 6.9$ Hz, 1H, H-4), 4.14 (q, $J_{8,9} = 7.0$ Hz, 2H, H-8), 2.69 (t, $J_{1,2} = 7.3$ Hz, 2H, H-1), 2.51–2.41 (m, 1H, H-6), 2.40–2.29

(m, 3H, H-2, H-5), 2.17–2.09 (m, 1H, H-5'), 1.27 (t, $J_{9,8} = 7.0$ Hz, 3H, H-9), 1.13 (d, $J_{7,6} = 6.8$ Hz, 3H, H-7). δ_C (100 MHz, $CDCl_3$): 176.3 (C=O), 142.0 (q, Ar-C), 132.0 (C-3), 128.4, 128.3 (Ar-C), 127.5 (C-4), 125.8 (Ar-C), 60.2 (C-8), 39.7 (C-6), 36.7 (C-5), 36.0 (C-1), 34.4 (C-2), 16.5 (C-7), 14.3 (C-9). ν_{max} (ATR)/ cm^{-1} : 1184 (C-O), 1732 (C=O). **HRMS**: (ESI) m/z calcd for $C_{16}H_{21}O_2$ ($[M-H]^-$): 245.1547; found: 245.1542.

(E)-2-Methyl-7-phenylhept-4-enoic acid (25)

General procedure B to yield the title compound as a yellow oil (1.021 g, 4.68 mmol, 98%) from **24** (1.176 g, 4.78 mmol). δ_H (400 MHz, $CDCl_3$): 11.14 (bs, 1H, CO_2H), 7.32–7.27 (m, 2H, Ar-H), 7.22–7.17 (m, 3H, Ar-H), 5.55 (dt, $J_{3,4} = 15.3$ Hz, $J_{3,2} = 6.4$ Hz, 1H, H-3), 5.41 (dt, $J_{4,3} = 15.3$ Hz, $J_{4,5} = 6.9$ Hz, 1H, H-4), 2.69 (t, $J_{1,2} = 7.7$ Hz, 2H, H-1), 2.56–2.46 (m, 1H, H-6), 2.43–2.30 (m, 3H, H-2, H-5), 2.20–2.12 (m, 1H, H-5'), 1.13 (d, $J_{7,6} = 6.8$ Hz, 3H, H-7). δ_C (100 MHz, $CDCl_3$): 181.8 (C=O), 141.9 (q, Ar-C), 132.4 (C-3), 128.5 (Ar-C), 128.3 (Ar-C), 127.1 (C-4), 125.8 (Ar-C), 39.4 (C-6), 36.3 (C-5), 35.9 (C-1), 34.3 (C-2), 16.2 (C-7). ν_{max} (ATR)/ cm^{-1} : 1704 (C=O), 3121 (O-H). **HRMS**: (APCI) m/z calcd for $C_{14}H_{17}O$ ($[M-H]^-$): 217.1234; found: 217.1234.

26 was prepared according to the following sequence:

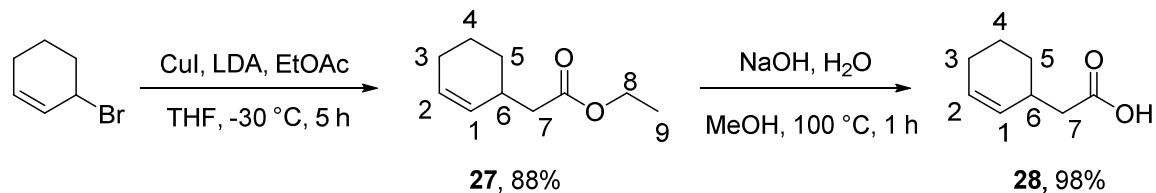


3,3-Dimethylpent-4-enoic acid (26)

To a stirred solution of prenyl alcohol (1.0 g, 11.6 mmol, 1.0 equiv.) in $MeC(OEt)_3$ (4.5 mL, 24.3 mmol, 2.1 equiv.) was added phenol (100 mg, 1.2 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 16 h in a Dean-Stark apparatus. After this time, the remaining $MeC(OEt)_3$ was distilled off, and 2.5 M NaOH solution in 10% $H_2O/MeOH$ (10 mL) was added. The mixture was heated at 100 °C for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (10 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH_2Cl_2 (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The Aqueous phase was extracted five times with CH_2Cl_2 . The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to yield the title compound as a fragrant colourless oil (1.41 g, 11.0 mmol, 95%), without further purification being required. δ_H (400 MHz, $CDCl_3$): 10.51 (bs, 1H, CO_2H), 5.90 (dd, $J_{2,1} = 17.6$ Hz, $J_{2,1'} = 10.8$ Hz, 1H, H-2), 5.02–4.93 (m, 2H, H-1), 2.33 (s, 2H, H-4),

1.15 (s, 6H, H-3). **LRMS:** (ESI) m/z calcd for $C_7H_{12}O_2Br$ ($[M+Br]^+$): 207.0; found: 207.1. The spectral data were in accordance with those reported in the literature.²⁴

28 was prepared according to the following sequence:



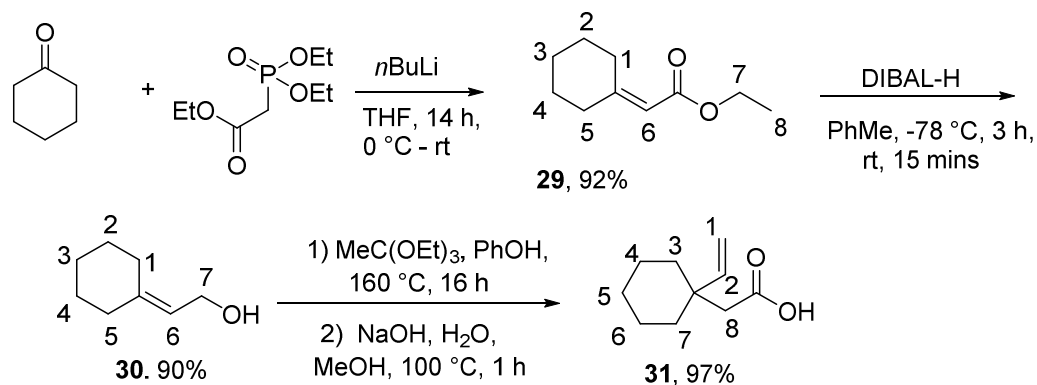
Ethyl 2-(cyclohex-2-en-1-yl)acetate (27)

General procedure A to yield the title compound as pleasant, fragrant colourless oil (448 mg, 2.64 mmol, 88%) from 2-cyclohexenyl bromide (483 mg, 3.00 mmol). Purification was achieved using 5% EtOAc/Hexane (v/v). δ_H (400 MHz, $CDCl_3$): 5.72–5.66 (m, 1H, H-1), 5.55–5.50 (m, 1H, H-2), 4.12 (q, $J_{8,9} = 7.3$ Hz, 2H, H-8), 2.62–2.53 (m, 1H, H-6), 2.31–2.20 (m, 2H, H-7), 1.99–1.93 (m, 2H, H-3), 1.85–1.77 (m, 1H, H-5), 1.73–1.65 (m, 1H, H-5'), 1.59–1.49 (m, 1H, H-4), 1.31–1.22 (m, 4H, H-4', H-9). **LRMS:** (ESI) m/z calcd for $C_{10}H_{16}O_2Cl$ ($[M+Cl]^+$): 203.1; found: 203.1. The spectral data were in accordance with those reported in the literature.²⁵

2-(Cyclohex-2-en-1-yl)acetic acid (28)

General procedure B to yield the title compound as a brown wax (206 mg, 1.47 mmol, 98%) from **27** (252 mg, 1.50 mmol). δ_H (400 MHz, $CDCl_3$): 10.95 (bs, 1H, CO_2H), 5.75–5.69 (m, 1H, H-1), 5.58–5.53 (m, 1H, H-2), 2.63–2.54 (m, 1H, H-6), 2.39–2.25 (m, 2H, H-7), 2.00–1.94 (m, 2H, H-3), 1.89–1.81 (m, 1H, H-5), 1.75–1.65 (m, 1H, H-5'), 1.61–1.50 (m, 1H, H-4), 1.35–1.21 (m, 1H, H-4'). **LRMS:** (ESI) m/z calcd for $C_8H_{11}O_2$ ($[M-H]^+$): 139.1; found: 139.0. The spectral data were in accordance with those reported in the literature.²⁶

31 was prepared according to the following sequence:



Ethyl 2-cyclohexylideneacetate (29)

To triethyl phosphonoacetate (2.4 mL, 12 mmol, 1.2 equiv.) in anhydrous THF (50 mL) under an atmosphere of argon at 0 °C was added 2.5 M *n*BuLi (6 mL, 15 mmol, 1.5 equiv.) and the mixture was stirred for 30 min. Cyclohexanone (1.03 mL, 10 mmol, 1.0 equiv.) was then added, and after 10 min, the reaction mixture was allowed to warm to rt, and was stirred for a further 14 h. The reaction was diluted CH₂Cl₂ (250 mL) and quenched with 2 M aqueous HCl (40 mL). After phase separation, the aqueous phase was extracted further with CH₂Cl₂ (2 x 50 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 3.0→4.0% EtOAc/Hexane (v/v) to afford the title compound as colourless oil (1.546 g, 9.21 mmol, 92%). δ_{H} (400 MHz, CDCl₃): 5.58 (s, 1H, H-6), 4.12 (q, $J_{7,8} = 7.2$ Hz, 2H, H-7), 2.81 (t, $J_{5,4} = 5.5$ Hz, 2H, H-5), 2.17 (t, $J_{1,2} = 5.9$ Hz, 2H, H-1), 1.67–1.52 (m, 6H, H-2, H-3, H-4), 1.26 (t, $J_{8,7} = 7.2$ Hz, 3H, H-8). LRMS: (ESI⁺) m/z calcd for C₁₀H₁₅O₂Na₂ ([M+2Na-H]⁺): 213.1; found: 213.1. The spectral data were in accordance with those reported in the literature.²⁷

2-Cyclohexylideneethan-1-ol (30)

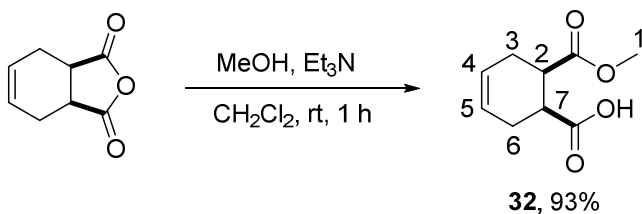
To a solution of **29** (1.176 g, 7 mmol, 1.0 equiv.) in anhydrous PhMe (56 mL) under an atmosphere of argon at –78 °C was added 1 M DIBAL-H in PhMe (17.5 mL, 17.5 mmol 2.5 equiv.), and the reaction was stirred at this temperature for 3 h. The reaction was then warmed to rt and H₂O (2 mL), then aqueous 1 M NaOH solution (15 mL), followed again by H₂O (5 mL), were added, with 5 minutes between each addition, maintaining vigorous stirring. The mixture was then poured into a separating funnel, and after phase separation, the aqueous phase was extracted with PhMe (2 x 25 mL). The combined organic layers were then washed with brine, dried over MgSO₄, filtered through a plug of

silica gel, and the solvent removed *in vacuo* to yield the title compound (794 mg, 6.31 mmol, 90%) without the requirement for further purification. δ_{H} (400 MHz, CDCl_3): 5.35 (t, $J_{6,7} = 7.0$ Hz, 1H, H-6), 4.12 (app-t, 2H, H-7), 2.17 (t, $J_{5,4} = 5.2$ Hz, 2H, H-5), 2.12–2.07 (m, 2H, H-1), 1.58–1.47 (m, 6H, H-2, H-3, H-4), 1.08 (t, $J_{\text{OH},7} = 5.1$ Hz, 1H, OH). **LRMS:** (ESI⁺) m/z calcd for $\text{C}_8\text{H}_{14}\text{OK}$ ($[\text{M}+\text{K}]^+$): 165.1; found: 165.1. The spectral data were in accordance with those reported in the literature.²⁷

2-(1-Vinylcyclohexyl)acetic acid (31)

To a stirred solution of **30** (600 mg, 4.76 mmol, 1.0 equiv.) in $\text{MeC}(\text{OEt})_3$ (1.83 mL, 10.0 mmol, 2.1 equiv.) was added phenol (45 mg, 0.476 mmol, 0.1 equiv.) and the mixture was heated at 160 °C for 16 h in a Dean-Stark apparatus. After this time, the remaining $\text{MeC}(\text{OEt})_3$ was distilled off, and 2.5 M NaOH solution in 10% $\text{H}_2\text{O}/\text{MeOH}$ (10 mL) was added. The mixture was heated at reflux for 1 h. The mixture was cooled to rt, diluted with an aqueous 1 M NaOH solution (15 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH_2Cl_2 (2 x 5 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and the solvent removed *in vacuo* to yield the title compound as a colourless oil (776 mg, 4.617 mmol, 97%), without further purification being required. δ_{H} (400 MHz, CDCl_3): 5.79 (dd, $J_{2,1} = 18.1$ Hz, $J_{2,1'} = 11.0$ Hz, 1H, H-2), 5.14–4.99 (m, 2H, H-1), 2.35 (s, 2H, H-8), 1.55–1.30 (m, 10H, H-3, H-4, H-5, H-6, H-7). **LRMS:** (ESI) m/z calcd for $\text{C}_{10}\text{H}_{15}\text{O}_2$ ($[\text{M}-\text{H}]^-$): 167.1; found: 167.1. The spectral data were in accordance with those reported in the literature.²⁸

32 was prepared according to the following sequence:

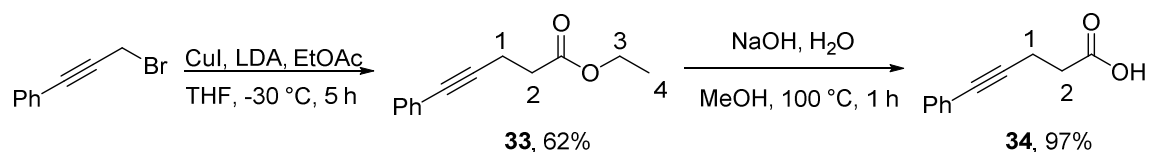


Cis-6-(methoxycarbonyl)cyclohex-3-ene-1-carboxylic acid (32)

To a stirred solution of *cis*-4-cyclohexene-1,2-dicarboxylic anhydride (760 mg, 5 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (10 mL) under argon at 0 °C was added Et_3N (2 mL, 15 mmol, 3.0 equiv.), then MeOH (0.2 mL, 5 mmol, 1.0 equiv.). The reaction was stirred for 5 mins at this temperature and then allowed to warm to rt. The mixture was poured into separating funnel, and 1 M NaOH solution (15 mL), was added. After phase separation the aqueous phase was extracted with CH_2Cl_2 (2 x 5 mL),

then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the title compound as a colourless wax (856 mg, 4.65 mmol, 93%), without further purification being required. δ_{H} (400 MHz, CDCl₃): 11.30 (bs, 1H, CO₂H), 5.96 (app-s, 2H, H-4, H-5), 3.70 (s, 3H, H-1), 3.17–3.03 (m, 2H, H-2, H-7), 2.65–2.53 (m, 2H, H-3, H-6), 2.44–2.31 (m, 2H, H-3', H-6'). **LRMS:** (ESI) m/z calcd for C₉H₁₁O₄ ([M-H]⁻): 183.1; found: 183.1. The spectral data were in accordance with those reported in the literature.²⁹

34 was prepared according to the following sequence:



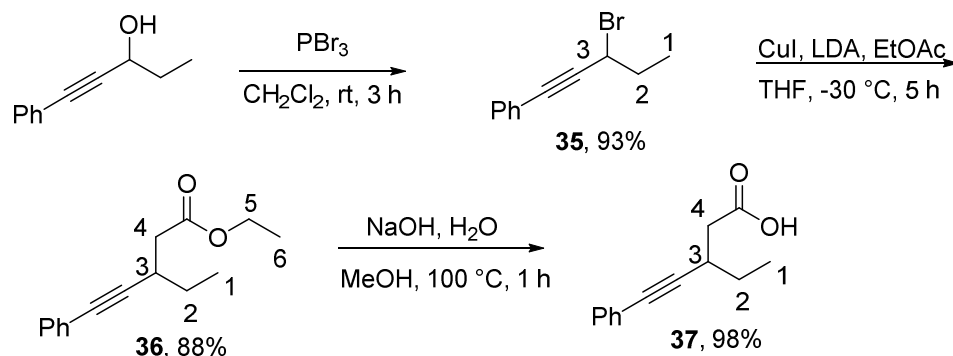
Ethyl 5-phenylpent-4-ynoate (33)

General procedure A to yield the title compound as pleasantly fragrant yellow oil (376 mg, 1.86 mmol, 62%) from 3-phenylpropargyl bromide (688 mg, 3.00 mmol). Purification was achieved using 5% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl₃): 7.38–7.23 (m, 5H, Ar-H), 4.16 (q, $J_{3-4} = 7.2$ Hz, 2H, H-3), 2.74–2.66 (m, 2H, H-2), 2.65–2.58 (m, 2H, H-1), 1.26 (t, $J_{4-3} = 7.2$ Hz, 3H, H-4). **LRMS:** (ESI⁺) m/z calcd for C₁₃H₁₄O₂ ([M+H]⁺): 203.1; found: 202.9. The spectral data were in accordance with those reported in the literature.³⁰

5-Phenylpent-4-ynoic acid (34)

General procedure B to yield the title compound as a yellow oil (253 mg, 1.46 mmol, 97%) from **33** (303 mg, 1.50 mmol). δ_{H} (400 MHz, CDCl₃): 10.04 (bs, 1H, CO₂H) 7.41–7.25 (m, 5H, Ar-H), 2.78–2.64 (m, 4H, H-1, H-2). **LRMS:** (ESI) m/z calcd for C₁₁H₉O₂ ([M-H]⁻): 173.1; found: 173.1. The spectral data were in accordance with those reported in the literature.³¹

37 was prepared according to the following sequence:



(3-Bromopent-1-yn-1-yl)benzene (35)

General procedure A to yield the title compound (425 mg, 1.92 mmol, 93%) as a colourless wax from 1-phenyl-1-pentyn-3-ol (330 mg, 2.06 mmol). Purification was achieved using 15% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 7.46–7.39 (m, 2H, Ar-H), 7.35–7.26 (m, 3H, Ar-H), 4.74 (t, $J_{3-2} = 6.4$ Hz, 1H, H-3), 2.16–2.07 (m, 2H, H-2), 1.15 (t, $J_{1-2} = 7.3$ Hz, 3H, H-1). **LRMS:** (ESI⁺) m/z calcd for $\text{C}_{11}\text{H}_{11}\text{Br}$ ($[\text{M}+\text{Na}]^+$): 245.0; found: 245.0. The spectral data were in accordance with those reported in the literature.³²

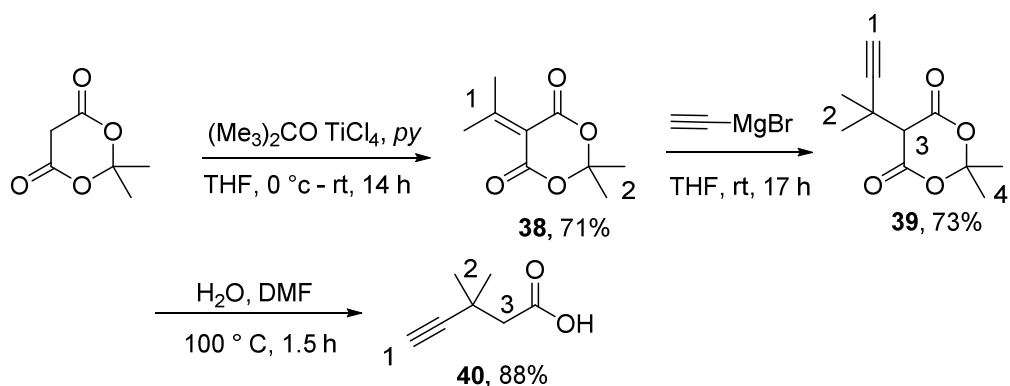
Ethyl 3-ethyl-5-phenylpent-4-ynoate (36)

General procedure B to yield the title compound as a yellow oil (314 mg, 1.36 mmol, 88%) from **35** (345 mg, 1.55 mmol). δ_{H} (400 MHz, CDCl_3): 7.38–7.26 (m, 4H, Ar-H), 7.20–7.15 (m, 1H, Ar-H) 5.67–5.62 (m, 1H, H-3), 4.13 (q, $J_{5-6} = 7.2$ Hz, 2H, H-5), 3.43 (d, $J_{4-3} = 2.3$ Hz, 2H, H-4), 2.18–2.10 (m, 2H, H-2), 1.21 (t, $J_{6-5} = 7.2$ Hz, 3H, H-6), 1.07 (t, $J_{1-2} = 7.5$ Hz, 3H, H-1). **LRMS:** (ESI⁺) m/z calcd for $\text{C}_{15}\text{H}_{18}\text{O}_2\text{Na}$ ($[\text{M}+\text{Na}]^+$): 253.1; found: 253.0. The spectral data were in accordance with those reported in the literature.³³

3-Ethyl-5-phenylpent-4-ynoic acid (37)

General procedure B to yield the title compound as a yellow oil (218 mg, 1.08 mmol, 98%) from **36** (253 mg, 1.10 mmol). δ_{H} (400 MHz, CDCl_3): 10.46 (bs, 1H, CO_2H), 7.47–7.43 (m, 2H, Ar-H), 7.38–3.33 (m, 3H, Ar-H), 5.95–5.80 (m, 1H, H-3), 2.26–2.12 (m, 1H, H-4), 1.69–1.60 (m, 2H, H-4'), 1.05 (dt, $J_{2-3} = 19.4$ Hz, $J_{2-1} = 7.4$ Hz, 2H, H-2), 0.78 (t, $J_{1-2} = 7.4$ Hz, 3H, H-1). **LRMS:** (ESI⁺) m/z calcd for $\text{C}_{13}\text{H}_{13}\text{O}_2$ ($[\text{M}-\text{H}]$): 201.1; found: 201.1. The spectral data were in accordance with those reported in the literature.³³

40 was prepared according to the following sequence:



2,2-Dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione (38)

TiCl_4 (1.73 mL, 15.75 mmol, 2.1 equiv.) was added slowly to anhydrous THF (35 mL) under argon at $0\text{ }^\circ\text{C}$. After stirring for 10 min, acetone (690 μL , 9.38 mmol, 1.25 equiv.) and Meldrum's acid (1.08 g, 7.50 mmol, 1.0 equiv.) in anhydrous THF (7.5 mL) were added, followed by pyridine (3.0 mL, 37.5 mmol, 5.0 equiv.). After 30 min the solution was warmed to rt, and stirred vigorously for 12 h. The mixture was then cooled to $0\text{ }^\circ\text{C}$ and H_2O (15 mL) was added. After stirring for 10 min, the solution was diluted with CH_2Cl_2 (150 mL), poured into a separating funnel, and quenched with saturated aqueous NaHCO_3 solution (80 mL). After phase separation, the aqueous phase was extracted with CH_2Cl_2 (4 x 50 mL). The combined organic layers were then washed with brine (60 mL), dried over MgSO_4 , filtered, and the solvent removed *in vacuo* to yield the title compound as an orange wax (969 mg, 5.33 mmol, 71%) without the requirement for further purification. δ_{H} (400 MHz, CDCl_3): 2.51 (s, 6H, H-1), 1.72 (s, 6H, H-2). **LRMS**: (ESI) m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_4\text{Cl}$ ($[\text{M}+\text{Cl}]^+$): 219.0; found: 219.0. The spectral data were in accordance with those reported in the literature.³⁴

2,2-Dimethyl-5-(2-methylbut-3-yn-2-yl)-1,3-dioxane-4,6-dione (39)

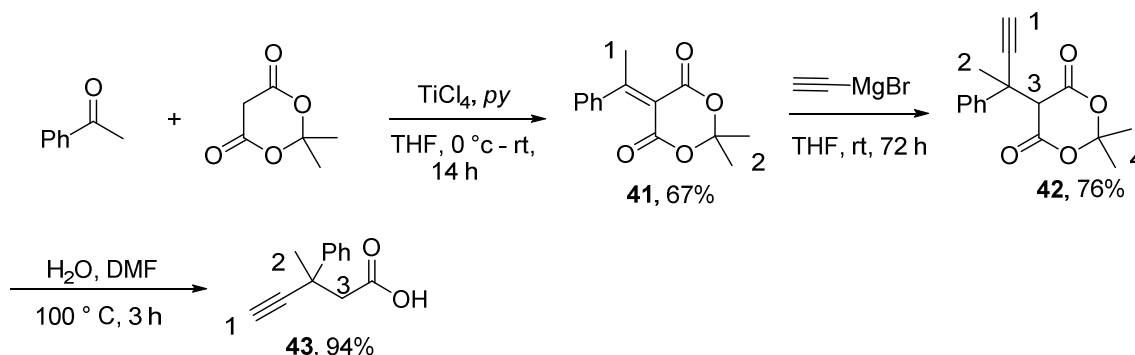
To a solution of **38** (600 mg, 3.26 mmol, 1.0 equiv.) in anhydrous THF (3 mL) under an atmosphere of argon at $0\text{ }^\circ\text{C}$ was added 0.5 M ethynyl magnesium bromide (18 mL, 9.0 mmol, 2.75 equiv.) in THF. The reaction was stirred at this temperature for 10 min and then allowed to react at rt for 72 h. The solution was diluted with Et_2O (100 mL) poured into a separating funnel and quenched with a saturated aqueous solution of NH_4Cl (40 mL). After phase separation, the aqueous phase was extracted with Et_2O (3 x 40 mL). The combined organic layers were washed with brine, dried over MgSO_4 and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 10 \rightarrow 25% $\text{EtOAc}/\text{Hexane}$ (v/v) to furnish the product as a colourless oil (500 mg, 2.38 mmol, 73%). δ_{H} (400 MHz, CDCl_3): 3.47 (s, 1H, H-3), 2.30 (s, 1H, H-1), 1.80 (s, 3H, H-2), 1.78 (s,

3H, H-2'), 1.60 (s, 6H, H-4). **LRMS:** (ESI) m/z calcd for $C_{11}H_{13}O_4$ ($[M-H]^-$): 209.1; found: 209.1. The spectral data were in accordance with those reported in the literature.³⁴

3,3-Dimethylpent-4-ynoic acid (40)

To a solution of **39** (367 mg, 1.75 mmol, 1.0 equiv.) in DMF (3.0 mL), was added H_2O (0.5 mL) and the resulting solution was heated at 100 °C for 1.5 h. The mixture was cooled to rt, diluted with an aqueous 2 M NaOH solution (25 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH_2Cl_2 (2 X 10 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH_2Cl_2 . The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to yield the carboxylic acid as a brown wax (194 mg, 1.536 mmol, 88%), without further purification being performed. δ_H (400 MHz, $CDCl_3$): 2.51 (s, 2H, H-3), 2.18 (s, 1H, H-1), 1.38 (s, 6H, H-2). **LRMS:** (ESI) m/z calcd for $C_7H_9O_2$ ($[M-H]^-$): 125.1; found: 125.1. The spectral data were in accordance with those reported in the literature.³⁵

43 was prepared according to the following sequence:



2,2-Dimethyl-5-(1-phenylethylidene)-1,3-dioxane-4,6-dione (41)

$TiCl_4$ (1.73 mL, 15.75 mmol, 2.1 equiv.) was added slowly to anhydrous THF (35 mL) under argon at 0 °C. After stirring for 10 mins, acetophenone (990 mg, 8.25 mmol, 1.1 equiv.) and Meldrum's acid (1.08 g, 7.5 mmol, 1.0 equiv.) in anhydrous THF (8.25 mL) were added, followed by pyridine (3.0 mL, 37.5 mmol, 5.0 equiv.). After 30 min the solution was warmed to rt, and stirred vigorously for 12 h. The mixture was then cooled to 0 °C and H_2O (15 mL) was added. After stirring for 10 min, the solution was diluted with CH_2Cl_2 (150 mL) poured into a separating funnel and quenched with saturated aqueous $NaHCO_3$ solution (80 mL). After phase separation, the aqueous phase was extracted with CH_2Cl_2 (4 x 50 mL). The combined organic layers were then washed with brine (60 mL), dried

over MgSO₄, filtered, and the solvent removed *in vacuo*. Purification was achieved by column chromatography using 10→20% EtOAc/Hexane (v/v) to yield the title compound as an orange wax (1.237 g, 5.03 mmol, 67%). δ_{H} (400 MHz, CDCl₃): 7.42–7.38 (m, 3H, Ar-H), 7.21–7.15 (m, 2H, Ar-H), 2.72 (s, 3H, H-1), 1.82 (s, 6H, H-2). **LRMS**: (ESI⁺) *m/z* calcd for C₁₄H₁₄O₄Na ([M+Na]⁺): 269.1; found: 269.1. The spectral data were in accordance with those reported in the literature.³⁶

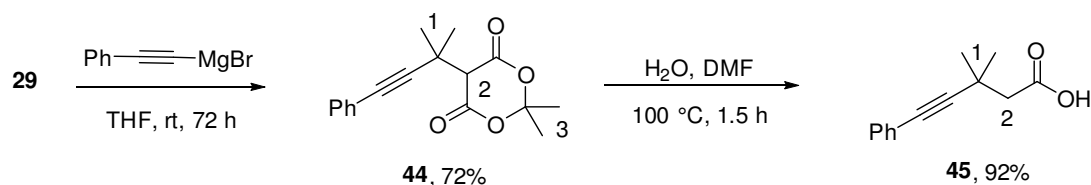
2,2-Dimethyl-5-(2-phenylbut-3-yn-2-yl)-1,3-dioxane-4,6-dione (42)

To a solution of **41** (615 mg, 2.50 mmol, 1.0 equiv.) in anhydrous THF (12.5 mL) under an atmosphere of argon at 0 °C was added 0.5 M ethynyl magnesium bromide (15 mL, 7.50 mmol, 3.0 equiv.) in THF. The reaction was stirred at this temperature for 10 min and then allowed to react at rt for 72 h. The solution was diluted with Et₂O (100 mL), poured into a separating funnel and quenched with a saturated aqueous solution of NH₄Cl (40 mL). After phase separation, the aqueous phase was extracted with Et₂O (3 x 40 mL). The combined organic layers were washed with brine, dried over MgSO₄ and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 15→25% EtOAc/Hexane (v/v) to furnish the product as a colourless oil (517 mg, 1.90 mmol, 76%). δ_{H} (400 MHz, CDCl₃): 7.57–7.53 (m, 2H, Ar-H), 7.38–7.32 (m, 2H, Ar-H), 7.30–7.36 (m, 1H, Ar-H), 3.92 (s, 1H, H-3), 2.59 (s, 1H, H-1), 1.99 (s, 3H, H-2), 1.71 (s, 3H, H-4), 1.53 (s, 3H, H-4'). **LRMS**: (ESI) *m/z* calcd for C₁₆H₁₅O₄ ([M-H]⁻): 271.1; found: 271.1. The spectral data were in accordance with those reported in the literature.³⁷

3-Methyl-3-phenylpent-4-ynoic acid (43)

To a solution of **42** (326 mg, 1.20 mmol, 1.0 equiv.) in DMF (3.0 mL), was added H₂O (0.5 mL) and the resulting solution was heated at 100 °C for 1.5 h. The mixture was cooled to rt, diluted with an aqueous 2 M NaOH solution (25 mL), and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 X 10 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the crude carboxylic acid as a brown wax (192 mg, 1.02 mmol, 85%), without further purification being performed. δ_{H} (400 MHz, CDCl₃): 7.39–7.26 (m, 5H, Ar-H), 2.91–2.72 (m, 2H, H-3), 2.46 (s, 1H, H-1), 1.72 (s, 2H, H-2). **LRMS**: (ESI) *m/z* calcd for C₇H₉O₂ ([M-H]⁻): 125.1; found: 125.1.

45 was prepared according to the following sequence:



2,2-Dimethyl-5-(2-methyl-4-phenylbut-3-yn-2-yl)-1,3-dioxane-4,6-dione (44)

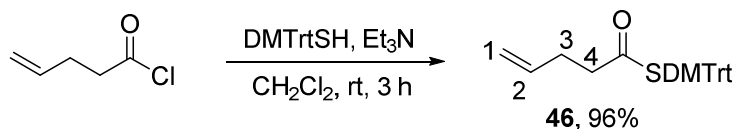
To a solution of **38** (283 mg, 1.54 mmol, 1.0 equiv.) in anhydrous THF (4 mL) under an atmosphere of argon at 0 °C was added 1.0 M phenylethynyl magnesium bromide (5.4 mL, 5.40 mmol, 3.5 equiv.) in THF. The reaction was stirred at this temperature for 10 min and then allowed to react at rt for 72 h. The solution was diluted with Et₂O (50 mL), poured into a separating funnel, and quenched with a saturated aqueous solution of NH₄Cl (30 mL). After phase separation, the aqueous phase was extracted with Et₂O (3 x 30 mL). The combined organic layers were washed with brine, dried over MgSO₄ and the solvent removed *in vacuo*. Purification was achieved by column chromatography on silica gel using 5→15% EtOAc/Hexane (v/v) to furnish the product as a colourless oil (316 mg, 1.11 mmol, 72%). *R_f* = 0.30 (30 % EtOAc/Hexane (v/v)). δ_{H} (400 MHz, CDCl₃): 7.44–7.41 (m, 2H, Ar-H), 7.33–7.29 (m, 3H, Ar-H), 3.50 (s, 1H, H-2), 1.80 (s, 3H, H-3), 1.78 (s, 3H, H-3'), 1.68 (s, 6H, H-1). δ_{C} (100 MHz, CDCl₃): 163.3 (C=O), 131.7, 128.2, 128.2 (Ar-C), 122.9 (q, Ar-C), 105.4, 92.9, 83.1 (q-C), 55.9 (C-2), 34.7 (q-C), 28.6 (C-1), 28.5 (C-3), 28.4 (C-3'). ν_{max} (ATR)/cm⁻¹: 1206 (C-O), 1751 (C=O). **HRMS**: (ESI⁻) *m/z* calcd for C₁₇H₁₇O₄ ([M-H]⁻): 285.1132; found: 235.1139.

3,3-Dimethyl-5-phenylpent-4-ynoic acid (45)

To a solution of **44** (139 mg, 0.486 mmol, 1.0 equiv.) in DMF (3.0 mL), was added H₂O (0.5 mL) and the resulting solution was heated at 100 °C for 1.5 h. The mixture was cooled to rt, diluted with an aqueous 2 M NaOH solution, and poured into a separating funnel. The aqueous phase was extracted twice with CH₂Cl₂ (2 x 10 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and the solvent removed *in vacuo* to yield the carboxylic acid (91 mg, 0.452 mmol, 92%), without requiring further purification. δ_{H} (400 MHz, CDCl₃): 7.43–7.39 (m, 2H, Ar-H), 7.30–7.26 (m, 3H, Ar-H), 2.62 (s, 2H, H-2), 1.41 (s, 6H, H-1). δ_{C} (100 MHz, CDCl₃): 175.6 (C=O), 131.6, 128.1, 127.8 (Ar-C), 123.5 (q, Ar-C), 95.1, 81.0 (q-C), 46.9 (C-2), 29.2 (C-1), 28.1 (q-C). ν_{max} (ATR)/cm⁻¹: 1740 (C=O), 2971 (O-H). **HRMS**: (ESI⁻) *m/z* calcd for C₁₃H₁₃O₂ ([M-H]⁻): 201.0921; found: 201.0927.

5. Synthesis of Protected Thioacids

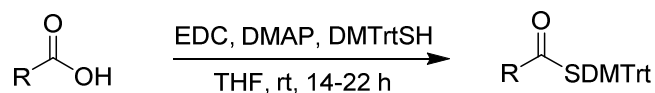
46 was prepared according to the following sequence:



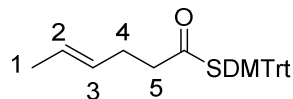
***S*-Dimethoxytrityl pent-4-enthioate (46)**

To a stirred solution of DMTrtSH (336 mg, 1.0 mmol, 1.0 equiv.) and Et₃N (0.3 mL, 2.0 mmol, 2.0 equiv.) in anhydrous CH₂Cl₂ (35 mL), under an atmosphere of argon at 0 °C was added dropwise 4-pentenoyl chloride (0.15 mL, 1.25 mmol, 1.25 equiv.). After 15 min the mixture was allowed to warm to rt and stirred for a further 3 h. The mixture was diluted with CH₂Cl₂ (60 mL) and quenched with water (60 mL). After phase separation, the aqueous phase was washed with CH₂Cl₂ (2 x 30 mL). The combined organic phases were washed with brine (50 mL), dried over MgSO₄, and the solvent evaporated *in vacuo*. Purification of the crude product by column chromatography on silica gel using 3.5% EtOAc/Hexane (v/v) afforded the thioester as a yellow wax (394 mg, 0.94 mmol, 94 %). **R_f** = 0.28 (10 % EtOAc/Hexane (v/v)). **δ_H** (400 MHz, CDCl₃): 7.26–7.19 (m, 5H, Ar-H), 7.10 (d, *J*_{*o-m*} = 8.9 Hz, 4H, Ar-H), 6.77 (d, *J*_{*m-o*} = 8.9 Hz, 4H, Ar-H), 5.78–5.68 (m, 1H, H-2), 5.05–4.96 (m, 2H, H-1), 3.78 (s, 6H, OMe), 2.56 (t, *J*_{*4-3*} = 7.0 Hz, H-4), 2.31 (app-q, 2H, H-3). **δ_C** (100 MHz, CDCl₃): 196.5 (C=O), 158.4 (Ar-OMe), 144.3 (q, Ar-C), 136.2 (C-2) 136.2 (q, Ar-C) 130.9, 129.7, 127.7, 127.0 (Ar-C), 115.8 (C-1) 113.0 (Ar-C), 69.8 (q-C), 55.2 (OMe), 42.9 (C-4), 29.5 (C-3). **v_{max}** (ATR)/cm⁻¹: 1033 (C-S), 1248 (C-O), 1725 (C=O). **LRMS**: (ESI) *m/z* calcd for C₂₆H₂₅O₃S ([M-H]⁻): 418.2; found: 418.2.

Thioester **47-57** were prepared according to the following sequence:



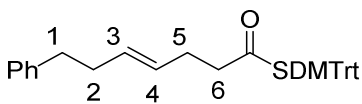
***S*-Dimethoxytrityl (E)-hex-4-enthioate (47)**



General procedure C to yield the title compound (359 mg, 0.832 mmol, 83 %) as a colourless wax from **2**. Purification was achieved by column chromatography on silica gel using 4→4.5 % EtOAc/Hexane (v/v). **R_f** = 0.28 (10 % EtOAc/Hexane (v/v)). **δ_H** (400 MHz, CDCl₃): 7.36–7.23 (m, 5H, Ar-H), 7.13 (d, *J*_{*o-m*} = 9.0 Hz, 4H, Ar-H), 6.76 (d, *J*_{*m-o*} = 9.0 Hz, 4H, Ar-H), 5.49–5.39 (m, 1H, H-3), 5.36–5.27 (m, 1H, H-2) 3.78 (s, 6H, OMe), 2.51 (t, *J*_{*5-4*} = 7.0 Hz, 2H, H-5), 2.23 (app-q, 2H, H-4), 1.63 (dd, *J*_{*1-2*} = 6.3 Hz, *J*_{*1-3*} = 1.4 Hz, 3H, H-1). **δ_C** (100 MHz, CDCl₃): 196.7 (C=O), 158.4 (Ar-COMe), 144.4, 136.3 (q, Ar-C), 130.9, 129.7 (Ar-C), 128.7 (C-3), 127.7, 127.0 (Ar-C), 126.6 (C-2), 113.0 (Ar-C), 69.6 (q-C), 55.2

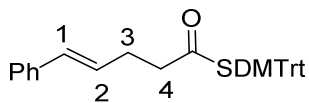
(OMe), 43.6 (C-5), 28.6 (C-4), 17.9 (C-1). ν_{\max} (ATR)/ cm^{-1} : 1175 (C-S), 1249 (C-O), 1707 (C=O). **LRMS**: (ESI) m/z calcd for $\text{C}_{27}\text{H}_{27}\text{O}_3\text{S}$ ($[\text{M}-\text{H}]^-$): 431.2; found: 431.2.

***S*-Dimethoxytrityl (E)-7-phenylhept-4-enethioate (48)**



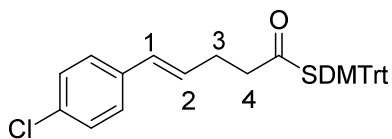
General procedure C to yield the title compound (323 mg, 0.62 mmol, 62 %, *E/Z* > 95:5) as a colourless wax from **6**. Purification was achieved by column chromatography on silica gel using 2.0→7.5% EtOAc/Hexane (v/v). R_f = 0.18 (10 % EtOAc/Hexane (v/v)). δ_{H} (400 MHz, CDCl_3): 7.30–7.18 (m, 10H, Ar-H), 7.14 (d, J_{o-m} = 8.8 Hz, 4H, Ar-H), 6.81 (d, J_{m-o} = 8.8 Hz, 4H, Ar-H), 5.56–5.47 (m, 1H, H-4), 5.42–5.33 (m, 1H, H-3), 3.81 (s, 6H, OMe), 2.88 (t, $J_{6,5}$ = 7.8 Hz, 2H, H-6), 2.55 (t, $J_{1,2}$ = 7.8 Hz, 2H, H-1), 2.36–2.24 (m, 4H, H-2, H-5). δ_{C} (100 MHz, CDCl_3): 196.7 (C=O), 158.4 (Ar-COMe), 144.4, 142.0, 136.3 (q, Ar-C), 132.6 (C-4), 131.1 (C-3), 130.9, 129.7, 128.4, 128.3, 127.7, 127.0, 125.8, 113.0 (Ar-C), 58.5 (q-C), 55.2 (OMe), 43.6 (C-6), 35.9 (C-1), 34.4 (C-2), 28.5 (C-5). ν_{\max} (ATR)/ cm^{-1} : 1037 (C-S), 1248 (C-O), 1709 (C=O). **LRMS**: (ESI) m/z calcd for $\text{C}_{34}\text{H}_{33}\text{O}_3\text{S}$ ($[\text{M}-\text{H}]^-$): 521.2; found: 521.3.

***S*-Dimethoxytrityl (E)-5-phenylpent-4-enethioate (49)**



General procedure C to yield the title compound (390 mg, 0.79 mmol, 79 %) as a colourless wax from **8**. Purification was achieved by column chromatography on silica gel using 4→6% EtOAc/Hexane (v/v). R_f = 0.16 (5% EtOAc/Hexane (v/v)). δ_{H} (400 MHz, CDCl_3): 7.36–7.23 (m, 10H, Ar-H), 7.13 (d, J_{o-m} = 9.0 Hz, 4H, Ar-H), 6.76 (d, J_{m-o} = 9.0 Hz, 4H, Ar-H), 6.43 (d, $J_{1,2}$ = 15.8 Hz, 1H, H-1), 6.15 (dt, $J_{1,2}$ = 15.8 Hz, $J_{2,3}$ = 7.0 Hz, 1H, H-2), 3.78 (s, 6H, OMe), 2.70 (t, $J_{4,3}$ = 7.0 Hz, 2H, H-4), 2.52 (app-q, 2H, H-3). δ_{C} (100 MHz, CDCl_3): 195.6 (C=O), 158.3 (Ar-COMe), 144.3, 137.3, 136.1 (q, Ar-C), 131.5 (C-1), 130.9, 129.6, 128.5 (Ar-C), 127.8 (C-2), 127.7, 127.2, 127.0, 126.2 (Ar-C), 113.7 (C-1), 113.0 (Ar-C), 69.8 (q-C), 55.2 (OMe), 43.2 (C-4), 28.9 (C-3). ν_{\max} (ATR)/ cm^{-1} : 1021 (C-S), 1251 (C-O), 1689 (C=O). **LRMS**: (EI⁺) m/z calcd for $\text{C}_{32}\text{H}_{29}\text{O}_3\text{S}$ ($[\text{M}]^+$): 493.2; found: 493.3.

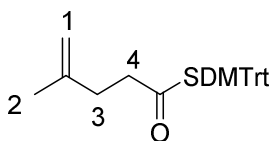
***S*-Dimethoxytrityl (E)-5-(4-chlorophenyl)pent-4-enethioate (50)**



General procedure C to yield the title compound (379 mg, 0.719 mmol, 72 %) as a colourless wax from **10**. Purification was

achieved by column chromatography on silica gel using 4→6 % EtOAc/Hexane (v/v). R_f = 0.13 (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.37–7.27 (m, 5H, Ar-H), 7.26–7.19 (m, 4H, Ar-H), 7.12 (d, J_{o-m} = 8.8 Hz, 4H, Ar-H), 6.75 (d, J_{m-o} = 8.8 Hz, 4H, Ar-H), 6.38 (d, J_{1-2} = 15.6 Hz, 1H, H-1), 6.12 (dt, J_{2-1} = 15.6 Hz, J_{2-3} = 6.9 Hz 1H, H-2), 3.79 (s, 6H, OMe), 2.69 (t, J_{4-3} = 7.1 Hz, 2H, H-4), 2.51 (app-q, 2H, H-3). δ_C (100 MHz, $CDCl_3$): 196.4 (C=O), 158.4 (Ar-COMe), 144.3, 136.1, 135.8 (q, Ar-C), 130.9 (Ar-C), 130.3 (C-2), 129.6, 129.1 (C-1), 128.7, 128.6, 127.7, 127.4, 127.0 (Ar-C), 113.0 (Ar-C), 69.8 (q-C), 55.2 (OMe), 43.0 (C-4), 28.9 (C-3). ν_{max} (ATR)/ cm^{-1} : 1181 (C-S), 1250 (C-O), 1703 (C=O). **LRMS**: (ESI) m/z calcd for $C_{32}H_{28}O_3SCl$ ([M-H]⁻): 527.1; found: 527.1.

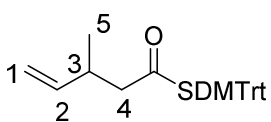
***S*-Dimethoxytrityl 4-methylpent-4-enethioate (51)**



General procedure C to yield the title compound (384 mg, 0.84 mmol, 84 % as a colourless wax from **12**. Purification was achieved by column chromatography on silica gel using 2.5→5% EtOAc/Hexane (v/v). R_f = 0.23 (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.34–7.24 (m,

5H, Ar-H), 7.17 (d, J_{o-m} = 8.8 Hz, 4H, Ar-H), 6.83 (d, J_{m-o} = 8.8 Hz, 4H, Ar-H), 4.78 (s, 1H, H-1), 4.72 (s, 1H, H-1'), 3.82 (s, 6H, OMe), 2.68 (t, J_{4-3} = 7.5 Hz, 2H, H-4), 2.35 (t, J_{3-4} = 7.5 Hz, 2H, H-3), 1.74 (s, 3H, H-2). δ_C (100 MHz, $CDCl_3$): 196.7 (C=O), 158.4 (Ar-COMe), 144.4 (q, Ar-C), 143.7 (q-C), 136.3 (q, Ar-C), 130.9, 129.7, 127.7, 127.0, 113.0 (Ar-C), 111.0 (C-1), 69.7 (q-C), 55.2 (OMe), 42.0 (C-4), 33.2 (C-3), 22.4 (C-2). ν_{max} (ATR)/ cm^{-1} : 1029 (C-S), 1247 (C-O), 1715 (C=O). **LRMS**: (ESI) m/z calcd for $C_{27}H_{27}O_3S$ ([M-H]⁻): 431.2; found: 431.2.

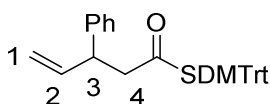
***S*-Dimethoxytrityl 3-methylpent-4-enethioate (52)**



General procedure C to yield the title compound (337 mg, 0.78 mmol, 78 %) as a colourless wax from 3-methyl-4-pentenoic acid. Purification was achieved by column chromatography on silica gel using 3→4.5% EtOAc/Hexane (v/v). R_f = 0.21 (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.31–7.24 (m,

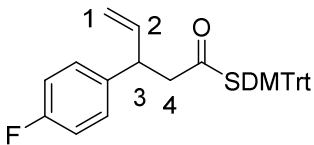
5H, Ar-H), 7.16 (d, J_{o-m} = 8.9 Hz, 4H, Ar-H), 6.82 (d, J_{m-o} = 8.9 Hz, 4H, Ar-H), 5.73 (m, 1H, H-2), 5.05–4.98 (m, 2H, H-1), 3.82 (s, 6H, OMe), 2.75–2.64 (m, 1H, H-3), 2.60–2.53 (m, 1H, H-4), 2.48–2.41 (m, 1H, H-4'), 1.02 (d, $J_{5,3}$ = 6.9 Hz, 3H, H-5). δ_C (100 MHz, $CDCl_3$): 196.1 (C=O), 158.4 (Ar-COMe), 144.4 (q, Ar-C), 142.1 (C-1), 136.3 (q, Ar-C), 130.9, 129.7, 127.7, 127.0 (Ar-C), 113.7 (C-2), 113.0 (Ar-C), 69.9 (q-C), 55.2 (OMe), 50.2 (C-4), 35.2 (C-3), 19.5 (C-5). ν_{max} (ATR)/ cm^{-1} : 1032 (C-S), 1248 (C-O), 1690 (C=O). **LRMS**: (ESI) m/z calcd for $C_{27}H_{27}O_3S$ ([M-H]⁻): 431.2; found: 431.3.

S-Dimethoxytrityl 3-phenylpent-4-enethioate (53)



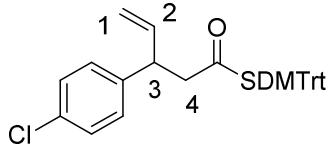
General procedure C to yield the title compound (400 mg, 0.81 mmol, 81 %) as a colourless wax from **13**. Purification was achieved by column chromatography on silica gel using 3→6% EtOAc/Hexane (v/v). $R_f = 0.16$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.33–7.28 (m, 2H, Ar-H), 7.23–7.07 (m, 8H, Ar-H), 6.99 (d, $J_{o-m} = 8.9$ Hz, 4H, Ar-H), 6.72 (d, $J_{m-o} = 8.9$ Hz, 4H, Ar-H), 5.97–5.87 (m, 1H, H-2), 5.07–4.99 (m, 2H, H-1), 3.83 (app-q, 1H, H-3), 3.77 (s, 6H, OMe), 2.88 (d, $J_{4,3} = 7.7$ Hz, 2H, H-4). δ_C (100 MHz, $CDCl_3$): 195.3 (C=O), 158.3 (Ar-COMe), 144.1, 141.9 (q, Ar-C), 140.0 (C-1), 136.0 (q, Ar-C), 130.9, 129.6, 128.6, 127.8, 127.7, 126.9, 126.8 (Ar-C), 115.1 (C-2), 113.0 (Ar-C), 69.9 (q-C), 55.2 (OMe), 48.9 (C-4), 46.0 (C-3). ν_{max} (ATR)/ cm^{-1} : 1029 (C-S), 1243 (C-O), 1718 (C=O). **LRMS**: (ESI) m/z calcd for $C_{32}H_{29}O_3S$ ([M-H]⁻): 493.2; found: 493.2.

S-Dimethoxytrityl 3-(4-fluorophenyl)pent-4-enethioate (54)



General procedure C to yield the title compound (387 mg, 0.756 mmol, 76 %) as a rotameric mixture (3:1) as a colourless wax from **16**. Purification was achieved by column chromatography on silica gel using 4→5.5 % EtOAc/Hexane (v/v). $R_f = 0.29$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): Major rotamer: 7.34–7.26 (m, 3H, Ar-H), 7.25–7.19 (m, 3H, Ar-H), 7.17–7.09 (m, 3H, Ar-H), 7.02 (d, $J_{o-m} = 8.9$ Hz, 4H, Ar-H), 6.76 (d, $J_{m-o} = 8.9$ Hz, 4H, Ar-H), 5.97–5.87 (m, 1H, H-2), 5.12–5.00 (m, 2H, H-1), 3.86 (app-q, 1H, H-3), 3.81 (s, 6H, OMe), 2.92–2.87 (m, 2H, H-4). δ_C (100 MHz, $CDCl_3$): 195.2 (C=O), 158.6 (Ar-CF), 158.4 (Ar-COMe), 144.1 (q, Ar-C), 139.8 (C-2), 136.0 (q, Ar-C), 131.3, 130.8, 129.9, 129.6, 129.4, 127.7, 127.0 (Ar-C), 115.2 (C-1), 112.9 (Ar-C), 70.0 (q-C), 55.2 (OMe), 48.9 (C-2), 45.1 (C-3). δ_F (367 MHz, $CDCl_3$): -116.2. ν_{max} (ATR)/ cm^{-1} : 1035 (C-F), 1180 (C-S), 1253 (C-O), 1691 (C=O). **LRMS**: (ESI⁺) m/z calcd for $C_{32}H_{29}O_3SFK$ ([M+K]⁺): 551.1; found: 551.2.

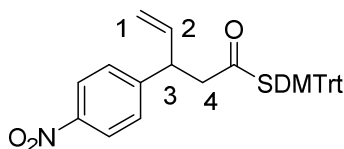
S-Dimethoxytrityl 3-(4-chlorophenyl)pent-4-enethioate (55)



General procedure C to yield the title compound (387 mg, 0.756 mmol, 76 %) as a rotameric mixture (3:1) as a colourless wax from **18**. Purification was achieved by column chromatography on silica gel using 4→6 % EtOAc/Hexane (v/v). $R_f = 0.16$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.34–7.30 (m, 2H, Ar-H), 7.25–7.21 (m, 3H, Ar-H), 7.15–7.09 (m, 4H, Ar-H), 7.00 (d, $J_{o-m} = 8.9$ Hz, 4H, Ar-H), 6.75 (d, $J_{m-o} = 8.9$ Hz, 4H, Ar-H), 5.96–5.86 (m, 1H, H-2), 5.13–5.00 (m, 2H, H-1), 3.85 (app-q, 1H, H-3), 3.81 (s, 6H, OMe), 2.90 (app-d, 2H, H-4). δ_C (100

MHz, CDCl₃): 195.1 (C=O), 158.3 (Ar-COMe), 144.0, 140.2 (q, Ar-C), 139.5 (C-2), 135.9 (q, Ar-C), 130.8, 129.6, 129.3, 128.2, 127.7, 127.0 (Ar-C), 115.4 (C-1), 112.9 (Ar-C), 70.0 (q-C), 55.2 (OMe), 48.6 (C-2), 45.3 (C-3). ν_{\max} (ATR)/cm⁻¹: 734 (C-Cl), 1180 (C-S), 1253 (C-O), 1690 (C=O). **LRMS**: (ESI) m/z calcd for C₃₂H₂₈O₃SCl ([M-H]⁻): 527.1; found: 527.2.

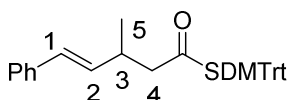
***S*-dimethoxytrityl 3-(4-nitrophenyl)pent-4-enethioate (56)**



General procedure C to yield the title compound (414 mg, 0.768 mmol, 77 % as a rotameric mixture) as a colourless wax from **19**. Purification was achieved by column chromatography on silica gel using 4→8 % EtOAc/Hexane (v/v). **R_f** = 0.16 (10 % EtOAc/Hexane

(v/v)). δ_{H} (400 MHz, CDCl₃): 8.19 (d, J_{o-m} = 8.8 Hz, 1H, Ar-H), 7.36–7.29 (m, 3H, Ar-H), 7.25–7.15 (m, 4H, Ar-H), 7.13 (m, 1H, Ar-H), 7.00 (d, J_{o-m} = 8.8 Hz, 3H, Ar-H), 6.88–6.82 (m, 2H, Ar-H), 6.74 (d, J_{m-o} = 8.8 Hz, 3H, Ar-H), 5.98–5.86 (m, 1H, H-2), 5.21–5.05 (m, 2H, H-2), 3.98 (app-q, 1H, H-3), 3.83 (s, 2H, OMe, minor rotamer) 3.80 (s, 4H, OMe, major rotamer), 3.02–2.89 (m, 2H, H-4). δ_{C} (100 MHz, CDCl₃): 194.6 (C=O), 158.4 (Ar-COMe), 149.4 (Ar-CNO₂), 146.8, 143.9 (q, Ar-C), 138.4 (C-2), 135.8 (q, Ar-C), 132.2, 130.8, 129.5, 129.1, 128.8, 127.9, 127.8, 127.7, 127.1, 123.8 (Ar-C), 116.4 (C-1), 113.2, 113.0 (Ar-C), 70.3 (q-C), 55.3 (OMe, minor rotamer) 55.2 (OMe, major rotamer), 48.3 (C-4), 45.6 (C-3). ν_{\max} (ATR)/cm⁻¹: 1180 (C-S), 1252 (C-O), 1347, 1509 (N-O), 1690 (C=O). **LRMS**: (ESI) m/z calcd for C₃₂H₂₈NO₅S ([M-H]⁻): 538.2; found: 538.2.

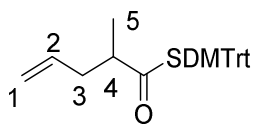
***S*-Dimethoxytrityl (E)-3-methyl-5-phenylpent-4-enethioate (57)**



General procedure C to yield the title compound (436 mg, 0.81 mmol, 81 %) as a colourless wax from **23**. Purification was achieved by column chromatography on silica gel using 3→5.5% EtOAc/Hexane (v/v). **R_f** =

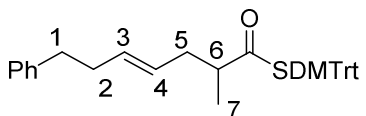
0.16 (10 % EtOAc/Hexane (v/v)). δ_{H} (400 MHz, CDCl₃): 7.40–7.30 (m, 5H, Ar-H), 7.27–7.20 (m, 5H, Ar-H), 7.14–7.09 (m, 4H, Ar-H), 6.72 (d, J_{m-o} = 8.9 Hz, 4H, Ar-H), 6.42 (d, J_{1-2} = 16.0 Hz, 1H, H-1), 6.10 (dd, J_{2-1} = 16.0 Hz, J_{2-3} = 7.7 Hz, 1H, H-2), 3.81 (s, 1H, OMe, minor rotamer), 3.76 (m, 5H, OMe, major rotamer), 2.93–2.82 (m, 1H, H-3), 2.67–2.52 (m, 2H, H-4), 1.11 (d, J_{5-3} = 6.8 Hz, 3H, H-5). δ_{C} (100 MHz, CDCl₃): 195.9 (C=O), 158.3 (Ar-COMe), 144.3, 137.4 (q, Ar-C), 136.1 (major rotamer), 136.1 (minor rotamer) (q, Ar-C), 133.6 (C-2), 130.9 (major rotamer), 130.9 (minor rotamer), 129.6 (Ar-C), 129.5 (C-1), 128.5, 127.7, 127.2, 126.9, 126.3, 113.0 (Ar-C), 69.8 (q-C), 55.2 (OMe), 50.7 (C-4), 35.0 (C-3), 20.2 (C-5). ν_{\max} (ATR)/cm⁻¹: 1034 (C-S), 1243 (C-O), 1708 (C=O). **LRMS**: (ESI) m/z calcd for C₃₃H₃₁O₃S ([M]⁻): 507.2; found: 507.2.

S-Dimethoxytrityl 2-methylpent-4-enethioate (58)



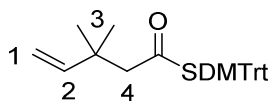
General procedure C to yield the title compound (340 mg, 0.79 mmol, 79 %) as a colourless wax from 2-methyl-4-pentenoic acid. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.30–7.22 (m, 5H, Ar-H), 7.14 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.81 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 5.76–5.65 (m, 1H, H-2), 5.09–5.03 (m, 2H, H-1), 3.82 (s, 6H, OMe), 2.78–2.69 (m, 1H, H-4), 2.44–2.35 (m, 1H, H-3), 2.13–2.04 (m, 1H, H-3'), 1.12 (d, $J_{5-4} = 6.9$ Hz, 3H, H-5). δ_C (100 MHz, $CDCl_3$): 200.5 (C=O), 158.4 (Ar-COMe), 144.4, 136.3 (q, Ar-C), 135.0 (C-2), 130.9, 129.5, 127.7, 127.0 (Ar-C), 117.0 (C-1), 112.9 (Ar-C), 69.6 (q-C), 55.2 (OMe), 48.0 (C-4), 38.0 (C-3), 17.2 (C-5). ν_{max} (ATR)/ cm^{-1} : 1037 (C-S), 1217 (C-O), 1739 (C=O). **LRMS**: (ESI) m/z calcd for $C_{27}H_{28}OSCl$ ([M+Cl]): 467.1; found: 467.0.

S-Dimethoxytrityl (E)-2-methyl-7-phenylhept-4-enethioate (59)



General procedure C to yield the title compound (443 mg, 0.83 mmol, 83 %) as a colourless wax from **25**. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.37–7.17 (m, 10H), 7.14 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.80 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 5.56–5.45 (m, 1H, H-3), 5.37–5.27 (m, 1H, H-4), 3.80 (s, 6H, OMe), 2.73–2.62 (m, 3H, H-1, H-6), 2.37–2.27 (m, 3H, H-2, H-5), 2.07–1.97 (m, 1H, H-5'), 1.06 (d, $J_{7-6} = 6.9$ Hz, 3H, H-7). δ_C (100 MHz, $CDCl_3$): 206.6 (C=O), 158.3 (Ar-COMe), 144.5, 141.9, 136.4 (q, Ar-C), 132.2 (C-3), 130.9, 129.7, 128.4, 128.3, 127.7 (Ar-C), 127.2 (C-4), 126.9, 125.8, 112.9 (Ar-C), 69.4 (q-C), 55.2 (OMe), 48.5 (C-6), 36.8 (C-5), 35.9 (C-1), 34.4 (C-2), 17.2 (C-7). ν_{max} (ATR)/ cm^{-1} : 1033 (C-S), 1251 (C-O), 1691 (C=O). **LRMS**: (ESI⁺) m/z calcd for $C_{35}H_{36}OS$ ([M+H]⁺): 537.2; found: 537.2.

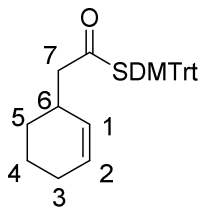
S-Dimethoxytrityl 3,3-dimethylpent-4-enethioate (60)



General procedure C to yield the title compound (374 mg, 0.84 mmol, 84 %) as a colourless wax from **26**. Purification was achieved by column chromatography on silica gel using 2.5→4.5% EtOAc/Hexane (v/v). $R_f = 0.17$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.30–7.23 (m, 5H, Ar-H), 7.15 (d, $J_{o-m} = 8.9$ Hz, 4H, *m*Ar-H), 6.80 (d, $J_{o-m} = 8.9$ Hz, 4H, Ar-H), 5.90–5.81 (m, 1H, H-2), 4.99–4.92 (m, 2H, H-1), 3.81 (s, 6H, OMe), 2.48 (s, 2H, H-4), 1.08 (s, 6H, H-3). δ_C (100 MHz, $CDCl_3$): 196.1 (C=O), 158.4 (Ar-COMe), 144.4 (q, Ar-C), 142.1 (C-2) 136.3 (q, Ar-C), 130.9, 129.7, 127.7, 127.0 (Ar-C), 113.7 (C-1), 113.0 (Ar-C), 69.9 (q-C), 55.2 (OMe), 50.2 (C-4) 41.0 (q-C), 26.9 (C-3). ν_{max} (ATR)/ cm^{-1} :

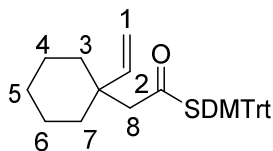
1031 (C-S), 1245 (C-O), 1712 (C=O). **LRMS:** (ESI) m/z calcd for $C_{28}H_{29}O_3S$ ([M-H]⁻): 445.2; found: 445.3.

***S*-Dimethoxytrityl 2-(cyclohex-2-en-1-yl)ethanethioate (61)**



General procedure C to yield the title compound (384 mg, 0.84 mmol, 84 %) as a colourless wax from **28**. Purification was achieved by column chromatography on silica gel using 2.5→6% EtOAc/Hexane (v/v). $R_f = 0.23$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.27–7.19 (m, 5H, Ar-H), 7.11 (d, $J_{o-m} = 8.9$ Hz, 4H, Ar-H), 6.77 (d, $J_{m-o} = 8.9$ Hz, 4H, Ar-H), 5.70–5.64 (m, 1H, H-1), 5.46–5.40 (m, 1H, H-2), 3.78 (s, 6H, OMe), 2.60–2.51 (m, 1H, H-6), 2.49–2.38 (m, 2H, H-7), 1.96–1.90 (m, 2H, H-3), 1.73–1.60 (m, 2H, H-5), 1.53–1.41 (m, 1H, H-4), 1.26–1.17 (m, 1H, H-4'). δ_C (100 MHz, $CDCl_3$): 196.5 (C=O), 158.4 (Ar-COMe), 144.4, 136.1 (q, Ar-C), 130.9, 129.8 (Ar-C), 129.7 (C-2), 128.3 (C-1), 127.7, 127.0, 113.0 (Ar-C), 69.8 (q-C), 55.2 (OMe), 49.8 (C-7), 33.1 (C-6), 28.5 (C-3), 25.0 (C-5), 20.9 (C-4). ν_{max} (ATR)/ cm^{-1} : 1041 (C-S), 1692 (C=O). **LRMS:** (ESI) m/z calcd for $C_{29}H_{29}OSNa$ ([M-H]⁻): 457.2; found: 457.2.

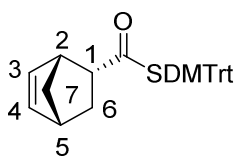
***S*-Dimethoxytrityl 2-(1-vinylcyclohexyl)ethanethioate (62)**



General procedure C to yield the title compound (402 mg, 0.828 mmol, 83 %) as a colourless wax from **31**. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.31$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.32–7.26 (m, 1H, Ar-H), 7.24–7.14 (m, 5H, Ar-H), 7.12–7.08 (m, 3H, *m*Ar-H), 6.81–6.73 (m, 4H, Ar-H), 5.68 (dd, $J_{2,1} = 18.8$ Hz, $J_{2,1'} = 10.9$ Hz, 1H, H-2, major rotamer), 5.56 (dd, $J_{2,1} = 18.3$ Hz, $J_{2,1'} = 10.9$ Hz, 1H, H-2, minor rotamer), 5.11–4.84 (m, 2H, H-1 (major + minor rotamers)), 3.79–3.76 (m, 6H, OMe (major + minor rotamer)), 2.46 (s, 1H, H-8, major rotamer), 2.35 (s, 1H, H-8, minor rotamer), 1.48–1.22 (m, 10H, H-3, H-4, H-5, H-6, H-7). δ_C (100 MHz, $CDCl_3$): 195.0 (C=O), 158.5 (Ar-COMe, minor rotamer), 158.3 (Ar-COMe, major rotamer), 144.6 (C-2), 144.4 (q, Ar-C), 136.3 (q, Ar-C, major rotamer), 135.8 (q, Ar-C, minor rotamer), 131.4 (Ar-C, minor rotamer), 131.0 (Ar-C, major rotamer), 130.0 (Ar-C, minor rotamer), 129.7 (Ar-C, major rotamer), 127.8 (Ar-C, minor rotamer), 127.6 (Ar-C, major rotamer), 127.1 (Ar-C, minor rotamer), 126.9 (Ar-C, major rotamer), 113.2 (C-1), 113.0 (Ar-C, minor rotamer), 112.9 (major rotamer), 69.9 (q-C), 55.2 (OMe), 40.5 (C-8, major rotamer), 40.2 (C-8, minor rotamer), 35.5 (C3/C7, major rotamer), 35.3 (C3/C7, minor rotamer), 26.1

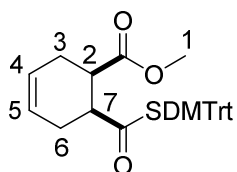
(C-5, major rotamer), 25.9 (C-5, minor rotamer), 22.7 (qC), 22.1 (C4/C6, major rotamer), 22.0 (C4/C6, minor rotamer). ν_{\max} (ATR)/ cm^{-1} : 1031 (C-S), 1239 (C-O), 1725 (C=O). **LRMS**: (ESI) m/z calcd for $\text{C}_{31}\text{H}_{33}\text{O}_3\text{S}$ ([M-H]⁻): 485.2; found: 485.3.

***S*-Dimethoxytrityl (1*R*,2*R*,4*R*)-bicyclo[2.2.1]hept-5-ene-2-carbothioate (63)**



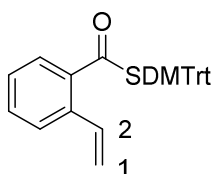
General procedure C to yield the title compound (367 mg, 0.802 mmol, 80 %) as a colourless wax from 5-norbornene-2-carboxylic acid. Purification was achieved by column chromatography on silica gel using 2.5→5.5% EtOAc/Hexane (v/v). **R_f** = 0.18 (10 % EtOAc/Hexane (v/v)). **δ_{H}** (400 MHz, CDCl_3): 7.28–7.21 (m, 5H, Ar-H), 7.14 (d, J_{o-m} = 8.8 Hz, 4H, Ar-H), 6.81 (d, J_{m-o} = 8.8 Hz, 4H, Ar-H), 6.13 (dd, J_{3-4} = 5.7 Hz, J_{3-2} = 3.1 Hz, 1H, H-3), 5.75 (dd, J_{4-3} = 5.7 Hz, J_{4-5} = 2.8 Hz, 1H, H-4), 3.88 (s, 6H, OMe), 3.28 (app-s, 1H, H-2), 3.20 (app-dt, 1H, H-1), 2.88 (app-s, 1H, H-5), 1.80–1.72 (m, 1H, H-6), 1.47–1.38 (m, 2H, H-6', H-7), 1.29–1.26 (, m, 1H, H-7'). **δ_{C}** (100 MHz, CDCl_3): 198.1 (C=O), 158.3 (Ar-COMe), 144.6 (q, Ar-C), 137.7 (C-3), 136.5 (q, Ar-C), 131.6 (C-4), 130.9, 129.7, 127.6, 126.9, 112.9 (Ar-C), 69.3 (q-C), 55.2 (OMe), 52.6 (C-1), 49.5 (C-7), 47.7 (C-2), 42.8 (C-5), 28.9 (C-6). ν_{\max} (ATR)/ cm^{-1} : 1213 (C-O), 1029 (C-O), 1698 (C=O). **HRMS**: (APCI⁺) m/z calcd for $\text{C}_{29}\text{H}_{28}\text{O}_3\text{S}$ ([M+H]⁺): 457.1837; found: 457.1832. **$[\alpha]_{\text{D}}^{22}$** = +88.42 (*c* 0.21, CHCl_3).

***Cis*-methyl-6-((dimethoxytritylthio)carbonyl)cyclohex-3-ene-1-carboxylate (64)**



General procedure C to yield the title compound (370 mg, 0.738 mmol, 74 %) as a colourless wax from **32**. Purification was achieved by column chromatography on silica gel using 4→10 % EtOAc/Hexane (v/v). **R_f** = 0.16 (10 % EtOAc/Hexane (v/v)). **δ_{H}** (400 MHz, CDCl_3): 7.34–7.22 (m, 5H, Ar-H), 7.16 (d, J_{o-m} = 8.8 Hz, 4H, Ar-H), 6.80 (d, J_{m-o} = 8.8 Hz, 4H, Ar-H), 5.70 (app-s, 2H, H-4, H-5), 3.81 (s, 6H, OMe), 3.66 (s, 3H, CO_2Me), 3.14–3.03 (m, 2H, H-2, H-7), 2.67–2.24 (m, 4H, H-3, H-6). **δ_{C}** (100 MHz, CDCl_3): 197.0 (C=O), 173.2 (C=O), 158.3 (Ar-COMe), 144.4, 136.3 (q, Ar-C), 131.0, 129.7, 127.7, 126.9 (Ar-C), 125.5 (C-5), 124.4 (C-5), 112.9 (Ar-C), 69.5 (q-C), 55.2 (OMe), 48.2 (C-7), 40.1 (C-2), 26.3 (C-6), 26.1 (C-3). ν_{\max} (ATR)/ cm^{-1} : 1035 (C-O), 1180 (C-S), 1252 (C-O), 1711 (C=O) 1733 (C=O). **LRMS**: (ESI⁺) m/z calcd for $\text{C}_{30}\text{H}_{30}\text{O}_5\text{SK}$ ([M+K]⁺): 541.1; found: 541.2.

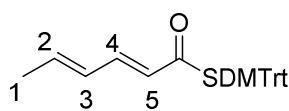
***S*-Dimethoxytrityl 2-vinylbenzothioate(64)**



General procedure C to yield the title compound (348 mg, 0.747 mmol, 75 %) as a colourless wax from 2-vinylbenzoic acid. Purification was achieved by column

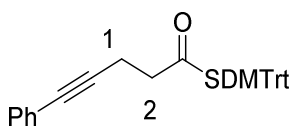
chromatography on silica gel using 2.5→5.5% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.72–7.69 (m, 1H, Ar-H), 7.59–7.57 (m, 1H, Ar-H), 7.46–7.41 (m, 1H, Ar-H), 7.38–7.29 (m, 6H, Ar-H), 7.26 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.94–6.88 (m, 1H, H-2), 6.84 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 5.67 (dd, $J_{1-2} = 17.4$ Hz, $J_{1-1'} = 1.0$ Hz, 1H, H-1), 5.29 (dd, $J_{1'-2} = 11.0$ Hz, $J_{1'-1} = 1.0$ Hz, 1H, H-1), 3.82 (s, 6H, OMe). δ_C (100 MHz, $CDCl_3$): 192.6 (C=O), 158.5 (Ar-COMe), 144.2, 137.2, 136.1, 135.9 (q, Ar-C), 134.1 (C-2), 131.3, 131.0, 129.8, 128.2, 127.8, 127.3, 127.1, 126.5 (Ar-C), 116.8 (C-1), 113.1 (Ar-C), 70.8 (q-C), 55.2 (OMe). ν_{max} (ATR)/ cm^{-1} : 1028 (C-S), 1248 (C-O), 1701 (C=O). **LRMS**: (ESI⁺) m/z calcd for $C_{30}H_{27}O_3S$ ([M+H]⁺): 467.2; found: 467.2.

***S*-Dimethoxytrityl (2E,4E)-hexa-2,4-dienethioate (65)**



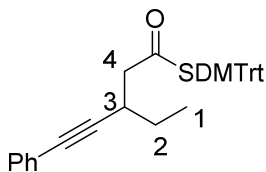
General procedure C to yield the title compound (341 mg, 0.794 mmol, 79 %) as a colourless wax from sorbic acid. Purification was achieved by column chromatography on silica gel using 2.5→5.5% EtOAc/Hexane (v/v). $R_f = 0.17$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.31–7.24 (m, 5H, Ar-H), 7.19 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 7.15–7.07 (m, 1H, H-4), 6.82 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 6.18–6.02 (m, 3H, H-2, H-3, H-5), 3.82 (s, 6H), 1.86 (d, $J_{1-2} = 5.5$ Hz, 3H, H-1). δ_C (100 MHz, $CDCl_3$): 188.0 (C=O), 158.3 (Ar-OMe), 144.5 (q, Ar-C), 140.9 (C-4), 140.8 (C-2), 136.4 (q, Ar-C), 131.0, 129.7 (Ar-C), 129.7 (C-5), 127.7, 127.0 (Ar-C), 125.8 (C-3), 113.0 (Ar-C), 69.6 (q-C), 55.2 (OMe), 18.8 (C-1). ν_{max} (ATR)/ cm^{-1} : 1034 (C-S), 1250 (C-O), 1728 (C=O). **LRMS**: (ESI⁺) m/z calcd for $C_{27}H_{27}O_3S$ ([M+H]⁺): 431.2; found: 431.2.

***S*-Dimethoxytrityl 5-phenylpent-4-ynethioate (66)**



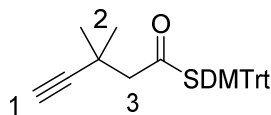
General procedure C to yield the title compound (340 mg, 0.786 mmol, 79 %) as a colourless wax from **34**. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.43–7.39 (m, 2H, Ar-H), 7.33–7.27 (m, 8H, Ar-H), 7.16 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.77 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 3.79 (s, 6H, OMe), 2.81 (t, $J_{2-1} = 6.8$ Hz, 2H, H-2), 2.69 (t, $J_{1-2} = 6.8$ Hz, 2H, H-1). δ_C (100 MHz, $CDCl_3$): 195.5 (C=O), 158.4 (Ar-OMe), 144.2 (q, Ar-C), 136.0 (q, Ar-C), 131.6, 130.9, 129.6, 128.2, 127.8, 127.7, 127.0 (Ar-C), 123.5 (q, Ar-C), 113.0 (Ar-C), 87.6, 81.7, 70.0 (q-C), 55.2 (OMe), 42.4 (C-2), 15.8 (C-1). ν_{max} (ATR)/ cm^{-1} : 1035 (C-S), 1253 (C-O), 1692 (C=O), 2157 (C≡C). **LRMS**: (ESI⁺) m/z calcd for $C_{32}H_{28}O_3SK$ ([M+K]⁺): 531.1; found: 531.0.

***S*-Dimethoxytrityl 3-ethyl-5-phenylpent-4-ynethioate (67)**



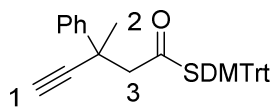
General procedure C to yield the title compound (419 mg, 0.81 mmol, 81 %) as a colourless wax from **37**. Purification was achieved by column chromatography on silica gel using 2.5→5.5% EtOAc/Hexane (v/v). $R_f = 0.17$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.37–7.29 (m, 5H, Ar-H), 7.28–7.20 (m, 5H, Ar-H) 7.17 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.80 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 3.78 (s, 6H, OMe), 3.77–3.74 (m, 1H, H-3), 2.18–2.07 (m, 2H, H-4), 1.26–1.22 (m, 1H, H-2), 1.06–0.90 (m, 1H, H-2'), 0.92 (t, $J_{1-2} = 7.5$ Hz, 3H, H-1). δ_C (100 MHz, $CDCl_3$): 195.8 (C=O), 158.6 (Ar-COMe), 139.5, 132.6 (q, Ar-C), 130.5, 129.7, 129.1, 128.7, 128.2, 127.8, 127.1, 126.8 (Ar-C), 126.4 (q, Ar-C), 113.0 (Ar-C), 93.0, 81.4, 68.9 (q-C), 55.3 (OMe), 46.2 (C-4), 45.8 (C-2), 28.0 (C-3), 11.4 (C-1). ν_{max} (ATR)/ cm^{-1} : 1032 (C-S), 1251 (C-O), 1729 (C=O), 2223 (C≡C). **LRMS**: (ESI) m/z calcd for $C_{34}H_{33}O_3S$ ($[M+H]^+$): 521.2; found: 521.1.

S-Dimethoxytrityl 3,3-dimethylpent-4-ynethioate (**68**)



General procedure C to yield the title compound (345 mg, 0.78 mmol, 77 %) as a colourless wax from **40**. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.20$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.30–7.23 (m, 5H, Ar-H), 7.19 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.81 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 3.82 (s, 6H, OMe), 2.62 (s, 2H, H-3), 2.21 (s, 1H, H-1), 1.29 (s, 6H, H-2). δ_C (100 MHz, $CDCl_3$): 194.1 (C=O), 158.4 (Ar-COMe), 144.2 (q, Ar-C), 136.2 (q, Ar-C), 131.0, 129.7, 127.7, 127.0, 113.0 (Ar-C), 90.0, 70.1, 69.0 (q-C), 55.2 (OMe), 54.6 (C-3), 30.6 (q-C), 29.2 (C-2). ν_{max} (ATR)/ cm^{-1} : 1034 (C-S), 1252 (C-O), 1738 (C=O), 2123 (C≡C). **LRMS**: (ESI) m/z calcd for $C_{28}H_{29}OS$ ($[M+H]^+$): 445.2; found: 445.2.

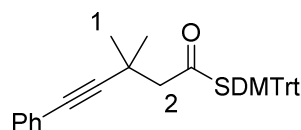
S-Dimethoxytrityl 3-methyl-3-phenylpent-4-ynethioate (**69**)



To a solution of **42** (340 mg, 1.25 mmol, 1.0 equiv.) in DMF (3.0 mL), was added H_2O (0.5 mL) and the resulting solution was heated at 100 °C for 1.5 h. The mixture was cooled to rt, diluted with an aqueous 2 M NaOH solution, and poured into a separating funnel. The aqueous phase was extracted twice with CH_2Cl_2 (2 x 10 mL), then acidified with aqueous 4 M HCl solution. The aqueous phase was extracted five times with CH_2Cl_2 . The combined organic layers were dried over $MgSO_4$, filtered and the solvent removed *in vacuo* to give **43**. General procedure C was then applied to the crude carboxylic acid (**43**) to yield the title compound (439 mg, 0.87 mmol, 69%) as a colourless wax. Purification was achieved by column chromatography on silica gel using 2.5→7.0% EtOAc/Hexane (v/v). $R_f = 0.14$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.56–7.52 (m, 2H, Ar-H), 7.40–7.34 (m, 2H, Ar-H),

7.31–7.29 (m, 1H, Ar-H), 7.26–7.21 (m, 3H, Ar-H), 7.17–7.13 (m, 2H, Ar-H), 7.05 (d, $J_{o-m} = 8.8$ Hz, 4H, Ar-H), 6.76 (d, $J_{m-o} = 8.8$ Hz, 4H, Ar-H), 3.81 (s, 6H, OMe), 2.99 (app-q, 2H, H-3), 2.51 (s, 1H, H-1), 1.71 (s, 3H, H-2). δ_C (100 MHz, CDCl₃): 193.2 (C=O), 158.3 (Ar-COMe.), 144.1, 143.3, 136.0 (q, Ar-C), 130.9, 129.6, 128.4, 127.7, 127.0, 126.9, 126.1, 112.9 (Ar-C), 87.8, 72.7, 70.0 (q-C), 55.7 (C-3), 55.2 (OMe), 39.0 (q-C), 29.3 (C-2). ν_{max} (ATR)/cm⁻¹: 1031 (C-S), 1249 (C-O), 1712 (C=O), 2123 (C≡C). **LRMS**: (ESI) m/z calcd for C₃₃H₃₃O₃S ([M-H]⁻): 505.2; found: 505.2.

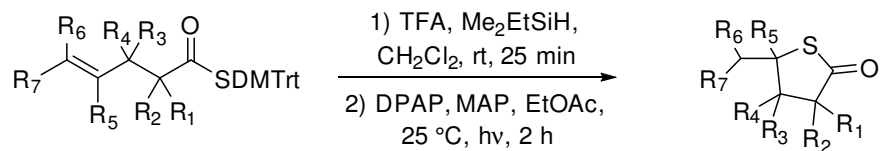
S-Dimethoxytrityl 3,3-dimethyl-5-phenylpent-4-ynethioate (70)



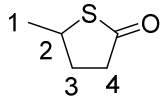
General procedure C to yield the title compound (375 mg, 0.721 mmol, 72 %) as a colourless wax from **45**. Purification was achieved by column chromatography on silica gel using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, CDCl₃): 7.35–7.12 (m, 14H, Ar-H), 6.78 (d, $J_{m-o} = 8.8$ Hz, 2H, Ar-H, minor rotamer), 6.73 (d, $J_{m-o} = 8.8$ Hz, 2H, Ar-H, major rotamer), 3.78 (s, 2H, OMe, minor rotamer), 3.76 (s, 4H, OMe, major rotamer), 2.66 (s, 1H, H-2, minor rotamer), 2.58 (s, 1H, H-2, major rotamer), 1.34 (s, 3H, H-1, major rotamer), 1.26 (s, 3H, H-1, minor rotamer). δ_C (100 MHz, CDCl₃): 194.4 (C=O), 158.6 (minor rotamer), 158.3 (major rotamer) (Ar-OMe.), 144.3(major rotamer), 144.0 (minor rotamer) (q, Ar-C), 136.2 (major rotamer), 135.8 (minor rotamer) (q, Ar-C), 132.6 (major rotamer), 131.9 (minor rotamer), 131.6 (major rotamer), 131.4 (minor rotamer), 131.0, 130.0 (minor rotamer), 129.7 (major rotamer), 128.2 (minor rotamer), 128.1 (major rotamer), 128.1, 127.8 (major rotamer), 127.7 (minor rotamer), 127.7 (major rotamer), 127.7 (minor rotamer), 127.2 (minor rotamer), 127.0 (major rotamer) (Ar-C), 123.6 (major rotamer), 123.5 (minor rotamer) (q, Ar-C), 95.4 (q-C), 81.7 (q-C), 72.5 (minor rotamer), 70.1 (major rotamer)(q-C), 55.3 (minor rotamer), 55.2 (major rotamer)(OMe), 55.2 (major rotamer), 53.8 (minor rotamer) (C-2), 33.3 (major rotamer), 30.9 (minor rotamer) (q-C), 29.5 (major rotamer), 28.9 (minor rotamer) (C-1). ν_{max} (ATR)/cm⁻¹: 1033 (C-S), 1257 (C-O), 1728 (C=O), 2213 (C≡C). **LRMS**: (ESI) m/z calcd for C₃₄H₃₂O₃SNa ([M-H]⁻): 543.2; found: 543.1.

6. Acyl-Thiol-Ene Cyclisation

Thiolactones **1a-1p** were prepared according to the following sequence:

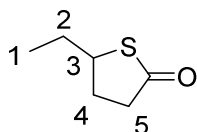


S-Methyldihydrothiophen-2(3H)-one (1a)



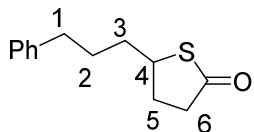
General procedure D to yield the title compound (63 mg, 0.44 mmol, 88%) as a colourless wax from **46**. Purification was achieved using 1.5→3.5% EtOAc/Hexane (v/v). $R_f = 0.14$ (5% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 4.00–3.90 (m, 1H, H-2), 2.71–2.55 (m, 2H, H-4), 2.45–2.37 (m, 1H, H-3), 1.91–1.81 (m, 1H, H-3'), 1.51 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1). δ_C (100 MHz, $CDCl_3$): 208.9 (C=O), 45.6 (C-2), 42.5 (C-4), 34.2 (C-3), 21.5 (C-1). ν_{max} (ATR)/ cm^{-1} : 1175 (C-S), 1707 (C=O). **HRMS**: (EI⁺) m/z calcd for C_5H_8OS ([M]⁺): 116.0296; found: 116.06289.

5-Ethylidihydrothiophen-2(3H)-one (1b)



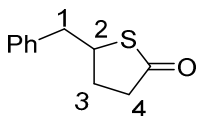
General procedure D to yield the title compound (43.7 mg, 0.34 mmol, 84%) as a colourless wax from **47** (172.9 mg, 0.400 mmol, 1.0 equiv.). Purification was achieved using 1.5% → 4.5% EtOAc/Hexane (v/v). $R_f = 0.14$ (5% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 3.86–3.78 (m, 1H, H-3), 2.70–2.53 (m, 2H, H-5), 2.45–2.36 (m, 1H, H-4), 1.97–1.87 (m, 1H, H-4'), 1.87–1.74 (m, 2H, H-2), 1.06 (t, $J_{1,2} = 7.3$ Hz, 1H, H-1). δ_C (100 MHz, $CDCl_3$): 208.9 (C=O), 50.0 (C-3), 42.1 (C-5), 31.8 (C-4), 29.5 (C-2), 12.6 (C-1). ν_{max} (ATR)/ cm^{-1} : 1168 (C-S), 1702 (C=O). **HRMS**: (EI⁺) m/z calcd for $C_6H_{10}OS$ ([M]⁺): 130.0452; found: 130.0451.

5-(3-Phenylpropyl)dihydrothiophen-2(3H)-one (1c)



General procedure D to yield the title compound (79.4 mg, 0.36 mmol, 90%) as a colourless wax from **48** (217 mg, 0.400 mmol). Purification was achieved using 1.5→3.0% EtOAc/Hexane (v/v). $R_f = 0.20$ (10% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.32–7.29 (m, 2H, Ar-H), 7.26–7.18 (m, 3H, Ar-H), 3.93–3.84 (m, 1H, H-4), 2.72–2.65 (m, 2H, H-1), 2.65–2.52 (m, 2H, H-6), 2.44–2.35 (m, 1H, H-5), 1.95–1.74 (m, 5H, H-2, H-3, H-5'). δ_C (100 MHz, $CDCl_3$): 208.4 (C=O), 141.6 (q, Ar-C), 128.5, 128.4, 126.0 (Ar-C), 51.2 (C-4), 42.0 (C-6), 36.0 (C-3), 35.6 (C-1), 32.2 (C-5), 30.0 (C-2). ν_{max} (ATR)/ cm^{-1} : 1052 (C-S), 1709 (C=O). **HRMS**: (ESI⁺) m/z calcd for $C_{13}H_{16}OSNa$ ([M+Na]⁺): 243.0820; found: 243.016.

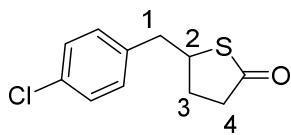
5-Benzylidihydrothiophen-2(3H)-one (1d)



General procedure D to yield the title compound (62 mg, 0.32 mmol, 64%) as a colourless wax from **49**. Purification was achieved using 1.5→4% EtOAc/Hexane

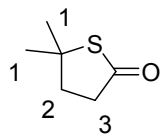
(v/v). $R_f = 0.16$ (10% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.36–7.26 (m, 3H, Ar-H), 7.23–7.18 (m, 2H, Ar-H), 4.13–4.09 (m, 1H, H-2), 3.13–3.00 (m, 2H, H-1), 2.61–2.49 (m, 2H, H-4), 2.36–2.28 (1H, H-3), 2.06–1.91 (m, 1H, H-3'). δ_C (100 MHz, $CDCl_3$): 208.1 (C=O), 138.2 (q, Ar-C), 128.9, 128.7, 128.1, 127.7, 127.0 (Ar-C), 52.2 (C-2), 42.4 (C-1), 41.9 (C-4), 31.6 (C-3). ν_{max} (ATR)/ cm^{-1} : 1157 (C-S), 1712 (C=O). **HRMS**: (APCI⁺) m/z calcd for $C_{11}H_{13}OS$ ($[M+H]^+$): 193.0682; found: 193.0690.

5-(4-chlorobenzyl)dihydrothiophen-2(3H)-one (1e)



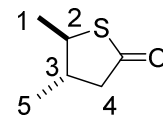
General procedure D to yield the title compound (36 mg, 0.16 mmol, 32%) as a colourless wax from **50**. Purification was achieved using 1.5→8.0% EtOAc/Hexane (v/v). $R_f = 0.11$ (10% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.33–7.25 (m, 2H, Ar-H), 7.17–7.12 (m, 2H, Ar-H), 4.11–4.02 (m, 1H, H-2), 3.04 (d, $J_{1,2} = 7.3$ Hz, 2H, H-1), 2.69–2.50 (m, 2H, H-4), 2.40–2.30 (m, 1H, H-3), 2.03–1.90 (m, 1H, H-3'). δ_C (100 MHz, $CDCl_3$): 207.7 (C=O), 136.7 (q, Ar-C), 130.2, 129.1, 128.9 (Ar-C), 51.9 (C-2), 41.9 (C-4), 41.7 (C-1), 31.6 (C-3). ν_{max} (ATR)/ cm^{-1} : 750 (C-Cl), 1173 (C-S), 1706 (C=O). **HRMS**: (ESI) m/z calcd for $C_{11}H_{10}OSCl$ ($[M-H]^-$): 225.0146; found: 225.0138.

5,5-Dimethyldihydrothiophen-2(3H)-one (1f)



General procedure D to yield the title compound (14.5 mg, 0.11 mmol, 48%) as a colourless wax from **51** (100 mg, 0.23 mmol). Purification was achieved using 1.5→8.0% EtOAc/Hexane (v/v). $R_f = 0.13$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 2.64 (t, $J_{3,2} = 8.2$ Hz, 2H, H-3), 2.07 (t, $J_{2,3} = 8.2$ Hz, 2H, H-2), 1.45 (s, 6H, H-1). δ_C (100 MHz, $CDCl_3$): 201.5 (C=O), 84.6 (q-C), 34.7 (C-3), 29.4 (C-2), 27.8 (C-1). ν_{max} (ATR)/ cm^{-1} : 1098 (C-S), 1718 (C=O). **HRMS**: (EI⁺) m/z calcd for $C_6H_{10}OS$ ($[M]^+$): 130.0451; found: 130.0452.

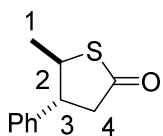
4,5-Dimethyldihydrothiophen-2(3H)-one (1g)



General procedure D to yield the title compound (55.4 mg, 0.426 mmol, 83% *anti:syn* > 19:1) as a colourless wax from **52**. Purification was achieved using 1.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.24$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 3.61–3.53 (m, 1H, H-2), 2.73 (dd, $J_{4,4'} = 16.6$ Hz, $J_{4,3} = 6.6$ Hz, 1H,

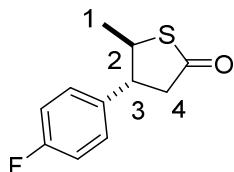
H-4), 2.38 (dd, $J_{4',4} = 16.6$ Hz, $J_{4',3} = 10.7$ Hz, 1H, H-4), 2.27–2.15 (m, 1H, H-3), 1.50 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1), 1.21 (d, $J_{5,3} = 6.4$ Hz, 3H, H-5). δ_C (100 MHz, CDCl₃): 207.1 (C=O), 51.5 (C-2), 50.5 (C-4), 41.9 (C-3), 19.4 (C-5), 16.9 (C-1). ν_{\max} (ATR)/cm⁻¹: 1107 (C-S), 1684 (C=O). **HRMS**: (EI⁺) m/z calcd for C₆H₁₀OS ([M]⁺): 130.0451; found: 130.0452.

5-Methyl-4-phenyldihydrothiophen-2(3H)-one (1f)



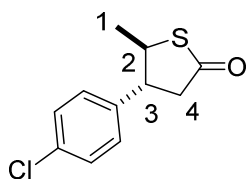
General procedure D to yield the title compound (81.6 mg, 0.43 mmol, 85%, *anti:syn*, 19:1) as a colourless wax from **53**. Purification was achieved using 1.5→5.0% EtOAc/Hexane (v/v). δ_H (600 MHz, CDCl₃): 7.41–7.37 (m, 2H, Ar-H), 7.34–7.31 (m, 1H, Ar-H), 7.26–7.24 (m, 2H, Ar-H), 4.19–4.14 (m, 1H, H-2), 3.95–3.91 (m, 1H, H-3), 3.11 (dd, $J_{4,4'} = 17.3$ Hz, $J_{4,3} = 10.9$ Hz, 1H, H-4), 2.85 (dd, $J_{4',4} = 17.3$ Hz, $J_{4',3} = 6.6$ Hz, 1H, H-4'), 1.16 (d, $J_{1,2} = 7.0$ Hz, 3H, H-1). δ_C (150 MHz, CDCl₃): 207.1 (C=O), 138.0 (q, Ar-C), 128.8 (Ar-C), 127.8 (Ar-C), 127.6 (Ar-C) 48.2 (C-2), 47.6 (C-3), 43.6 (C-4), 17.8 (C-1). ν_{\max} (ATR)/cm⁻¹: 1109 (C-S), 1719 (C=O). **HRMS**: (EI⁺) m/z calcd for C₁₁H₁₂OS ([M]⁺): 192.0609; found: 192.0608.

4-(4-Fluorophenyl)-5-methyldihydrothiophen-2(3H)-one (1i)



General procedure D to yield the title compound (88 mg, 0.42 mmol, 84%, *anti:syn* > 19:1) as a colourless wax from **54**. Purification was achieved using 1.5→4.0% EtOAc/Hexane (v/v). $R_f = 0.12$ (5% EtOAc/Hexane (v/v)). δ_H (400 MHz, CDCl₃): 7.31–7.25 (m, 2H, Ar-H), 7.12–7.06 (m, 2H, Ar-H), 4.03–3.94 (m, 1H, H-2), 3.24 (app-q, 1H, H-3), 2.93 (app-s, 1H, H-4), 2.91 (app-d, 1H, H-4'), 1.40 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1). δ_C (100 MHz, CDCl₃): 205.0 (C=O), 162.3 (d, $J_{C-F} = 245.7$ Hz, Ar-CF), 134.1 (d, $J_{C-F} = 3.0$ Hz, q-Ar-C), 129.0 (d, $J_{C-F} = 8.1$ Hz, Ar-C), 115.9 (d, $J_{C-F} = 20.9$ Hz, Ar-C), 52.7 (C-4), 50.7 (C-2), 50.4 (C-3), 18.9 (C-1). δ_F (367 MHz, CDCl₃): -114.4 ν_{\max} (ATR)/cm⁻¹: 1161 (C-S), 1224 (C-F), 1704 (C=O). **HRMS**: (ESI⁺) m/z calcd for C₁₁H₁₀OSF ([M-H]⁺): 209.0442; found: 209.0442.

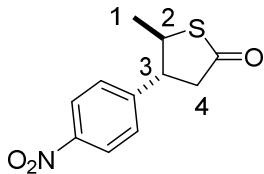
4-(4-chlorophenyl)-5-methyldihydrothiophen-2(3H)-one (1j)



General procedure D to yield the title compound (86 mg, 0.38 mmol, 76% *anti:syn* > 19:1) as a colourless wax from **55**. Purification was achieved using 1.5→4.0% EtOAc/Hexane (v/v). $R_f = 0.14$ (5% EtOAc/Hexane (v/v)). δ_H (400 MHz, CDCl₃): 7.39–7.34 (m, 2H, Ar-H), 7.26–7.23 (m, 2H, Ar-H), 4.03–3.95 (m, 1H, H-2), 3.23 (app-q, 1H, H-3), 2.93 (app-s, 1H, H-4), 2.91 (app-d, 1H, H-4'), 1.39 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1). δ_C (100 MHz, CDCl₃): 204.9 (C=O), 136.9 (q, Ar-

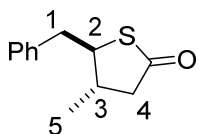
C), 133.6, 129.2, 128.9 (Ar-C), 52.8 (C-3) 50.5 (C-2), 50.3 (C-4), 18.9 (C-1). ν_{\max} (ATR)/ cm^{-1} : 749 (C-Cl), 1091 (C-S), 1703 (C=O). **HRMS**: (APCI) m/z calcd for $\text{C}_{11}\text{H}_{10}\text{OSCl}$ ($[\text{M-H}]^-$): 225.0146; found: 225.0151.

5-methyl-4-(4-nitrophenyl)dihydrothiophen-2(3H)-one (1k)



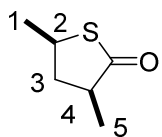
General procedure D to yield the title compound (73 mg, 0.31 mmol, 62%) as a colourless wax from **56**. Purification was achieved using 1.5→12% EtOAc/Hexane (v/v). $R_f = 0.08$ (10% EtOAc/Hexane (v/v)). δ_{H} (400 MHz, CDCl_3): 8.29–8.25 (m, 2H, Ar-H), 7.53–7.49 (m, 2H, Ar-H), 4.11–4.02 (m, 1H, H-2), 3.44–3.35 (m, 1H, H-3), 3.04–2.91 (m, 2H, H-4), 1.43 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1). δ_{C} (100 MHz, CDCl_3): 203.8 (C=O), 147.6 (Ar-CNO₂), 146.1 (q, Ar-C), 128.5, 124.3 (Ar-C), 52.9 (C-3) 50.1 (C-2), 50.0 (C-4), 19.1 (C-1). ν_{\max} (ATR)/ cm^{-1} : 1177 (C-S), 1348, 1520 (N-O), 1703 (C=O). **HRMS**: (ESI) m/z calcd for $\text{C}_{11}\text{H}_{10}\text{NO}_3\text{S}$ ($[\text{M-H}]^-$): 236.0387; found: 236.0381.

5-Benzyl-4-methyldihydrothiophen-2(3H)-one (1l)



General procedure D to yield the title compound (62.8 mg, 0.31 mmol, 61% (*anti:syn*, 10:1) as a colourless wax from **57**. Purification was achieved using 1.5→5.0% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 7.39–7.19 (m, 5H, Ar-H), 3.83–3.76 (m, 1H, H-2), 3.30 (dd, $J_{4,4'} = 14.1$ Hz, $J_{4,3} = 5.0$ Hz, 1H, H-4), 2.92 (dd, $J_{4',4} = 14.1$ Hz, $J_{4',3} = 9.5$ Hz, 1H, H-4'), 2.80–2.71 (m, 1H, H-1), 2.44–2.34 (m, 2H, H-1', H-3), 1.26 (d, $J_{5,3} = 6.4$ Hz, 3H, H-5). δ_{C} (100 MHz, CDCl_3): 206.7 (C=O), 138.6 (q, Ar-C), 128.8, 128.7, 126.9 (Ar-C), 58.8 (C-2), 49.9 (C-1), 41.0 (C-4), 38.9 (C-3), 18.0 (C-5). ν_{\max} (ATR)/ cm^{-1} : 1132 (C-S), 1694 (C=O). **HRMS**: (EI⁺) m/z calcd for $\text{C}_{12}\text{H}_{14}\text{OS}$ ($[\text{M}]^+$): 1206.0765; found: 206.0765.

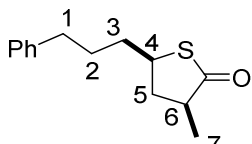
3,5-Dimethyldihydrothiophen-2(3H)-one (1m)



General procedure D to yield the title compound (52.9mg, 0.41 mmol, 81%, 3:2 *syn:anti*) as a colourless wax, inseparable from DMTrtH from **58**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). *Syn Isomer*: δ_{H} (400 MHz, CDCl_3): 3.99–3.89 (m, 1H, H-2), 2.84–2.75 (m, 1H, H-4), 2.17–2.07 (m, 2H, H-3), 1.52 (d, $J_{1,2} = 7.0$ Hz, 3H, H-1), 1.22 (app-t, 3H, H-5). δ_{C} (100 MHz, CDCl_3): 211.1 (C=O), 45.6 (C-4), 43.4 (C-2), 41.4 (C-3), 22.4 (C-1), 15.3 (C-5). *Anti Isomer*: δ_{H} (400 MHz, CDCl_3): 3.85–3.76 (m, 1H, H-2), 2.73–2.63 (m, 1H, H-4), 2.58–2.51 (m, 1H, H-3), 2.17–2.07 (m, 1H, H-3'), 1.50 (d, $J_{1,2} = 6.6$ Hz, 3H, H-1), 1.22 (app-t, 3H, H-5). δ_{C} (100 MHz, CDCl_3): 210.3 (C=O), 49.5 (C-4), 42.0 (C-2), 41.6 (C-3),

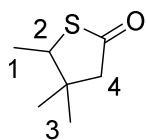
21.0 (C-1), 14.4 (C-5). ν_{\max} (ATR)/ cm^{-1} : 1035 (C-S), 1699 (C=O). **HRMS**: (EI^+) m/z calcd for $\text{C}_6\text{H}_{10}\text{OS}$ ($[\text{M}]^+$): 130.0452; found: 130.0451.

3-Methyl-5-(3-phenylpropyl)dihydrothiophen-2(3H)-one (1n)



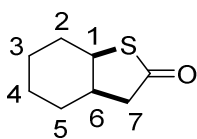
General procedure D to yield the title compound (108.8 mg, 0.47 mmol, 93%, 3:2 *syn:anti*) as a colourless wax from **59**. Purification was achieved using 2.5→5.0% EtOAc/Hexane (v/v). $R_f = 0.23$ (10 % EtOAc/Hexane (v/v)). *Syn Isomer*: δ_{H} (400 MHz, CDCl_3): 7.35–7.28 (m, 2H, Ar-H), 7.25–7.18 (m, 3H, Ar-H), 3.80–3.71 (m, 1H, H-4), 2.71–2.59 (m, 3H, H-1, H-6), 2.57–2.49 (m, 3H, H-3, H-5), 1.88–1.74 (m, 2H, H-2), 1.52 (app-q, 1H, H-5'), 1.19 (d, $J_{7-6} = 6.8$ Hz, 3H, H-7). δ_{C} (100 MHz, CDCl_3): 209.7 (C=O), 141.6 (q, Ar-C), 128.4, 128.4, 126.0 (Ar-C), 48.8 (C-6), 47.6 (C-4), 41.4 (C-5), 35.9 (C-2), 35.6 (C-1), 30.0 (C-3), 14.4 (C-7). *Anti Isomer*: δ_{H} (400 MHz, CDCl_3): 7.35–7.28 (m, 2H, Ar-H), 7.25–7.18 (m, 3H, Ar-H), 3.82–3.75 (m, 1H, H-4), 2.77–2.67 (m, 2H, H-1, H-6), 2.22–2.14 (m, 3H, H-2, H-3), 2.11–2.02 (m, 2H, H-5), 1.85–1.73 (m, 2H, H-1', H-2'), 1.21 (d, $J_{7-6} = 7.1$ Hz, 3H, H-7). δ_{C} (100 MHz, CDCl_3): 210.9 (C=O), 141.6 (q, Ar-C), 128.4, 128.4, 126.0 (Ar-C), 47.3 (C-4), 45.4 (C-6), 39.5 (C-5), 36.3 (C-2), 35.5 (C-1), 30.1 (C-3), 15.4 (C-7). ν_{\max} (ATR)/ cm^{-1} : 1145 (C-S), 1698 (C=O). **HRMS**: (APCI^+) m/z calcd for $\text{C}_{14}\text{H}_{19}\text{OS}$ ($[\text{M}+\text{H}]^+$): 235.1157; found: 235.1151.

4,4,5-Trimethyldihydrothiophen-2(3H)-one (1o)



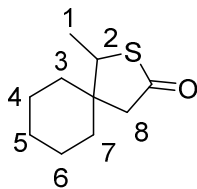
General procedure D to yield the title compound (37.7 mg, 0.26 mmol, 92%) as a colourless wax from **60**. Purification was achieved using 2.0→5.0% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 3.75 (q, $J_{2-1} = 7.0$ Hz, 1H, H-2), 2.54–2.41 (m, 2H, H-4), 1.36 (d, $J_{1-2} = 7.0$ Hz, 3H, H-1), 1.22 (s, 3H, H-3), 1.10 (s, 3H, H-3'). δ_{C} (100 MHz, CDCl_3): 209.9 (C=O), 57.2 (C-2), 54.0 (C-4), 41.4 (qC), 26.0 (C-1), 20.9 (C-3), 15.2 (C-3'). ν_{\max} (ATR)/ cm^{-1} : 1108 (C-S), 1702 (C=O). **HRMS**: (EI^+) m/z calcd for $\text{C}_7\text{H}_{12}\text{OS}$ ($[\text{M}]^+$): 144.0609; found: 144.0611.

Hexahydrobenzo[b]thiophen-2(3H)-one (1p)



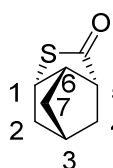
General procedure D to yield the title compound (57.1 mg, 0.37 mmol, 73%) as a colourless wax from **61**. Purification was achieved using 1.5→3.0% EtOAc/Hexane (v/v). δ_{H} (400 MHz, CDCl_3): 4.02 (app-q, 1H, H-1), 2.62–2.54 (m, 1H, H-7), 2.53–2.40 (m, 2H, H-7', H-6), 1.92–1.85 (m, 2H, H-2), 1.69–1.49 (m, 4H, H-5, H-4, H-3), 1.48–1.31 (m, 2H, H-4', H-3'). δ_{C} (100 MHz, CDCl_3): 208.8 (C=O), 50.2 (C-1), 47.9 (C-7), 38.3 (C-6), 29.0 (C-2), 26.5 (C-5), 22.8 (C-3), 21.4 (C-4). ν_{\max} (ATR)/ cm^{-1} : 1101 (C-S), 1711 (C=O). **HRMS**: (EI^+) m/z calcd for $\text{C}_8\text{H}_{12}\text{OS}$ ($[\text{M}]^+$): 156.0609; found: 156.0614.

1-Methyl-2-thiaspiro[4.5]decan-3-one (1q)



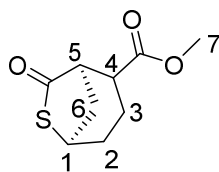
General procedure D to yield the title compound (74.5 mg, 0.41 mmol, 81%, inseparable from DMTrtH) as a colourless wax from **62**. Purification was achieved using 2.0→4.0% EtOAc/Hexane (v/v). $R_f = 0.31$ (10 % EtOAc/Hexane (v/v)). δ_H (600 MHz, $CDCl_3$): 3.72 (q, $J_{2-1} = 7.6$ Hz, 1H, H-2), 2.74 (d, $J_{8-8'} = 16.7$ Hz, 1H, H-8), 2.40 (d, $J_{8'-8} = 16.7$ Hz, 1H, H-8'), 1.72–1.25 (m, 13H, H-1, H-3, H-4, H-5, H-6, H-7). δ_C (150 MHz, $CDCl_3$): 207.5 (C=O), 53.2 (C-2), 51.1 (C-8), 44.5 (C-7), 35.6 (C-3), 29.9 (q-C), 26.0 (C-5), 23.4 (C-4), 22.6 (C-6), 16.3 (C-1). ν_{max} (ATR)/ cm^{-1} : 1245 (C-S), 1698 (C=O). **HRMS**: (APCI⁺) m/z calcd for $C_{10}H_{17}OS$ ($[M+H]^+$): 185.1000; found: 185.0997.

(3R,3aS,5R,6aS)-Hexahydro-2H-3,5-methanocyclopenta[b]thiophen-2-one (1r)



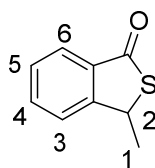
General procedure D to yield the title compound (64.7 mg, 0.42 mmol, 84%) as a colourless wax from **63**. Purification was achieved using 1.5→35% EtOAc/Hexane (v/v). $R_f = 0.20$ (10 % EtOAc/Hexane (v/v)). δ_H (600 MHz, $CDCl_3$): 3.72–3.66 (m, 1H, H-1), 3.19–3.15 (m, 1H, H-6), 2.66–2.60 (m, 1H, H-5), 2.47 (app-s, 1H, H-3), 2.20–2.12 (m, 1H, H-2), 2.06–1.96 (m, 1H, H-7), 1.73–1.63 (m, 4H, H-2', H-4, H-7'). δ_C (150 MHz, $CDCl_3$): 213.1 (C=O), 52.4 (C-5), 49.9 (C-6), 47.0 (C-1), 41.9 (C-2), 39.5 (C-4), 38.4 (C-3), 34.9 (C-7). ν_{max} (ATR)/ cm^{-1} : 1156 (C-S), 1711 (C=O). **HRMS**: (APCI⁺) m/z calcd for $C_8H_{11}OS$ ($[M+H]^+$): 155.0531; found: 155.0529. $[\alpha]_D^{24} = +110.43$ (c 0.15, $CHCl_3$).

Cis-methyl-7-oxo-6-thiabicyclo[3.2.1]octane-2-carboxylate (1s)



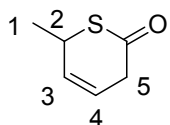
General procedure D to yield the title compound (91 mg, 0.46 mmol, 92%) as a colourless wax from **64**. Purification was achieved using 1.5→14.0% EtOAc/Hexane (v/v). $R_f = 0.11$ (10% EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 4.04 (app-s, 1H, H-1), 3.72 (s, 3H, H-7), 3.09–3.05 (m, 1H, H-5), 2.63–2.51 (m, 2H, H-3, H-4), 2.44–2.31 (m, 1H, H-6), 2.06–1.88 (m, 4H, H-2, H-3', H-6'). δ_C (100 MHz, $CDCl_3$): 206.5 (C=O), 172.2 (C=O), 52.1 (OMe), 49.4 (C-5), 46.9 (C-1), 43.4 (C-4), 40.3 (C-3), 29.2 (C-2), 19.9 (C-6). ν_{max} (ATR)/ cm^{-1} : 1200 (C-S), 1228 (C-O), 1701 (C=O), 1735 (C=O). **HRMS**: (ESI⁺) m/z calcd for $C_9H_{12}O_3SNa$ ($[M+Na]^+$): 223.0405; found: 223.0402.

3-Methylbenzo[c]thiophen-1(3H)-one (1t)



General procedure D to yield the title compound (30.3 mg, 0.18 mmol, 37%) as a colourless wax from **65**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). $R_f = 0.18$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.82 (d, $J_{6-5} = 7.6$ Hz, 1H, H-6), 7.69–7.63 (m, 1H, H-4), 7.58–7.55 (m, 1H, H-5), 7.48 (app-t, 1H, H-3), 4.90 (q, $J_{2-1} = 7.1$ Hz, 1H, H-2), 1.81 (d, $J_{1-2} = 7.1$ Hz, 3H, H-1). δ_C (100 MHz, $CDCl_3$): 197.1 (C=O), 152.4, 135.6 (q, Ar-C), 133.3 (C-4), 128.1 (C-3), 124.8 (C-5), 123.7 (C-7), 43.3 (C-2), 22.0 (C-1). ν_{max} (ATR)/ cm^{-1} : 1081 (C-S), 1703 (C=O). **HRMS**: (EI⁺) m/z calcd for C_9H_8OS ($[M]^+$): 164.0296; found: 164.0291.

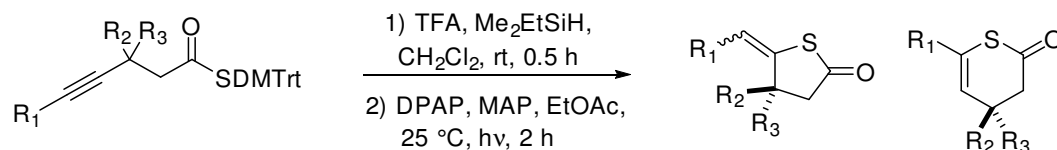
6-Methyl-5,6-dihydro-2H-thiopyran-2-one (1u)



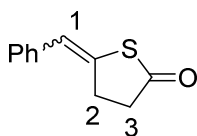
General procedure D for 4 h to yield the title compound (26.5 mg, 0.21 mmol, 41%) as a colourless wax from **66**. Purification was achieved using 1.5→4.5% EtOAc/Hexane (v/v). $R_f = 0.13$ (10 % EtOAc/Hexane (v/v)). δ_H (600 MHz, $CDCl_3$): 6.06–6.00 (m, 1H, H-4), 5.98–5.92 (m, 1H, H-3), 4.18–4.09 (m, 1H, H-2), 3.21 (dd, $J_{5-5'} = 19.1$ Hz, $J_{5-4} = 5.5$ Hz, 1H, H-3), 3.11–3.03 (m, 1H, H-5'), 1.53 (d, $J_{1-2} = 7.4$ Hz, 3H, H-1). δ_C (150 MHz, $CDCl_3$): 202.5 (C=O), 131.4 (C-4), 124.9 (C-3), 41.1 (C-5), 38.9 (C-2), 21.1 (C-1). ν_{max} (ATR)/ cm^{-1} : 1131 (C-S), 1684 (C=O). **HRMS**: (EI⁺) m/z calcd for C_6H_8OS ($[M]^+$): 128.0296; found: 128.0297.

7. Acyl-Thiol-Yne Cyclisation

Thiolactones **2a-2e** were prepared according to the following sequence:



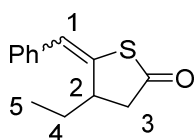
5-Benzylidenedihydrothiophen-2(3H)-one (2a)



General procedure D to yield the title compound (49.8 mg, 0.262 mmol, 52%) as a colourless wax from **53**. Purification was achieved using 2.0→5.0%

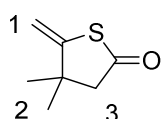
EtOAc/Hexane (v/v). $R_f = 0.19$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.42–7.25 (m, 5H, Ar-H), 6.71 (s, 1H, H-1), 3.13 (t, $J_{2,3} = 7.9$ Hz, 2H, H-2), 2.75 (t, $J_{3,2} = 7.9$ Hz, 2H, H-3). δ_C (100 MHz, $CDCl_3$): 206.2 (C=O), 136.0 (q, Ar-C), 135.7 (q-C), 128.6, 128.2, 127.3 (Ar-C), 123.8 (C-1), 39.9 (C-3), 34.1 (C-2). ν_{max} (ATR)/ cm^{-1} : 1107 (C-S), 1712 (C=O). **HRMS**: (ESI) m/z calcd for $C_{11}H_9OS$ ($[M-H]$): 189.0380; found: 189.0377.

5-Benzylidene-4-ethylidihydrothiophen-2(3H)-one (2b)



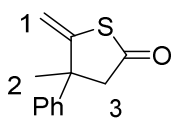
General procedure D to yield the title compound (59.7 mg, 0.27 mmol, 55% (with traces of DMTrtH)) as a colourless wax from **67**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). $R_f = 0.19$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.53–7.48 (m, 3H, Ar-H), 7.47–7.43 (m, 2H, Ar-H), 6.44 (s, 1H, H-1), 3.65–3.57 (m, 1H, H-2), 3.13 (dd, $J_{3,3'} = 17.4$ Hz, $J_{3,2} = 3.6$ Hz, 1H, H-3), 2.94–2.85 (m, 1H, H-3'), 1.85 (p, $J_{4,2} = J_{4,5} = 7.3$ Hz, 2H, H-4), 1.10 (t, $J_{5,4} = 7.3$ Hz, 3H, H-5). δ_C (100 MHz, $CDCl_3$): 190.9 (C=O), 139.4 (q, Ar-C), 130.1, 128.9 (Ar-C), 128.2 (q-C), 126.2 (Ar-C), 124.6 (C-1), 45.0 (C-3), 34.4 (C-4), 29.7 (C-2), 11.4 (C-5). ν_{max} (ATR)/ cm^{-1} : 1123 (C-S), 1714 (C=O). **HRMS**: (ESI) m/z calcd for $C_{13}H_{14}OS$ ($[M]^+$): 218.0765; found: 218.0769.

4,4-Dimethyl-5-methylenedihydrothiophen-2(3H)-one (2c)



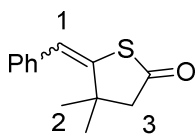
General procedure D to yield the title compound (33.4 mg, 0.236 mmol, 47%, inseparable from DMTrtH) as a colourless wax from **68**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). $R_f = 0.18$ (10 % EtOAc/Hexane (v/v)). δ_H (600 MHz, $CDCl_3$): 5.35 (d, $J_{1,1'} = 1.7$ Hz, 1H, H-1), 5.18 (d, $J_{1',1} = 1.7$ Hz, 1H, H-1'), 2.62 (s, 2H, H-3), 1.40 (s, 6H, H-2). δ_C (150 MHz, $CDCl_3$): 203.8 (C=O), 154.1 (q-C), 107.2 (C-1), 56.8 (C-3), 43.8 (q-C), 27.6 (C-2). ν_{max} (ATR)/ cm^{-1} : 1129 (C-S), 1728 (C=O). **HRMS**: (ESI) m/z calcd for C_7H_9OS ($[M-H]$): 141.0380; found: 141.0377.

4-Methyl-5-methylene-4-phenyldihydrothiophen-2(3H)-one (2d exo)



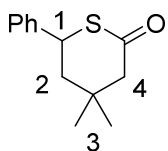
General procedure D to yield the title compound (60.2 mg, 0.29 mmol, 59% inseparable from DMTrtH) as a colourless wax from **69**. Purification was achieved using 1.0→2.0% EtOAc/Hexane (v/v). $R_f = 0.22$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.50–7.45 (m, 2H, Ar-H), 7.41–7.35 (m, 2H, Ar-H), 7.33–7.29 (m, 1H, Ar-H), 5.39 (d, $J_{1,1'} = 1.4$ Hz, 1H, H-1), 5.35 (d, $J_{1',1} = 1.4$ Hz, 1H, H-1'), 3.31 (d, $J_{3,3'} = 16.6$ Hz, 1H, H-3), 2.92 (d, $J_{3',3} = 16.6$ Hz, 1H, H-3), 1.77 (s, 3H, H-2). δ_C (100 MHz, $CDCl_3$): 202.7 (C=O), 153.6 (q-C), 146.6 (q, Ar-C), 130.3, 128.6, 126.3 (Ar-C), 57.1 (C-3), 51.6 (q-C), 27.2 (C-2). ν_{max} (ATR)/ cm^{-1} : 1125 (C-S), 1703 (C=O). **HRMS**: (EI⁺) m/z calcd for $C_{12}H_{12}OS$ ($[M]^+$): 204.0609; found: 204.0613.

5-Benzylidene-4,4-dimethyldihydrothiophen-2(3H)-one (2e exo)



General procedure D to yield the title compound as a mixture of isomers (32.7 mg, 0.15 mmol, 30%, Z:E = 2:1, inseparable from DMTrtH) as a colourless wax, inseparable from DMTrtH, from **70**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). $R_f = 0.16$ (10 % EtOAc/Hexane (v/v)). Z-Isomer: δ_H (400 MHz, $CDCl_3$): 7.40–7.34 (m, 3H, Ar-H), 7.33–7.29 (m, 2H, Ar-H), 6.73 (s, 1H, H-1), 2.66 (s, 2H, H-3), 1.27 (s, 6H, H-2). δ_C (100 MHz, $CDCl_3$): 204.2 (C=O), 146.8 (q, Ar-C), 129.6, 128.5, 128.3 (Ar-C), 128.5 (q-C), 125.0 (C-1), 59.6 (C-3), 44.2 (q-C), 27.8 (C-2). E-Isomer: δ_H (400 MHz, $CDCl_3$): 7.40–7.34 (m, 3H, Ar-H), 7.33–7.29 (m, 2H, Ar-H), 6.70 (s, 1H, H-1), 2.64 (s, 2H, H-3), 1.51 (s, 6H, H-2). δ_C (100 MHz, $CDCl_3$): 204.1 (C=O), 145.4 (q, Ar-C), 129.9, 129.0, 128.4 (Ar-C), 128.4 (q-C), 121.2 (C-1), 55.1 (C-3), 44.7 (q-C), 28.2 (C-2). ν_{max} (ATR)/ cm^{-1} : 1108 (C-S), 1708 (C=O). HRMS: (APCI⁺) m/z calcd for $C_{13}H_{15}OS$ ($[M+H]^+$): 219.0837; found: 219.0838.

4,4-Dimethyl-6-phenyltetrahydro-2H-thiopyran-2-one (2e endo)



General procedure D to yield the title compound (34.7 mg, 0.16 mmol, 32%) as a colourless wax from **70**. Purification was achieved using 1.5→2.5% EtOAc/Hexane (v/v). $R_f = 0.15$ (10 % EtOAc/Hexane (v/v)). δ_H (400 MHz, $CDCl_3$): 7.42–7.31 (m, 5H, Ar-H), 4.66 (dd, $J_{1-2} = 12.4$ Hz, $J_{1-2'} = 4.4$ Hz, 1H, H-1), 2.55 (dd, $J_{4-4} = 16.6$ Hz, $J_{4-2} = 1.4$ Hz, 1H, H-4), 2.42 (d, $J_{4'-4} = 16.6$ Hz, 1H, H-4'), 2.09 (ddd, $J_{2-2'} = 14.9$ Hz, $J_{2-1} = 4.4$ Hz, $J_{2-4} = 1.4$ Hz, 1H, H-2), 1.99 (app-t, 1H, H-2'), 1.20 (s, 3H, H-3), 1.13 (s, 3H, H-3'). δ_C (100 MHz, $CDCl_3$): 201.5 (C=O), 140.2 (q, Ar-C), 128.9, 128.1, 127.8 (Ar-C), 53.8 (C-4), 47.4 (C-1), 45.9 (C-2), 32.7 (q-C), 31.7 (C-3), 25.4 (C-3'). ν_{max} (ATR)/ cm^{-1} : 1091 (C-S), 1689 (C=O). HRMS: (APCI⁺) m/z calcd for $C_{13}H_{17}OS$ ($[M+H]^+$): 221.0988; found: 221.0995.

8. Acyl-Thiol-Ene Cyclisation on Large Scale

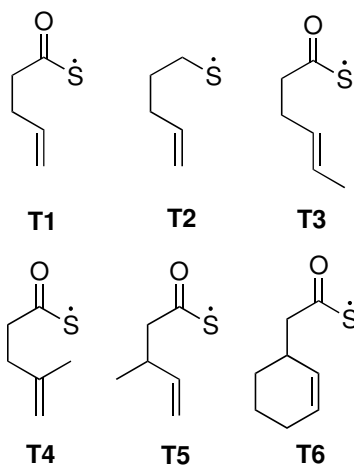
To a stirred solution of **46** (2.10 g, 5.0 mmol, 1.0 equiv.) in CH_2Cl_2 (10 mL) was added TFA (3.33 mL), followed immediately by the addition of Me_2EtSiH (2 mL, 15 mmol, 3.0 equiv.). The reaction was stirred for 25 min, and the solvent, TFA and Me_2EtSiH were removed *in vacuo*, maintaining the temperature below 30 °C. To the crude thioacid was added 2,2-dimethoxy-2-phenyl-acetophenone (DPAP) (256 mg, 1.0 mmol, 0.2 equiv.) and 4-methoxyacetophenone (MAP) (150 mg, 1.0 mmol, 0.2 equiv.), and the mixture was dried under vacuum for 120 seconds, before the transfer of anhydrous, degassed EtOAc (125 mL) *via* cannula. The reaction mixture was placed in the UV oven for 2 h at 25 °C. The solvent was removed *in vacuo* and the crude product was purified by column chromatography

on silica gel using 1.0→4.0% EtOAc/Hexane (v/v) to yield **1a** as a colourless oil (453 mg, 3.91 mmol, 78%).

9. Computational Studies

Compounds studied:

The set of compounds studied consist of **T1** (1a) from our research, **T2** from the literature, **T3** (1b), **T4** (1e), **T5** (1f) and **T6** (1l) as presented in Scheme S1.



Scheme S1. Six compound selected for the computational study, T1 (1a), T2, T3(1b), T4 (1e), T5 (1f) and T6 (1l) .

Benchmark

A benchmark on the relative energies for the compound **T1** has been carried out using UMP2³⁸ and DFT methods including UB3LYP,³⁹⁻⁴⁰ UB3PW1,⁴¹ UCAM-B3LYP,⁴² UWB97XD,⁴³ UM06-2X⁴⁴ and UMN15⁴⁵ functionals with 6-311++G(d,p)⁴⁶ basis set. The complete potential energy surface (PES) for the compound **T1** was obtained at those levels. As observed in **Table S1**, *ab initio* UMP2 results show a very selective profile with a large energy different between both 5-*exo* and 6-*endo* products. DFT methods fairly predict the relative energy of the products but the transition barriers are very different with respect to MP2. However, M06-2X and MN15 are able to describe the relative energy between both TS5_{exo} and TS6_{endo} giving similar values than MP2. Despite the MP2 method will be used from now on, M06-2X will be considered to perform Natural Bond Orbital (NBO)⁴⁷

calculations in order to obtain natural atomic charges and evaluate the Wiberg bond indexes (WBI) within the natural resonance theory (NRT).⁴⁸⁻⁴⁹

All the calculations have been carried out using Gaussian 16 (rev. A01) programs. NBO analysis was performed using NBO-3.1 program included in Gaussian 16 package.

Table S1. Potential energy surface corresponding to the **T1** compound at different computational levels. Energies are in kJ·mol⁻¹.

Compound	UMP2	UB3LYP	UCAM-B3LYP	UB3PW1	UWB97XD	UM062X	UMN15
React	0.0	0.0	0.0	0.0	0.0	0.0	0.0
TS _{5exo}	28.8	5.0	6.4	0.0	6.1	7.8	7.3
TS _{6endo}	37.7	14.1	15.5	9.3	14.2	15.1	16.4
Prod _{5exo}	-38.9	-13.0	-24.2	-31.3	-29.2	-28.3	-26.9
Prod _{6endo}	-21.1	-6.8	-17.9	-24.0	-23.3	-21.0	-18.1

Once the methodology is selected (MP2), the potential energy surface for **T1** and **T2** have been obtained.

Structural Discussion

In order to provide a further insight on the reaction and the structure of each system, in **Table S2**, selected structural parameters have been summarised for the reactant in compounds **T1** and **T2**.

As seen, bond distance between C and S atoms in **T1** is 1.774 Å, 0.032 Å shorter than in the **T2**. This would be caused mainly by the presence of the carbonyl group which withdraws density and somehow stabilises the radical. This bond shortening is corroborated by the Wiberg bond index (WBI) showing larger values for **T1** than for **T2**. The angle formed by the carbon chain and S (C-C-S) in both cases (**T1** and **T2**) is very similar. However, the dihedral angle between then C_γ-C_β-C_α-S is narrower in compound **T1** (42.2°) than in compound **T2** (74.0) which may indicate a different arrangement of the S atom in each compound. The withdrawing effect of the carbonyl group in **T1** may reduce the electron density on the terminal S atom and therefore allows attacking the C(5-exo) carbon, which in **T2** is less favourable.

This is corroborated by the natural charges on the terminal atoms in the reactants. In the case of **T2**, the terminal S atom bears +0.005e close (almost neutral) which correspond to the situation with the radical located at the S atom. In case of compound **T1**, the charge on the S atoms is +0.13e indicating a loss of charge with respect to **T2** due to the electro withdrawing nature of CO group. This is also corroborated by the spin densities (SD) on the S atom in the reactants. SDs indicate that the radical is more stabilised in **T1** (0.99 e) than in the thio-ene (0.92e). Furthermore, SD on S atom for compound **T4** (0.95e) also show that **T4** is less stabilised than **T1**, but at the same time more localised than in the thio-ene compound (**T2**). This stabilisation of the radical makes the compounds favouring 5-exo product over 6-endo product. The SD on the O atom in **T1** and **T4** (-0.03 and -0.04e) show without any further doubt that the radical is located on the S atom (Figure S2).

Table S2. Structural parameters from reactant **T2** and **T1**, bond distance between C and S (d_{C-S}) and its corresponding Wiberg bond index (WBI), C-C-S angle, C-C-C-S dihedral angle in the reactant compound. All distances are given in Å and angles in degrees.

	d_{C-S}	WBI	C-C-S	C-C-C-S
T1	1.774	1.15	118.5	42.2
T2	1.806	1.04	114.7	74.0

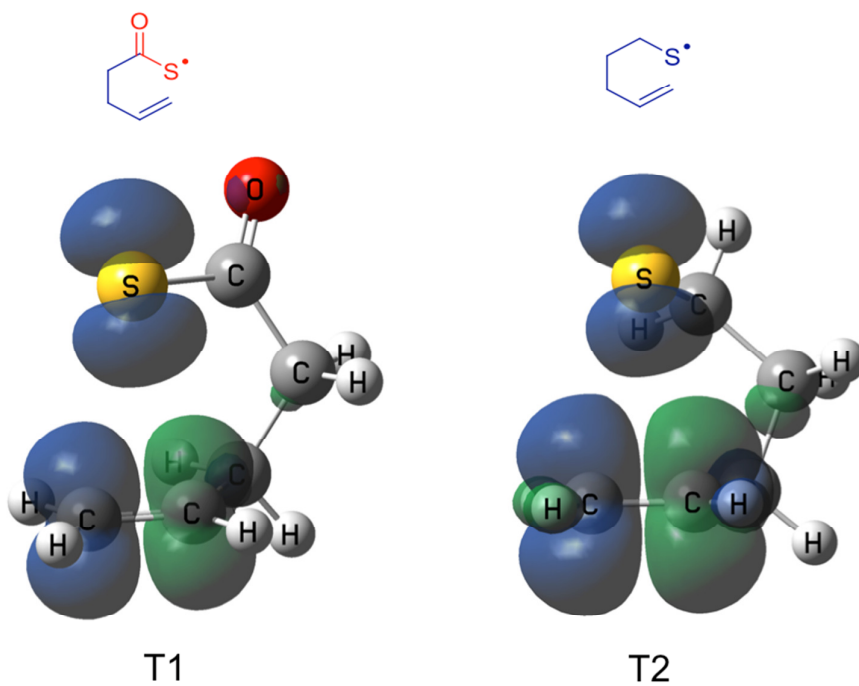


Figure S1. Spin Density different plots for T1 and T2 respectively. Blue and green areas corresponding to alpha and beta electrons.

Table S3. Potential energy surface corresponding to the T1, T2, T3, T4, T5 and T6 compounds at the UMP2/6-311++G(d,p) computational level. Energies are in $\text{kJ}\cdot\text{mol}^{-1}$.

Compound	T1 (1a)	T2	T3 (1b)	T4(1e)	T5(1f)	T6(1l)
React	0.0	0.0	0.0	0.0	0.0	0.0
TS _{5exo}	28.8	40.2	25.6	30.8	24.2	16.7
TS _{6endo}	37.7	40.4	46.1	30.4	33.6	47.0
Prod _{5exo}	-38.9	-19.1	-33.0	-33.8	-44.3	-42.3
Prod _{6endo}	-21.1	-24.9	-10.0	-22.5	-25.0	1.1

Table S4. Cartesian Coordinates of all the compounds obtained at the UMP2/6-311++G(d,p) computational level.

T2											
React			5-exo-product			6-endo-product					
C	-0.99992	1.47866	0.25976	C	0.59537	1.39717	-0.18680	C	1.11964	1.47050	0.30419
C	0.45079	1.43249	-0.25250	C	-0.86422	1.35678	0.25590	C	-0.31820	1.50907	-0.26175
C	1.10904	0.08347	0.03873	C	-1.36503	-0.04466	-0.09261	C	-1.08512	0.22685	0.05787
S	0.54555	-1.27473	-1.00989	S	0.00589	-1.17845	0.33046	S	-0.33169	-1.25393	-0.67497
H	-0.99472	1.33259	1.34696	H	0.65153	1.32997	-1.28043	H	1.63984	2.39902	0.05074
H	0.47856	1.63190	-1.32968	H	-0.92437	1.51690	1.33823	H	-0.85664	2.36381	0.16665
H	1.02699	2.22127	0.24719	H	-1.46540	2.12472	-0.24171	H	-0.27910	1.64601	-1.34818
H	-1.41805	2.47189	0.05892	H	1.10173	2.31474	0.12997	H	1.05114	1.41566	1.40040
C	-1.84837	0.42337	-0.38376	C	2.53052	-0.23420	-0.27124	C	1.86616	0.28271	-0.21315
C	-2.18021	-0.73479	0.21956	H	3.32534	-0.74343	0.26022	C	1.32006	-1.05637	0.11796
H	-2.75442	-1.49743	-0.29747	H	2.54324	-0.24947	-1.35598	H	1.18726	-1.18716	1.19779
H	-1.89800	-0.93000	1.25155	C	1.28840	0.17443	0.42548	H	2.45755	0.38377	-1.11915
H	-2.14647	0.58508	-1.41970	H	1.48326	0.35123	1.48702	H	1.94155	-1.86850	-0.26575
H	2.18734	0.15051	-0.15903	H	-1.59063	-0.11885	-1.15943	H	-1.15834	0.08899	1.14326
H	0.98773	-0.17953	1.09459	H	-2.25037	-0.32423	0.48256	H	-2.10096	0.27662	-0.34511
			5-exo-TS			6-endo-TS					
C	0.77734	1.44667	-0.14216	C	1.07197	1.52091	0.21256	C	-0.34961	1.43959	-0.38808
C	-0.71148	1.42291	0.21175	C	-0.34961	1.43959	0.21175	C	-1.06223	0.16478	0.06461
C	-1.24189	0.03016	-0.10901	C	-1.06223	0.16478	-0.10901	C	-0.34035	-1.36467	-0.59597
S	-0.26214	-1.17311	0.82151	S	-0.34035	-1.36467	0.82151	S	1.56940	2.43060	-0.13687
H	0.89299	1.38332	-1.23024	H	1.56940	2.43060	-1.23024	H	-0.92573	2.31444	-0.06121
H	-0.84484	1.62508	1.27984	H	-0.92573	2.31444	1.27984	H	-0.29359	1.46161	-1.48197
H	-1.24984	2.19207	-0.35475	H	-0.29359	1.46161	-0.35475	H	0.98454	1.57469	1.30420
H	1.22604	2.39097	0.18835	H	0.98454	1.57469	0.18835	H	1.84532	0.30506	-0.18173
C	1.54486	0.31378	0.49838	C	1.84532	0.30506	0.49838	C	1.69140	-0.87655	0.46391
C	2.35719	-0.49578	-0.23946	C	1.69140	-0.87655	-0.23946	C	1.27467	-0.90457	1.46643
H	3.01491	-1.21674	0.23218	H	1.27467	-0.90457	0.23218	H	2.38606	0.32296	-1.12488
H	2.29254	-0.50327	-1.32278	H	2.38606	0.32296	-1.32278	H	2.24696	-1.75262	0.14584
H	1.73476	0.39800	1.56501	H	2.24696	-1.75262	1.56501	H	-1.08514	0.12274	1.15991
H	-2.28550	-0.07743	0.20594	H	-1.08514	0.12274	0.20594	H	-2.09977	0.18021	-0.28692
H	-1.18184	-0.16454	-1.18432	H	-2.09977	0.18021	-1.18432				
T1 (1a)											
React			5-exo-product			6-endo-product					
C	0.69558	0.69483	0.20452	C	0.60871	0.87372	0.06583	C	-1.61961	-0.87296	-0.40191
C	0.88907	2.21419	0.07550	C	1.15426	2.29302	0.14003	C	-1.44329	0.58972	0.04706
C	0.30254	2.82552	-1.18112	C	0.06162	3.22216	-0.36551	C	-0.03314	1.14392	-0.04260
S	-1.29886	2.28256	-1.71887	S	-1.53701	2.44396	-0.20945	S	1.39428	0.09249	0.12536
H	1.04350	0.19496	-0.70676	H	0.60600	0.52893	-0.97423	H	-2.65900	-1.16870	-0.23465
H	0.42083	2.72122	0.92936	H	1.36427	2.57650	1.17976	H	-2.07955	1.26706	-0.53138
O	0.87036	3.70086	-1.81565	O	0.22140	4.33770	-0.81625	O	0.16848	2.34220	-0.15215

H	1.95189	2.47430	0.07381	H	2.05990	2.45291	-0.44998	H	-1.73300	0.68511	1.10148		
H	1.32810	0.35077	1.03112	H	1.19470	0.17131	0.66589	H	-1.41777	-0.94377	-1.47818		
C	-0.73227	0.32678	0.47820	C	-1.63830	-0.28119	0.21406	C	-0.66972	-1.74021	0.35033		
C	-1.48833	-0.40454	-0.36323	H	-2.44205	-0.62594	0.85192	C	0.75233	-1.64120	-0.03918		
H	-2.52884	-0.62152	-0.14221	H	-1.54614	-0.69839	-0.78257	H	0.89738	-1.92419	-1.08587		
H	-1.06732	-0.82109	-1.27434	C	-0.83996	0.91429	0.57342	H	-0.92951	-2.08724	1.34563		
H	-1.17627	0.72191	1.39255	H	-0.85556	1.08038	1.65471	H	1.40239	-2.24715	0.59376		
				5-exo-TS			6-endo-TS						
				C	-0.88247	1.23198	0.32772	C	1.15535	1.43528	0.38584		
				C	0.52322	1.46938	-0.21185	C	-0.26149	1.46794	-0.22205		
				C	1.37040	0.21585	-0.09551	C	-1.08286	0.20361	-0.01061		
				S	0.46792	-1.29797	-0.24875	S	-0.34251	-1.39546	-0.23928		
				H	-0.85171	1.06465	1.40944	H	1.64383	2.39250	0.18102		
				H	0.47829	1.72297	-1.27937	H	-0.84322	2.29677	0.19207		
				O	2.58150	0.23636	0.05823	O	-2.28085	0.27335	0.22727		
				H	1.03468	2.28461	0.30714	H	-0.18716	1.61558	-1.30685		
				H	-1.49762	2.12085	0.14186	H	1.08759	1.30453	1.47070		
				C	-1.54791	0.05656	-0.34040	C	1.90035	0.29917	-0.22621		
				C	-2.39765	-0.76778	0.31540	C	1.89234	-0.92636	0.35312		
				H	-2.96217	-1.52892	-0.21063	H	1.69120	-1.02425	1.41442		
				H	-2.48157	-0.73214	1.39697	H	2.25613	0.40943	-1.24808		
				H	-1.56690	0.06527	-1.42885	H	2.36970	-1.76889	-0.13678		
T3 (1b)													
React				5-exo-product				6-endo-product					
C	-0.70322	-1.15248	-0.82283	C	-0.11042	1.55136	-0.21856	C	0.14804	1.81436	0.28460		
C	0.57066	-1.41862	-0.00807	C	-1.52427	1.24798	0.25860	C	-1.27240	1.29389	-0.00064		
C	1.54165	-0.25625	0.06164	C	-1.77109	-0.23423	0.02453	C	-1.43273	-0.21065	0.08416		
S	0.89023	1.38624	0.21942	S	-0.22305	-1.11828	-0.04998	S	-0.09051	-1.30796	-0.32872		
H	-0.42893	-0.85486	-1.84094	H	-0.08467	1.57897	-1.31378	H	0.15524	2.90153	0.16646		
H	0.31593	-1.67984	1.02652	H	-1.61757	1.42424	1.33842	H	-2.00657	1.72542	0.68721		
O	2.75305	-0.41546	0.06365	O	-2.85417	-0.76908	-0.09748	O	-2.50251	-0.72404	0.36830		
H	1.12947	-2.26111	-0.42728	H	-2.29986	1.82370	-0.25228	H	-1.56695	1.57408	-1.02033		
H	-1.25645	-2.09763	-0.89101	H	0.26084	2.50658	0.16445	H	0.40650	1.59237	1.32613		
C	-1.59047	-0.10230	-0.20596	C	2.10269	0.32762	-0.42322	C	1.10562	1.16235	-0.65365		
C	-1.80632	1.07096	-0.84388	H	2.11060	0.51387	-1.49442	C	1.44949	-0.26421	-0.42683		
H	-2.42818	1.84547	-0.40289	C	0.79189	0.40856	0.26331	H	1.23097	1.57894	-1.64881		
H	-1.38595	1.25812	-1.82749	H	0.93132	0.46781	1.34888	H	1.97312	-0.66036	-1.30083		
C	-2.20149	-0.40615	1.13540	C	3.25222	-0.38702	0.20603	C	2.29402	-0.50932	0.82808		
H	-2.86568	0.40043	1.45549	H	3.10938	-1.47853	0.16930	H	2.50329	-1.57612	0.94633		
H	-2.77865	-1.33669	1.08421	H	4.19084	-0.16356	-0.30686	H	3.24452	0.02641	0.73744		
H	-1.43455	-0.54109	1.90568	H	3.35517	-0.11365	1.26164	H	1.77593	-0.16120	1.72513		
				5-exo-TS			6-endo-TS						
				C	-0.05717	1.62949	-0.22069	C	0.35002	1.79542	0.14207		
				C	-1.44021	1.24224	0.29355	C	-1.11649	1.36931	-0.09558		
				C	-1.74312	-0.21538	-0.00478	C	-1.39656	-0.10904	0.13596		

			S	-0.33587	-1.28198	0.05250	S	-0.33969	-1.31843	-0.62859	
			H	-0.04099	1.60540	-1.31561	H	0.44911	2.84974	-0.13223	
			H	-1.47930	1.35709	1.38495	H	-1.79441	1.93458	0.55073	
			O	-2.87139	-0.62815	-0.22993	O	-2.39063	-0.46979	0.75068	
			H	-2.23149	1.85987	-0.14021	H	-1.38120	1.57759	-1.13954	
			H	0.17556	2.65289	0.09799	H	0.59498	1.70044	1.20232	
			C	1.00798	0.70818	0.31368	C	1.22794	0.94386	-0.70897	
			C	2.07116	0.30810	-0.42555	C	1.73020	-0.25744	-0.29390	
			H	2.06055	0.51409	-1.49501	H	1.27224	1.17855	-1.76997	
			H	1.06856	0.61180	1.39771	H	2.27806	-0.83132	-1.03974	
			C	3.20769	-0.49582	0.10738	C	2.01065	-0.63547	1.13635	
			H	3.21899	-1.48407	-0.36839	H	2.03174	-1.72056	1.24839	
			H	4.16211	-0.01566	-0.13268	H	2.99957	-0.24444	1.40422	
			H	3.13308	-0.62542	1.18909	H	1.27536	-0.23123	1.83220	
T4 (1e)											
React			5-exo-product				6-endo-product				
C	0.68527	0.76798	0.24577	C	0.61086	0.88627	0.10039	C	-1.61480	-0.89958	-0.44454
C	0.87978	2.26942	-0.00964	C	1.16567	2.30445	0.09648	C	-1.45213	0.54734	0.05837
C	0.23812	2.79199	-1.28008	C	0.05891	3.22466	-0.39505	C	-0.03922	1.10218	0.04370
S	-1.35042	2.15875	-1.75177	S	-1.53474	2.44398	-0.20985	S	1.38041	0.03653	0.19523
H	1.07032	0.20028	-0.60853	H	0.60387	0.49661	-0.92315	H	-2.65983	-1.19874	-0.31323
H	0.46350	2.85590	0.81876	H	1.44680	2.63682	1.10304	H	-2.06541	1.24532	-0.52063
O	0.75240	3.66708	-1.96022	O	0.20850	4.33677	-0.85877	O	0.16663	2.30467	0.01094
H	1.94388	2.51573	-0.07901	H	2.03729	2.42680	-0.55182	H	-1.78484	0.61324	1.10270
H	1.28922	0.49989	1.12177	H	1.20309	0.20949	0.72514	H	-1.38485	-0.93567	-1.51642
C	-0.75178	0.39336	0.50105	C	-1.62103	-0.25789	0.18582	C	-0.69016	-1.79819	0.31112
C	-1.41436	-0.40594	-0.36635	H	-2.44615	-0.62160	0.78752	C	0.73009	-1.68187	-0.08900
H	-2.45641	-0.66933	-0.20571	H	-1.50023	-0.63937	-0.82205	H	0.86834	-1.89440	-1.15245
H	-0.91289	-0.82864	-1.23184	C	-0.84003	0.92827	0.62305	H	1.38278	-2.32873	0.50212
C	-1.40945	0.95208	1.73402	C	-0.89900	1.10561	2.14197	C	-1.02368	-2.18593	1.71660
H	-1.45910	2.04583	1.70310	H	-1.93506	1.21699	2.47450	H	-2.09323	-2.38884	1.82625
H	-2.42710	0.56920	1.84330	H	-0.46989	0.22083	2.62574	H	-0.46459	-3.07582	2.02319
H	-0.83349	0.67750	2.62536	H	-0.33984	1.98811	2.46472	H	-0.76396	-1.38430	2.42714
			5-exo-TS				6-endo-TS				
			C	-0.89621	1.22568	0.25858	C	1.11509	1.45506	0.32163	
			C	0.54498	1.47792	-0.16848	C	-0.32233	1.40013	-0.23678	
			C	1.39708	0.23161	0.00034	C	-1.07905	0.10421	0.02143	
			S	0.51401	-1.29302	-0.13288	S	-0.27713	-1.45660	-0.24039	
			H	-0.94385	1.09577	1.34415	H	1.55151	2.42389	0.05723	
			H	0.59821	1.75873	-1.22759	H	-0.92576	2.20943	0.18472	
			O	2.60586	0.27506	0.17523	O	-2.26892	0.13174	0.30819	
			H	1.00095	2.28942	0.40616	H	-0.29994	1.53492	-1.32532	
			H	-1.51244	2.09561	-0.00349	H	1.08383	1.37520	1.41274	
			C	-1.50970	0.01543	-0.41479	C	1.90872	0.32969	-0.26383	
			C	-2.29079	-0.82521	0.31809	C	1.91291	-0.86221	0.38771	

			H	-2.84778	-1.62737	-0.15470	H	1.67989	-0.90396	1.44573	
			H	-2.31419	-0.76115	1.40057	H	2.43651	-1.71478	-0.03529	
			C	-1.64206	0.05925	-1.91821	C	2.45334	0.49570	-1.64663	
			H	-1.98832	-0.90022	-2.30763	H	3.22993	1.26940	-1.64290	
			H	-2.37983	0.82983	-2.17269	H	2.88216	-0.43466	-2.02408	
			H	-0.70306	0.31761	-2.41045	H	1.67084	0.83163	-2.33677	
T5 (If)											
React			5-exo-product				6-endo-product				
C	-1.33007	0.41911	-0.42636	C	-0.89118	0.72409	-0.30979	C	1.43997	-0.06511	-0.32299
C	0.06420	0.50065	-1.10078	C	0.41068	1.40092	0.10290	C	0.50032	-1.17729	0.18144
C	1.19351	0.50604	-0.09574	C	1.52546	0.37770	-0.01635	C	-0.98912	-0.94328	0.00988
S	2.07196	-1.02468	0.05287	S	0.85939	-1.27373	0.08903	S	-1.67988	0.69768	0.04160
H	0.17769	-0.34323	-1.78985	H	-0.87323	0.57601	-1.39837	H	0.72227	-2.13146	-0.30985
O	1.49407	1.46713	0.59245	H	0.35940	1.70937	1.15722	O	-1.76977	-1.87770	-0.07138
H	0.13526	1.43365	-1.67202	O	2.70695	0.61423	-0.16674	H	0.66060	-1.31657	1.26010
H	-2.04816	0.31654	-1.24997	H	0.65954	2.27836	-0.50049	H	1.29989	0.02135	-1.41048
C	-1.44491	-0.80075	0.44637	C	-1.85264	-1.62160	-0.25176	C	1.02455	1.22029	0.30869
C	-2.18750	-1.87110	0.14861	H	-2.31149	-2.39574	0.34984	C	-0.22863	1.83164	-0.17984
H	-2.24056	-2.72608	0.81566	H	-1.97374	-1.65409	-1.32915	H	-0.17130	2.05367	-1.24935
H	-2.76312	-1.91680	-0.77313	C	-0.87713	-0.67289	0.33602	H	1.38984	1.46196	1.30390
H	-0.88615	-0.78208	1.38375	H	-1.02687	-0.57999	1.41729	H	-0.49076	2.73962	0.36575
C	-1.66535	1.68880	0.36376	C	-2.13295	1.51933	0.08268	C	2.89433	-0.43219	-0.03005
H	-1.57941	2.57491	-0.27341	H	-2.12039	2.50679	-0.38887	H	3.15110	-1.39405	-0.48467
H	-2.68969	1.62992	0.74402	H	-3.04445	1.00134	-0.22920	H	3.57249	0.33010	-0.42401
H	-0.98916	1.81455	1.21427	H	-2.16802	1.65851	1.16896	H	3.05355	-0.51029	1.05122
			5-exo-TS				6-endo-TS				
			C	-1.04292	-0.60943	-0.28518	C	1.43997	-0.06511	-0.32299	
			C	0.20758	-1.33770	0.19801	C	0.50032	-1.17729	0.18144	
			C	1.45994	-0.51386	-0.02319	C	-0.98912	-0.94328	0.00988	
			S	1.22467	1.23436	0.10472	S	-1.67988	0.69768	0.04160	
			H	-0.97417	-0.46703	-1.37118	H	0.72227	-2.13146	-0.30985	
			H	0.13094	-1.52016	1.27975	O	-1.76977	-1.87770	-0.07138	
			O	2.55665	-1.00412	-0.24334	H	0.66060	-1.31657	1.26010	
			H	0.33345	-2.30488	-0.29827	H	1.29989	0.02135	-1.41048	
			C	-1.14640	0.75087	0.35858	C	1.02455	1.22029	0.30869	
			C	-1.65918	1.82272	-0.28712	C	-0.22863	1.83164	-0.17984	
			H	-1.82339	1.79580	-1.36012	H	-0.17130	2.05367	-1.24935	
			H	-1.09215	0.76996	1.44699	H	1.38984	1.46196	1.30390	
			C	-2.30470	-1.42286	0.03673	H	-0.49076	2.73962	0.36575	
			H	-3.19612	-0.92286	-0.35138	C	2.89433	-0.43219	-0.03005	
			H	-2.23675	-2.41805	-0.41342	H	3.15110	-1.39405	-0.48467	
			H	-2.41709	-1.54141	1.12000	H	3.57249	0.33010	-0.42401	
			H	-1.85852	2.75339	0.23189	H	3.05355	-0.51029	1.05122	
T6 (If)											
React			5-exo-product				6-endo-product				

C	-1.13995	-1.21530	0.77114	C	1.30156	1.16432	0.76902	C	1.13396	1.41221	0.43832
C	-1.83280	-0.22300	-0.14890	C	1.96053	0.15908	-0.16351	C	1.72648	0.15828	-0.18193
S	-1.27606	1.46449	-0.19082	S	0.97803	-1.32403	-0.27246	S	0.90452	-1.42050	-0.05777
H	-1.44883	-2.21246	0.43846	H	1.53195	2.17752	0.42563	H	1.44505	2.25023	-0.19659
O	-2.79569	-0.53951	-0.83259	O	3.00961	0.31564	-0.75568	O	2.80573	0.17854	-0.75110
H	-1.54317	-1.05457	1.78007	H	1.75387	1.02317	1.76015	H	1.61981	1.53641	1.41497
C	0.39418	-1.10003	0.79389	C	-0.19175	0.86053	0.80278	C	-0.39617	1.37041	0.60063
C	0.98262	-1.34658	-0.60636	C	-0.91473	1.42475	-0.42475	C	-1.08576	1.29722	-0.78555
C	0.76657	0.24347	1.35451	C	-0.31868	-0.67572	0.89835	C	-0.72225	0.17496	1.43812
H	0.75690	-1.87769	1.48110	H	-0.64859	1.28366	1.70678	H	-0.70428	2.28512	1.12011
C	2.34766	-0.67873	-0.76853	C	-2.37124	0.96355	-0.48474	C	-2.30874	0.37979	-0.73789
H	0.30770	-0.93825	-1.37052	H	-0.39724	1.10637	-1.34021	H	-0.38511	0.91248	-1.53881
H	1.04514	-2.42586	-0.78512	H	-0.85683	2.51916	-0.38694	H	-1.36425	2.30634	-1.10668
C	1.46332	1.16889	0.65334	C	-1.66753	-1.19426	0.55837	C	-0.78387	-1.09579	0.68685
C	2.19658	0.83703	-0.61858	C	-2.43950	-0.56890	-0.55834	C	-1.89287	-1.05904	-0.39598
H	2.78088	-0.92271	-1.74400	H	-2.87269	1.40290	-1.35398	H	-2.83823	0.39231	-1.69625
H	3.03461	-1.05177	0.00198	H	-2.90197	1.30960	0.41165	H	-3.00461	0.75451	0.02248
H	3.17719	1.32667	-0.59289	H	-3.47743	-0.91634	-0.53899	H	-2.75789	-1.61280	-0.01406
H	1.66256	1.25228	-1.48358	H	-2.01825	-0.88606	-1.52816	H	-1.54652	-1.57829	-1.29583
H	0.34196	0.51352	2.32167	H	-1.97570	-2.14974	0.97100	H	-0.48839	0.17916	2.49909
H	1.59861	2.16050	1.08370	H	-0.01456	-1.01092	1.89478	H	-0.91845	-1.95395	1.34917
				5-exo-TS			6-endo-TS				
C	1.22951	1.09559	0.89623	C	1.10142	1.34052	0.61478	C	1.10142	1.34052	0.61478
C	1.99590	0.19371	-0.06311	C	1.72912	0.20936	-0.19410	C	1.72912	0.20936	-0.19410
S	1.06242	-1.28575	-0.41320	S	1.10463	-1.44910	-0.06962	S	1.10463	-1.44910	-0.06962
H	1.45335	2.13988	0.65824	H	1.39829	2.27741	0.13040	H	1.39829	2.27741	0.13040
O	3.08941	0.42571	-0.53821	O	2.71016	0.42440	-0.89464	O	2.71016	0.42440	-0.89464
H	1.60533	0.88197	1.90610	H	1.55867	1.31516	1.61257	H	1.55867	1.31516	1.61257
C	-0.24898	0.74541	0.77583	C	-0.43508	1.25212	0.73149	C	-0.43508	1.25212	0.73149
C	-0.86559	1.39106	-0.47479	C	-1.08684	1.35511	-0.66371	C	-1.08684	1.35511	-0.66371
C	-0.31314	-0.79114	0.72140	C	-0.71314	-0.04689	1.41520	C	-0.71314	-0.04689	1.41520
H	-0.79579	1.07459	1.66790	H	-0.76653	2.08210	1.36791	H	-0.76653	2.08210	1.36791
C	-2.27118	0.84992	-0.84083	C	-2.32552	0.46727	-0.76730	C	-2.32552	0.46727	-0.76730
H	-0.18377	1.23149	-1.31823	H	-0.37043	1.03935	-1.43356	H	-0.37043	1.03935	-1.43356
H	-0.90113	2.47318	-0.30716	H	-1.33004	2.40217	-0.87172	H	-1.33004	2.40217	-0.87172
C	-1.64202	-1.29086	0.27490	C	-1.06361	-1.14792	0.67436	C	-1.06361	-1.14792	0.67436
C	-2.73354	-0.28888	0.08943	C	-1.92252	-0.99579	-0.56839	C	-1.92252	-0.99579	-0.56839
H	-2.25472	0.46534	-1.86562	H	-2.80949	0.59199	-1.74103	H	-2.80949	0.59199	-1.74103
H	-3.01062	1.65699	-0.81307	H	-3.05089	0.75629	0.00319	H	-3.05089	0.75629	0.00319
H	-3.01775	0.14200	1.06403	H	-2.81036	-1.62191	-0.41904	H	-2.81036	-1.62191	-0.41904
H	-3.63196	-0.76411	-0.31496	H	-1.40831	-1.37811	-1.45494	H	-1.40831	-1.37811	-1.45494
H	-1.83622	-2.35802	0.26185	H	-0.35642	-0.17041	2.43532	H	-0.35642	-0.17041	2.43532
H	-0.04648	-1.20577	1.70346	H	-1.11285	-2.10618	1.18795	H	-1.11285	-2.10618	1.18795

Substitution Study

In order to verify the effect of the substitution on the relative stability of the radical and thus, on the relative stability of the *5-exo* and *6-endo* products, we have carried out a computational experiment. One of the hydrogens of the C_α has been substituted by a strong electron withdrawing group (EWG), NO_2 (compound **T3**), and by an electron donating group (EDG), NH_2 (compound **T4**) as shown in **Scheme 1**.

All the results are showed in **Table S3** and **Figures S2** and **S3**. In both cases, the transition barriers are very similar and they are not the limiting factor of the reaction. However, when the NH_2 (EDG) is considered, the relative energy shows that *6-endo* product is $8.5 \text{ kJ}\cdot\text{mol}^{-1}$ more stable than the *5-exo*, while the NO_2 (EWG) is taken into account is the *5-exo* which is more stable than *6-endo* one, as it happened in SO compound.

Table S3. Potential energy surface corresponding to the NH_2 and NO_2 compounds at the UMP2/6-311++G(d,p) computational level. Energies are in $\text{kJ}\cdot\text{mol}^{-1}$.

Compound	NH_2	NO_2
React	0.0	0.0
$\text{TS}_{5\text{exo}}$	37.2	30.6
$\text{TS}_{6\text{endo}}$	36.0	30.1
$\text{Prod}_{5\text{exo}}$	-24.1	-33.7
$\text{Prod}_{6\text{endo}}$	-32.6	-27.2

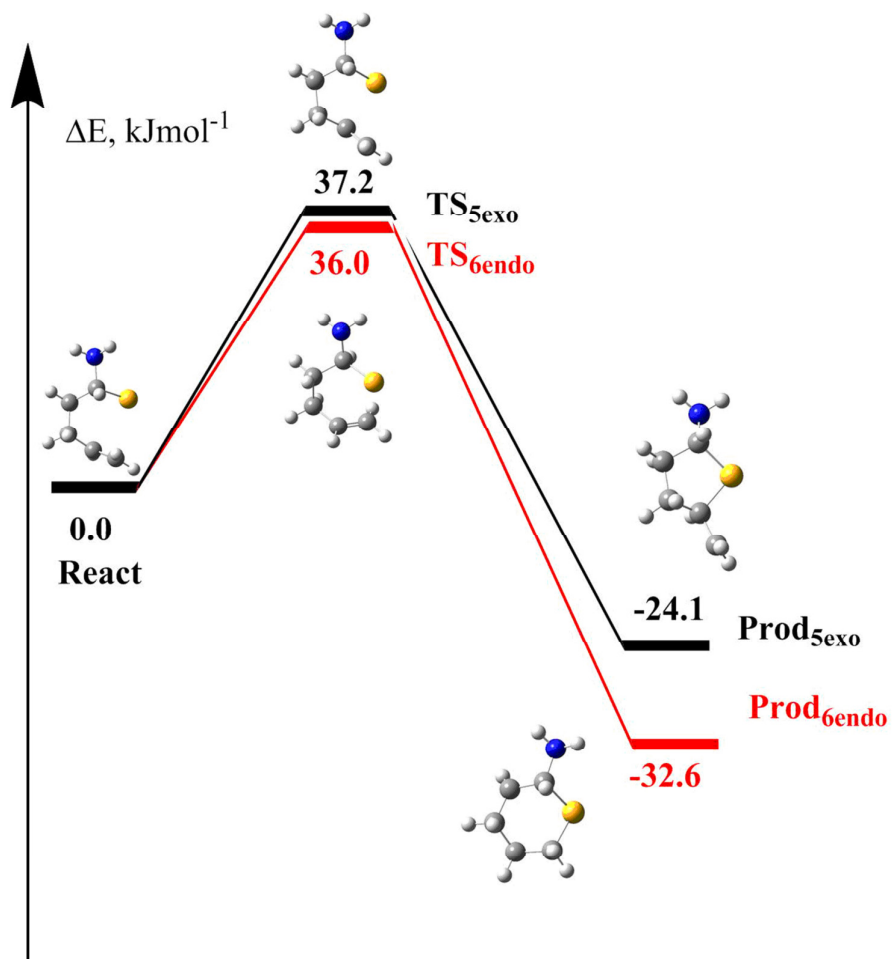


Figure S2. Potential Energy Surface (in $\text{kJ}\cdot\text{mol}^{-1}$) corresponding to the cyclisation processes leading to the 5-*exo* and 6-*endo* products for compound **T3**.

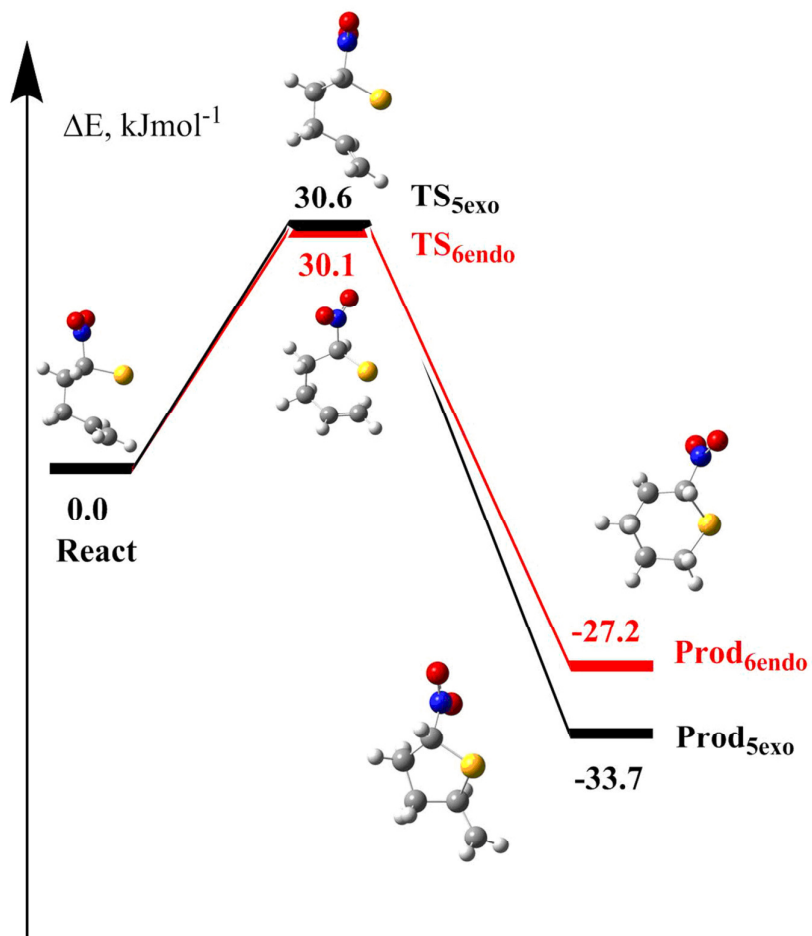
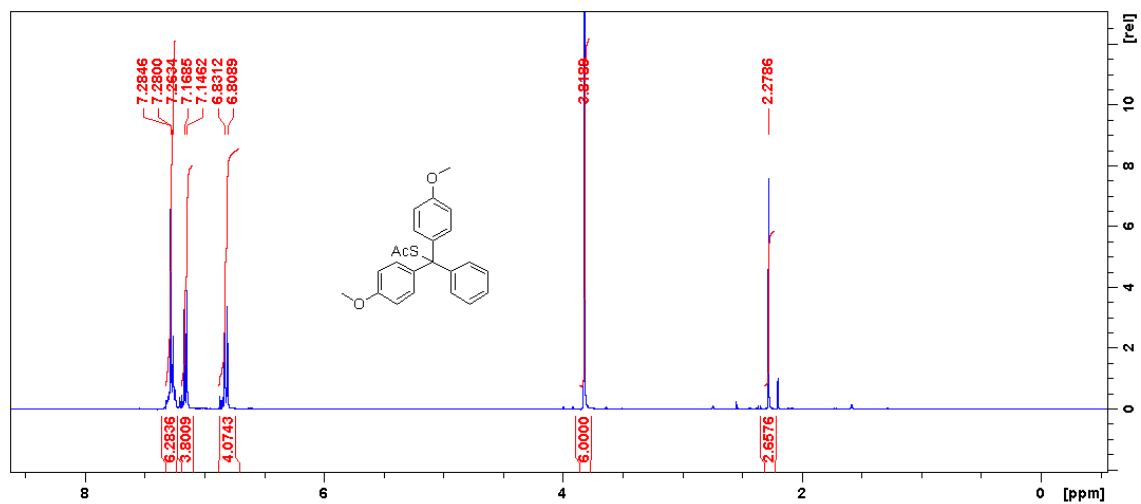


Figure S3. Potential Energy Surface (in $\text{kJ}\cdot\text{mol}^{-1}$) corresponding to the cyclisation processes leading to the 5-*exo* and 6-*endo* products for compound **T4**.

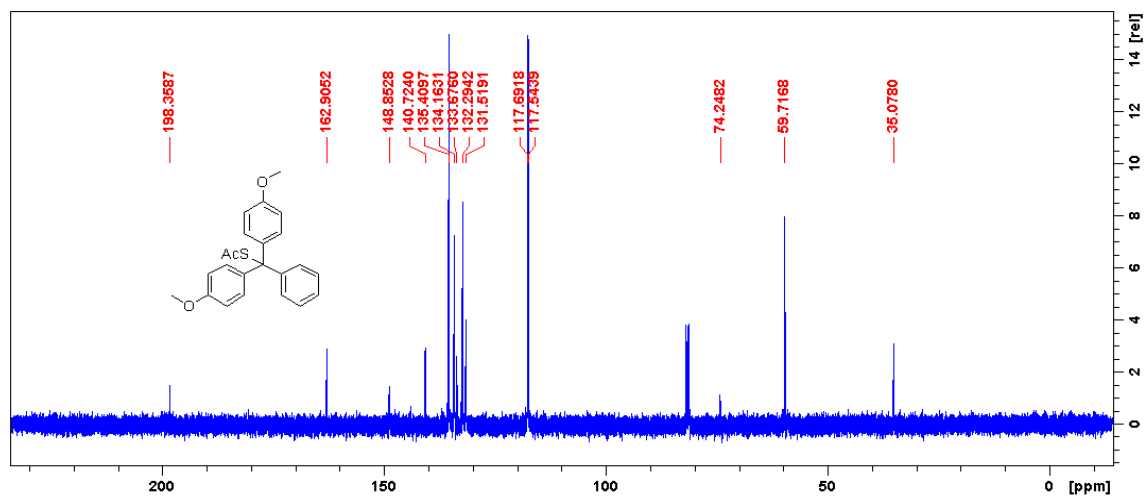
10. NMR Spectra

Supplementary Figure S4.

DMTrtSAc ^1H NMR (400 MHz, CDCl_3):

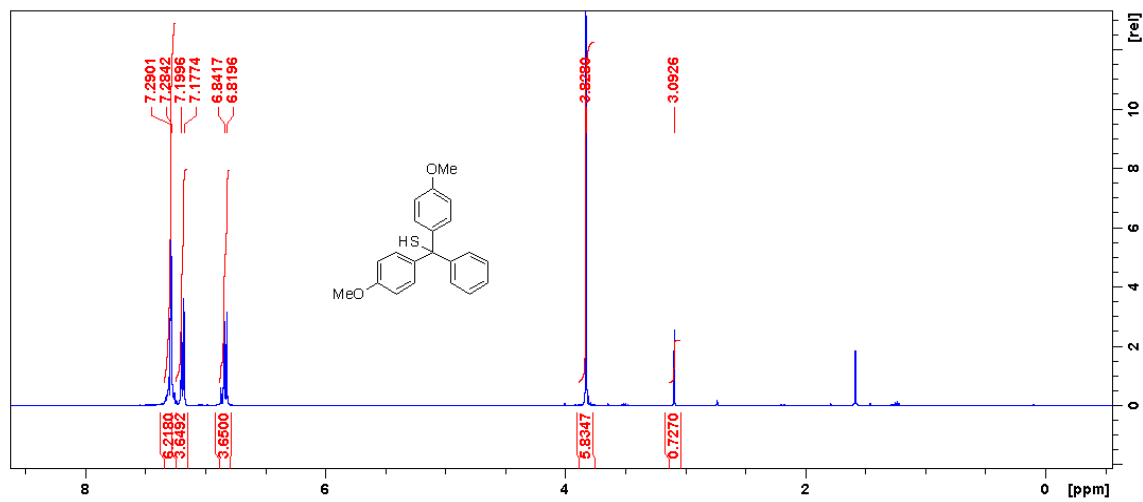


DMTrtSAc ^{13}C NMR (100 MHz, CDCl_3):

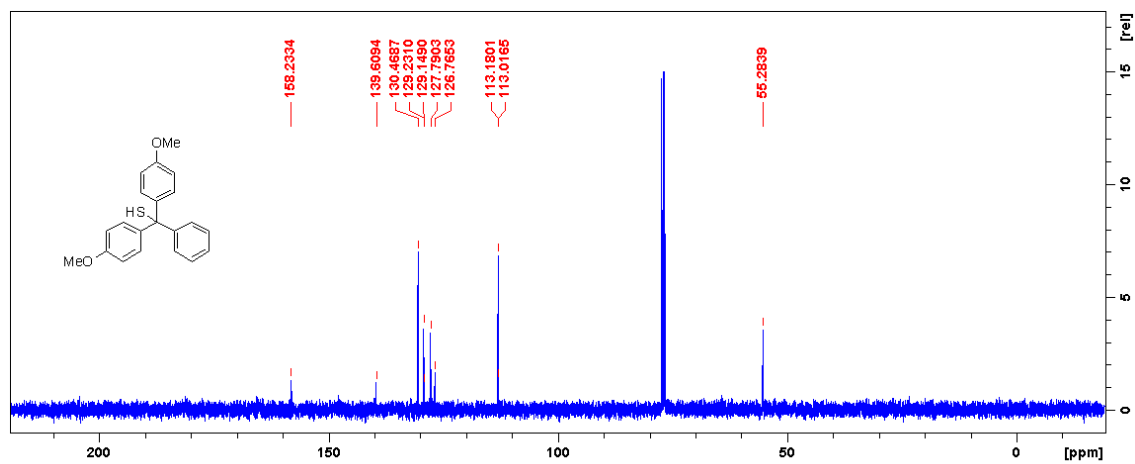


Supplementary Figure S5.

DMTrtSH ^1H NMR (400 MHz, CDCl_3):

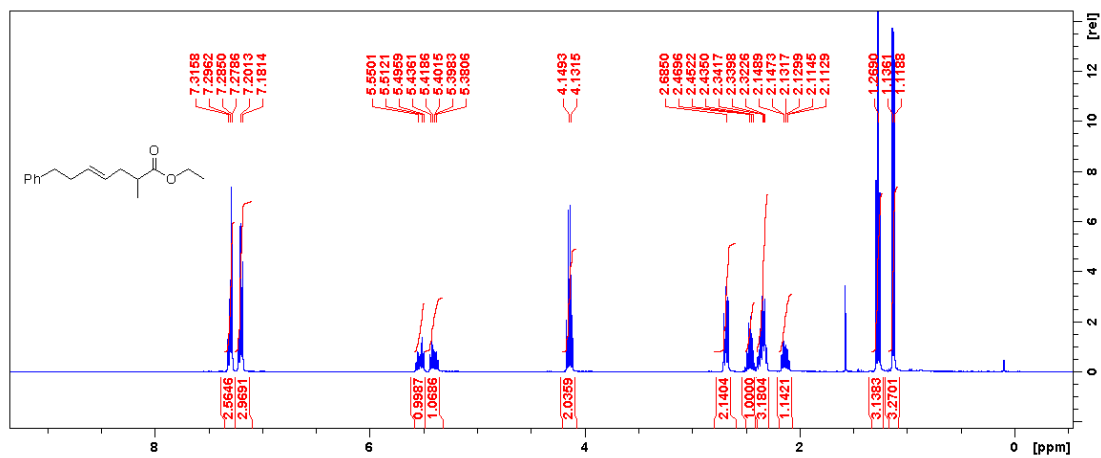


DMTrtSH ^{13}C NMR (100 MHz, CDCl_3):

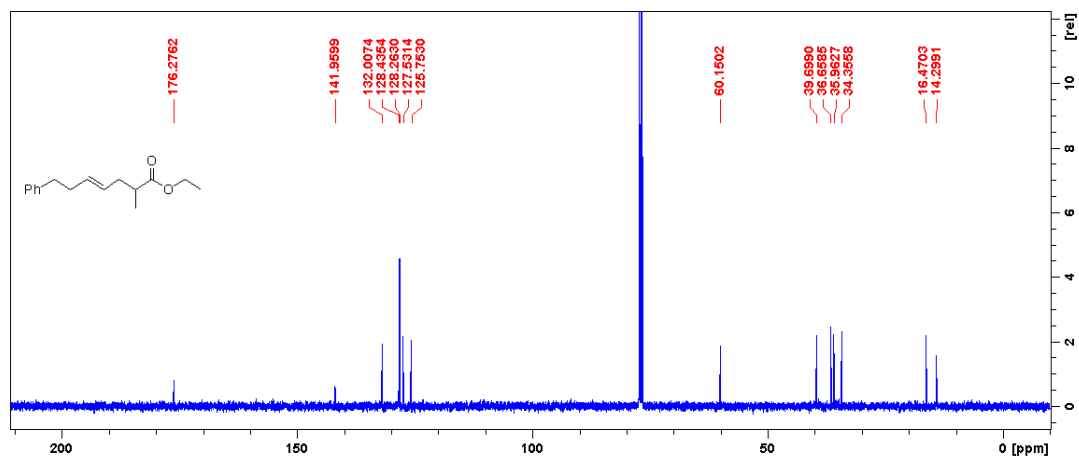


Supplementary Figure S6.

22 ^1H NMR (400 MHz, CDCl_3):

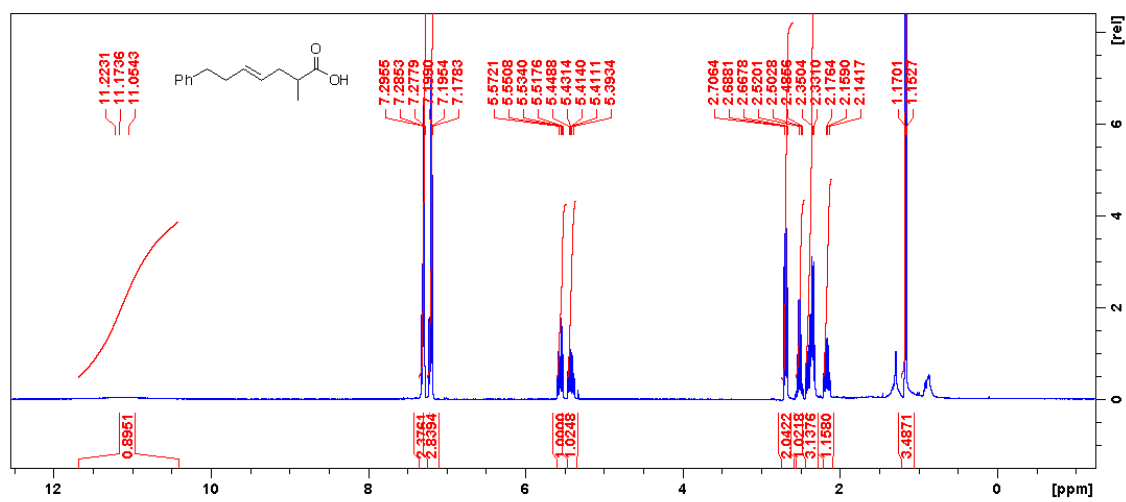


22 ^{13}C NMR (100 MHz, CDCl_3):

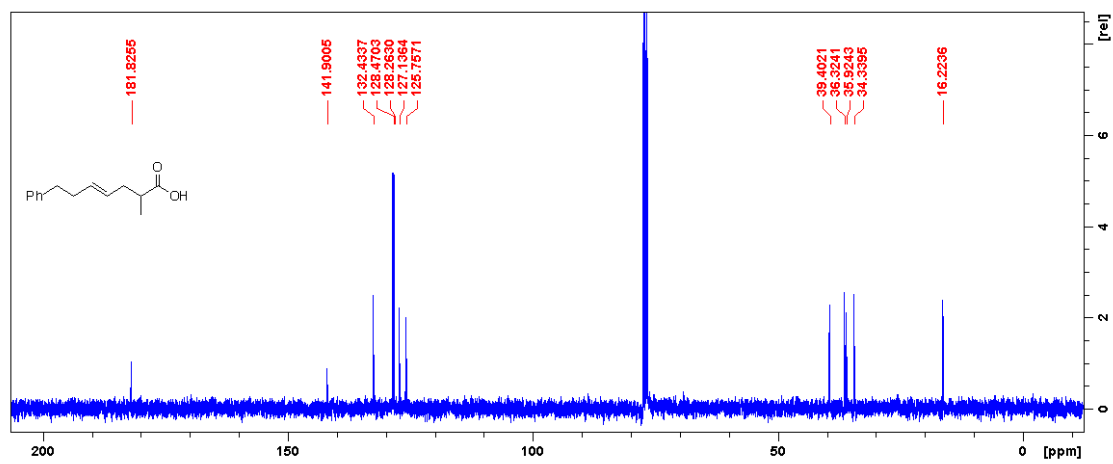


Supplementary Figure S7.

^{23}H NMR (400 MHz, CDCl_3):

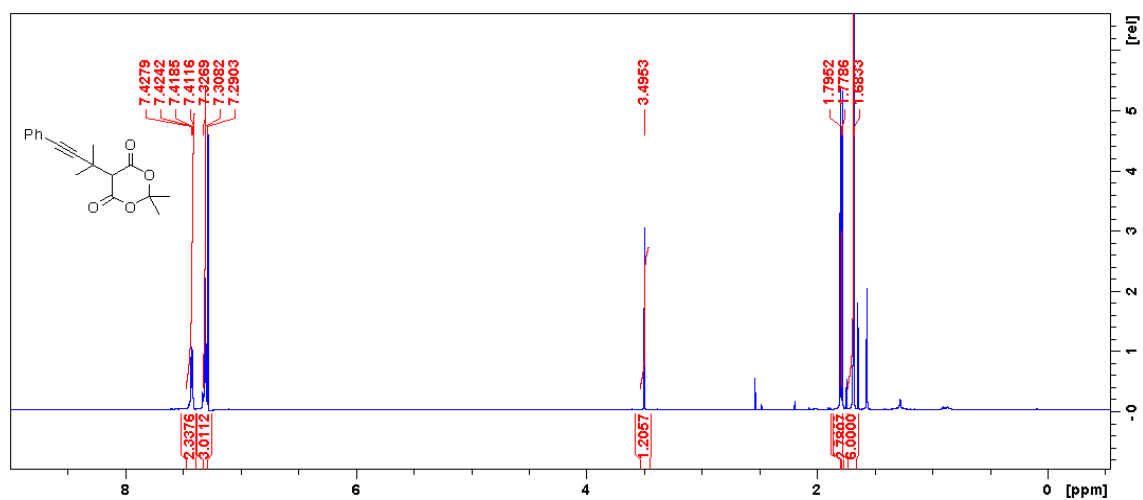


^{13}C NMR (100 MHz, CDCl_3):

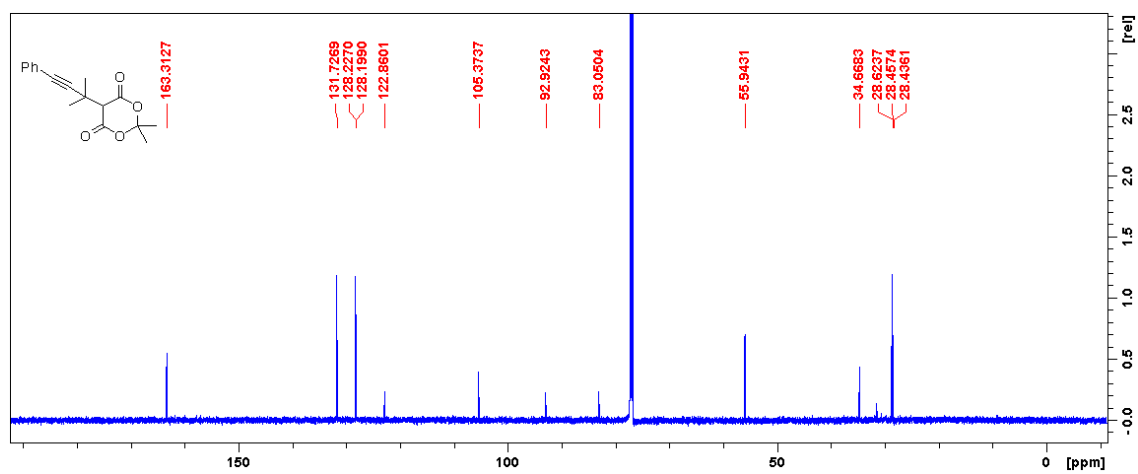


Supplementary Figure S8.

44 ^1H NMR (600 MHz, CDCl_3):

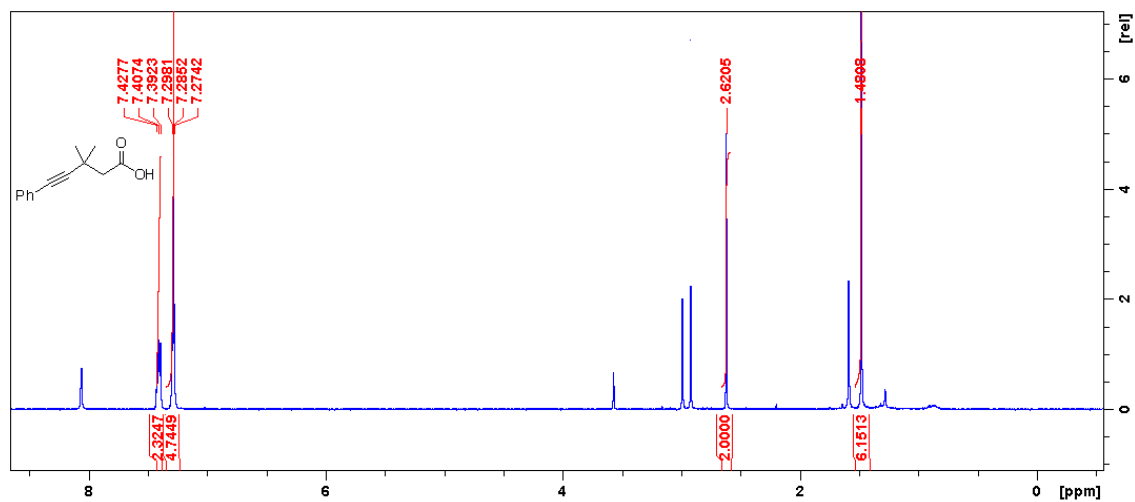


44 ^{13}C NMR (150 MHz, CDCl_3):

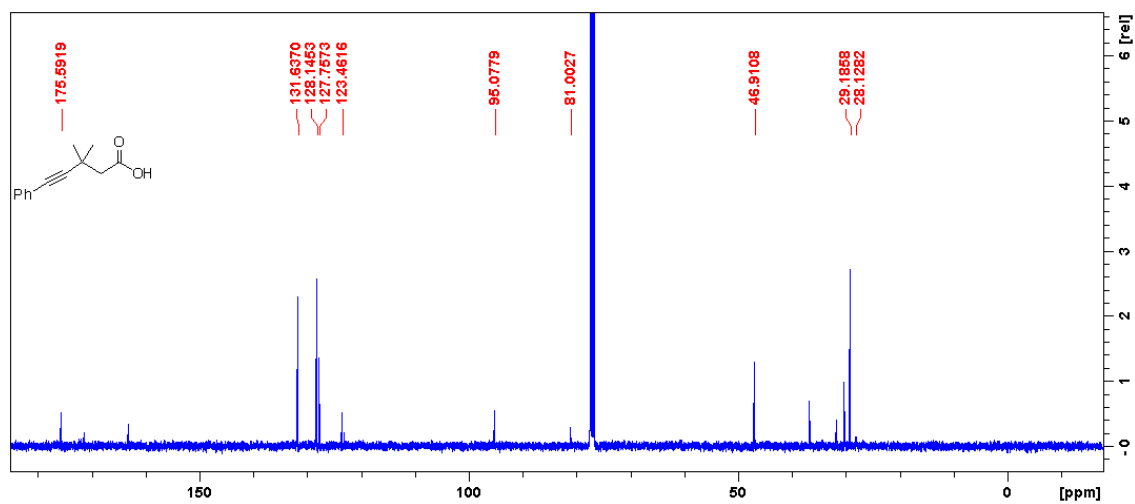


Supplementary Figure S9.

$45\text{ }^1\text{H NMR}$ (400 MHz, CDCl_3):

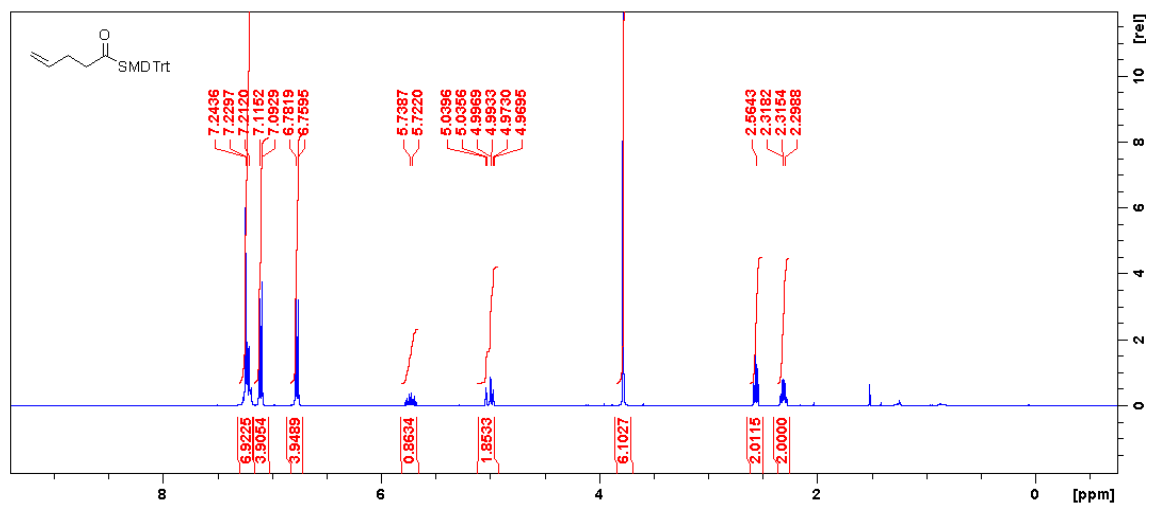


$45\text{ }^{13}\text{C NMR}$ (100 MHz, CDCl_3):

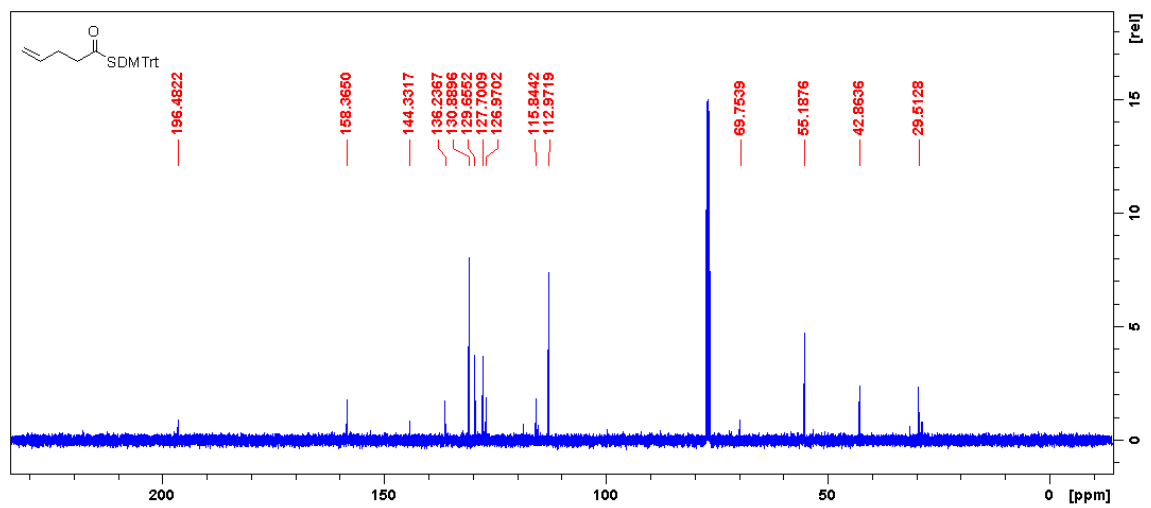


Supplementary Figure S10.

46 ^1H NMR (400 MHz, CDCl_3):

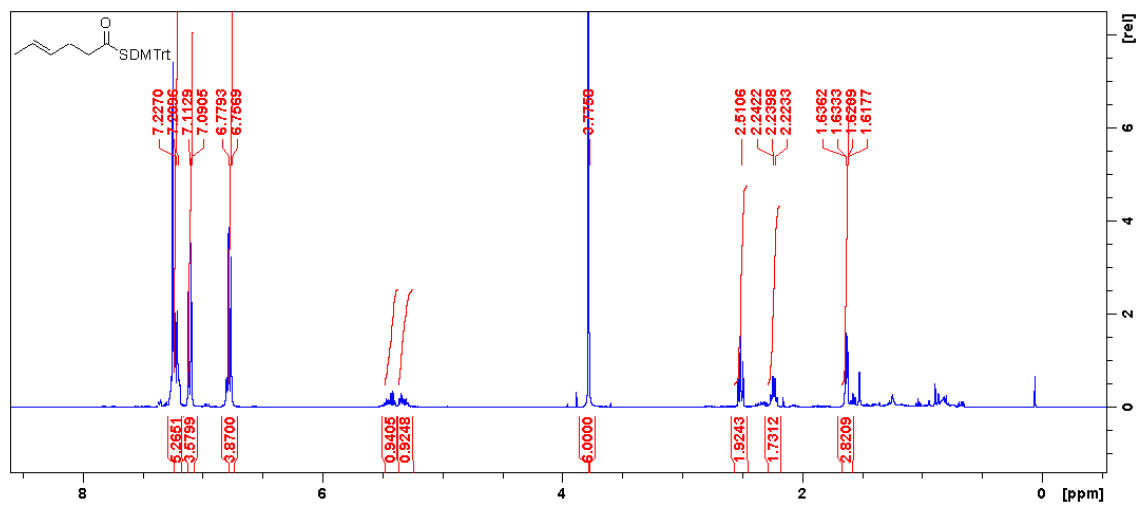


46 ^{13}C NMR (100 MHz, CDCl_3):

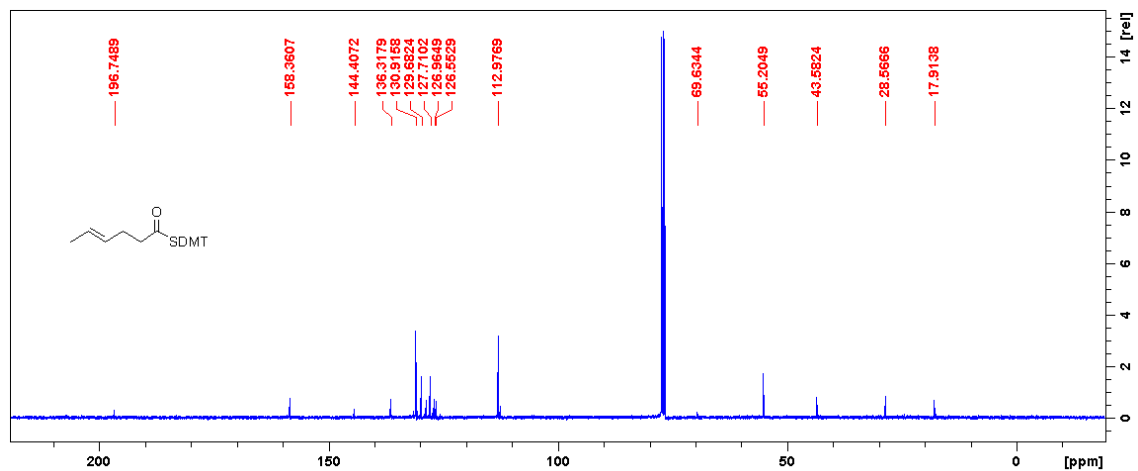


Supplementary Figure S11.

47 ^1H NMR (400 MHz, CDCl_3):

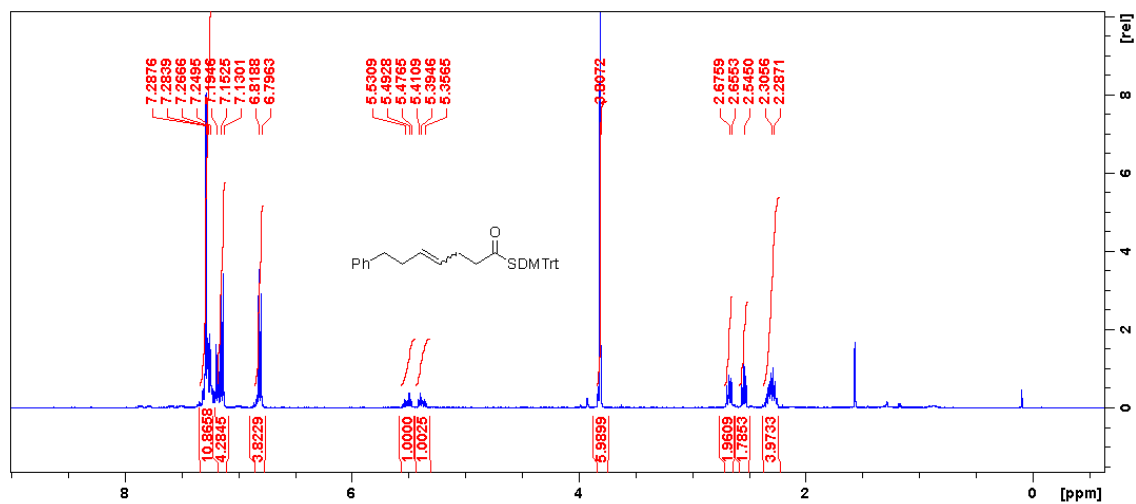


47 ^{13}C NMR (100 MHz, CDCl_3):

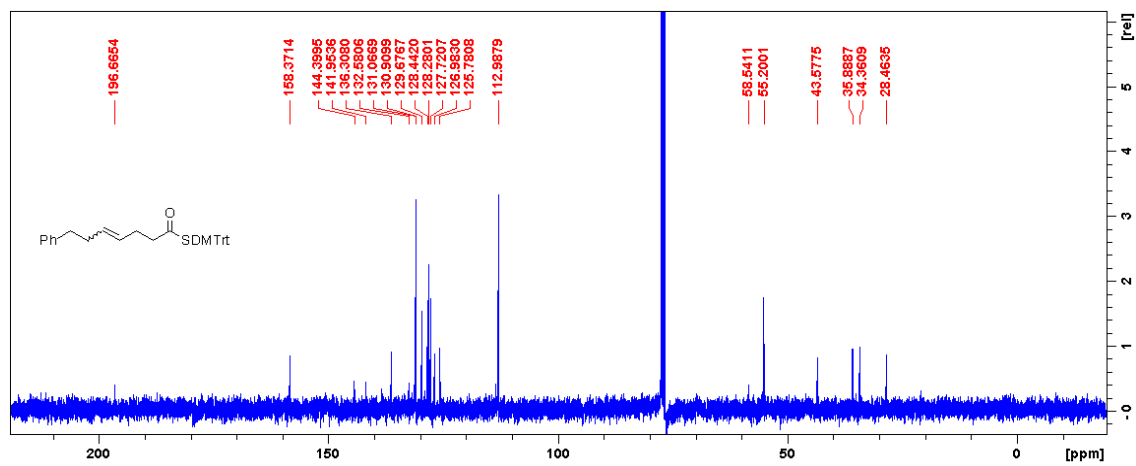


Supplementary Figure S11.

48 ^1H NMR (400 MHz, CDCl_3):

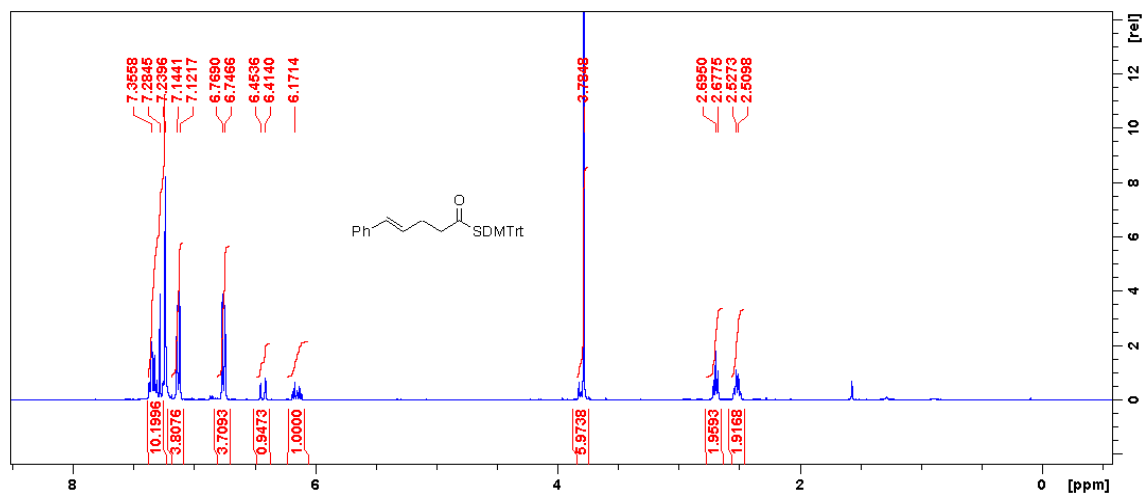


48 ^{13}C NMR (100 MHz, CDCl_3):

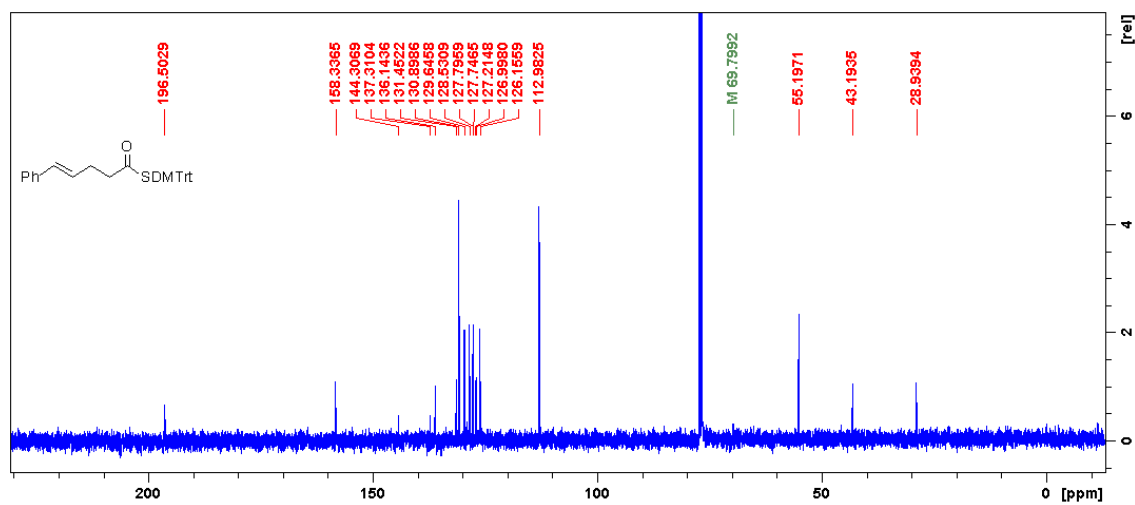


Supplementary Figure S12.

49 ^1H NMR (400 MHz, CDCl_3):

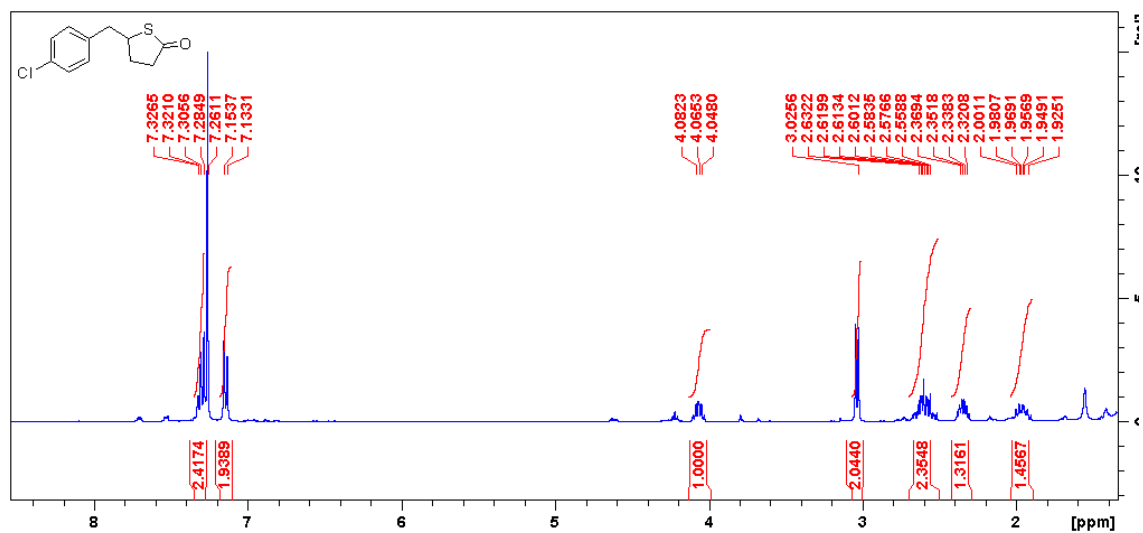


49 ^{13}C NMR (100 MHz, CDCl_3):

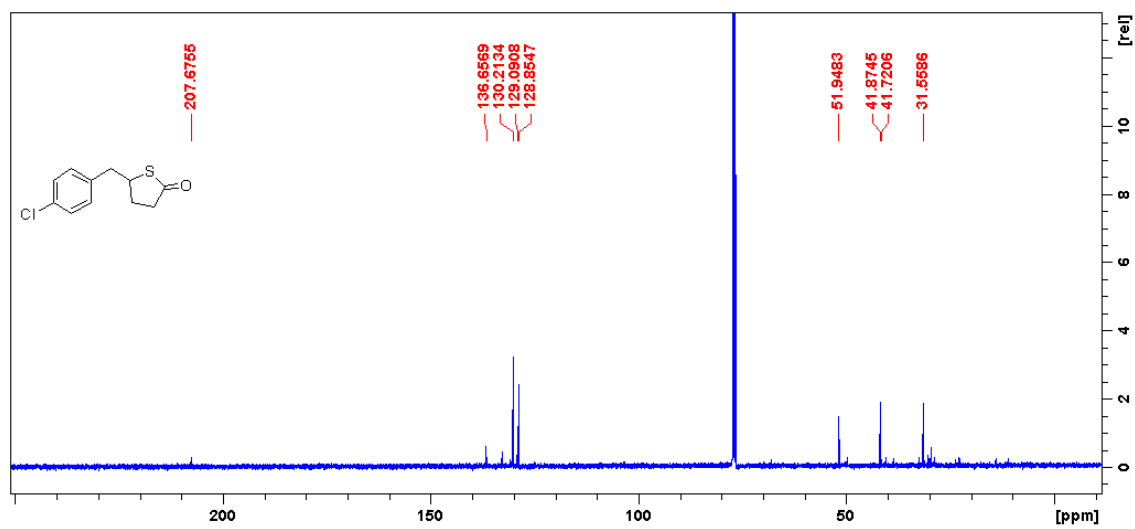


Supplementary Figure S13.

50 ^1H NMR (400 MHz, CDCl_3):

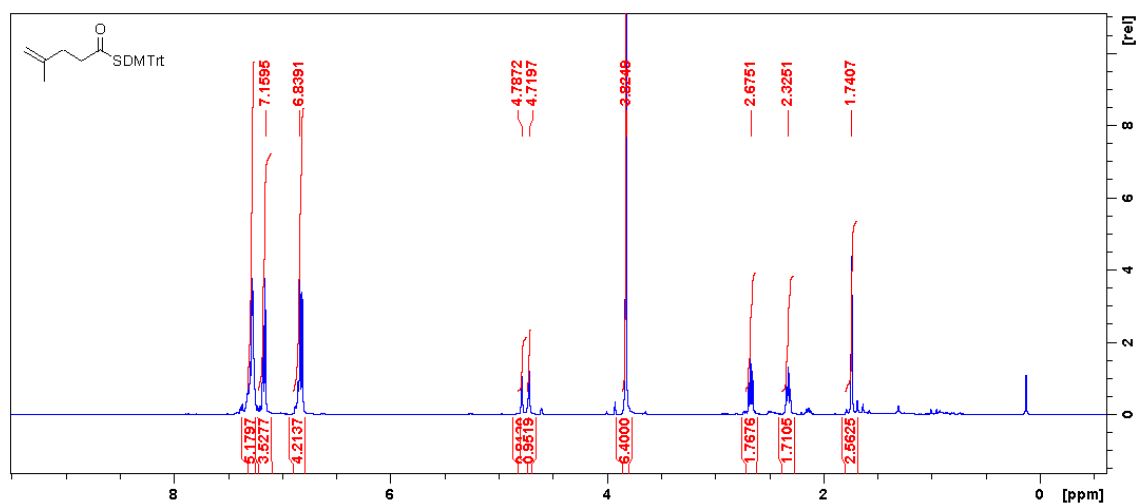


50 ^{13}C NMR (100 MHz, CDCl_3):

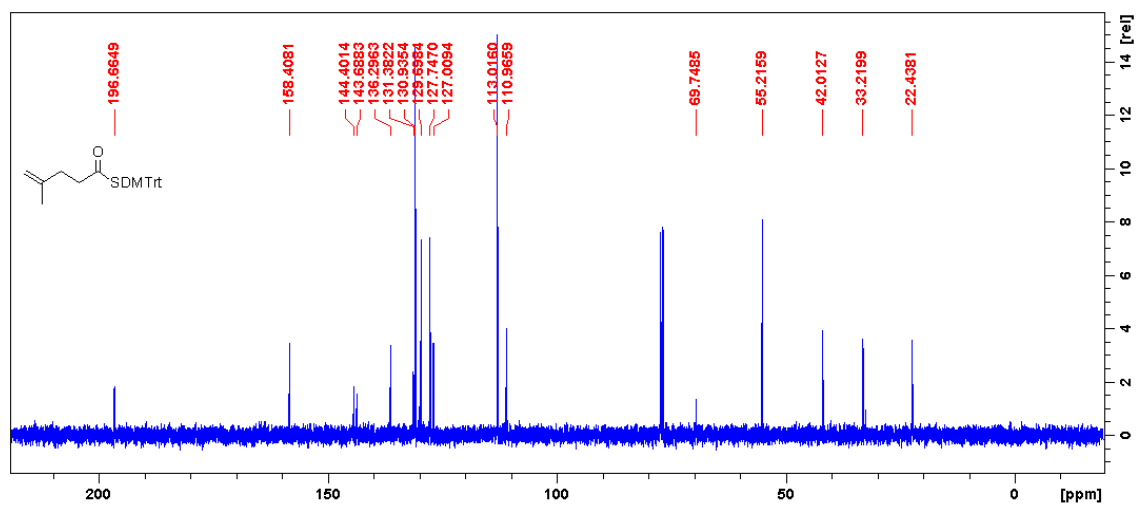


Supplementary Figure S14.

51 ^1H NMR (400 MHz, CDCl_3):

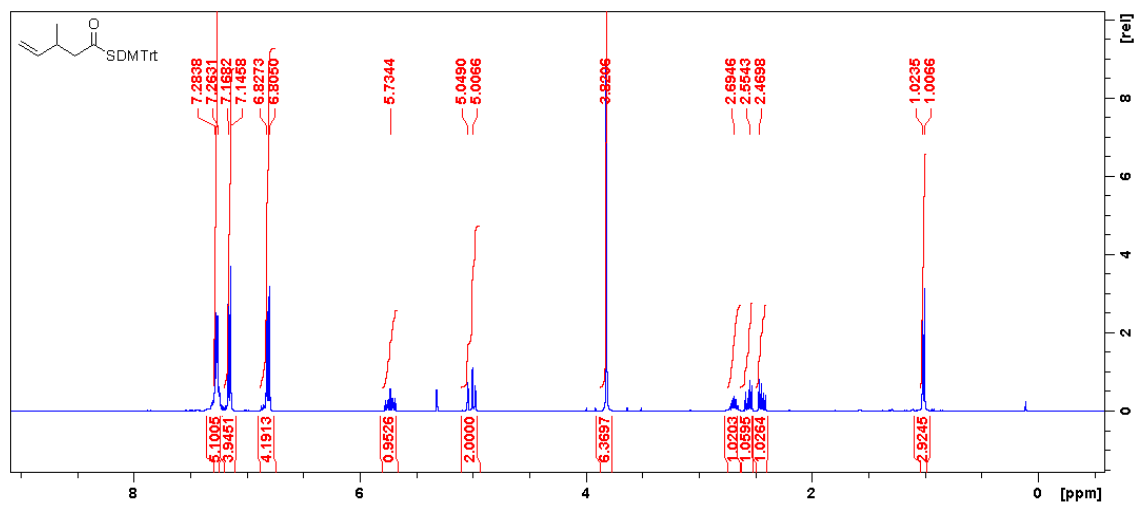


51 ^{13}C NMR (100 MHz, CDCl_3):

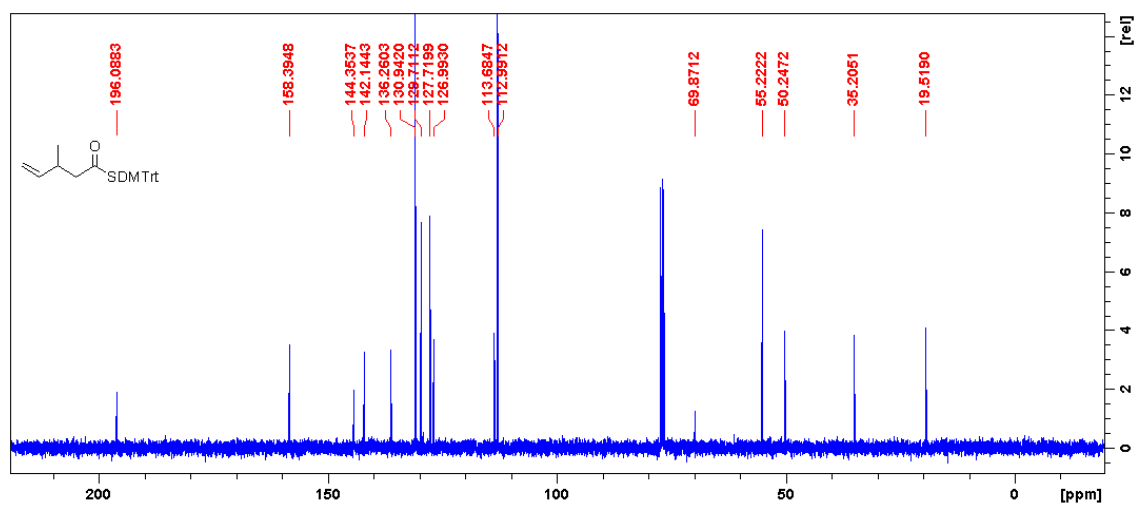


Supplementary Figure S15.

52 ^1H NMR (400 MHz, CDCl_3):

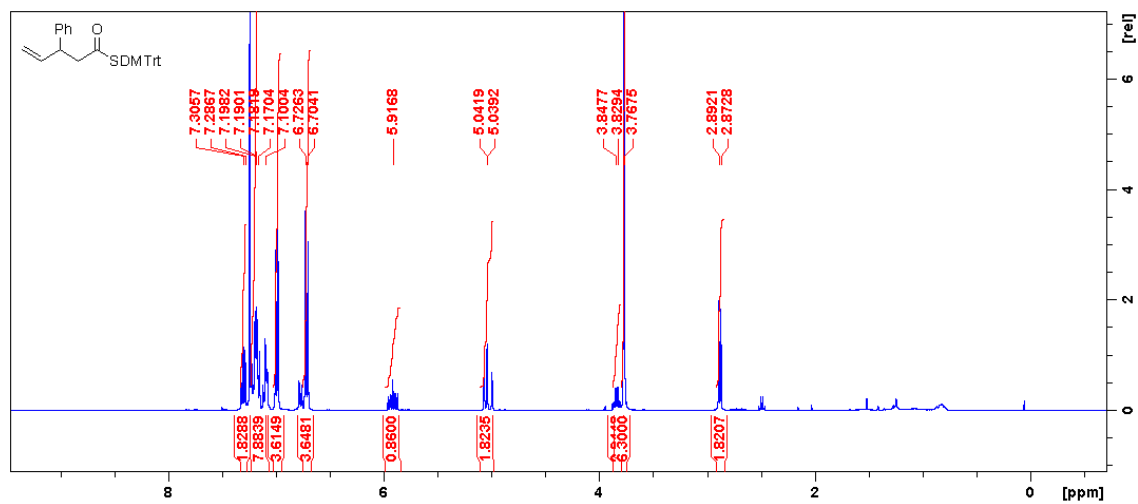


52 ^{13}C NMR (100 MHz, CDCl_3):

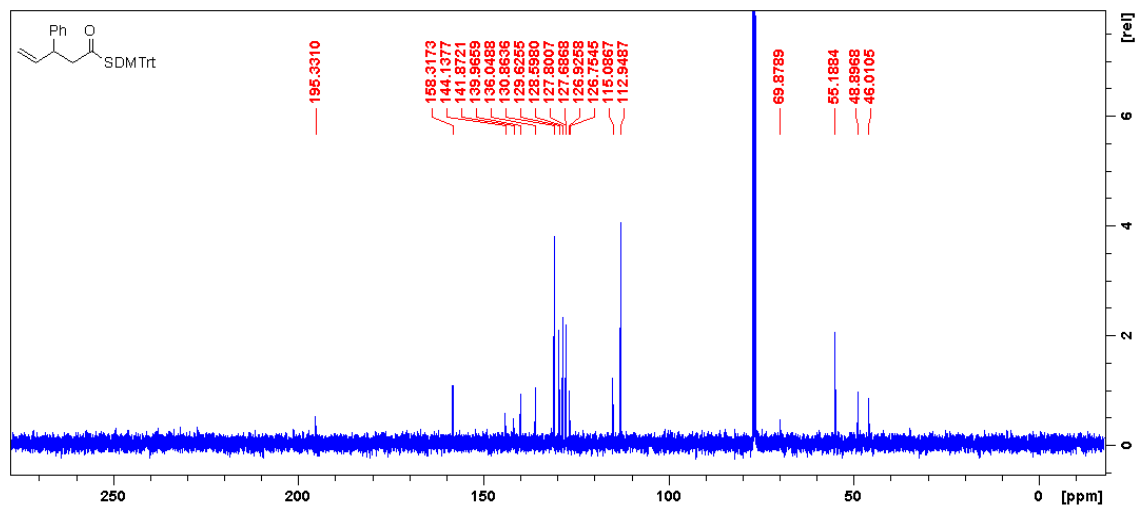


Supplementary Figure S16.

53 ^1H NMR (400 MHz, CDCl_3):

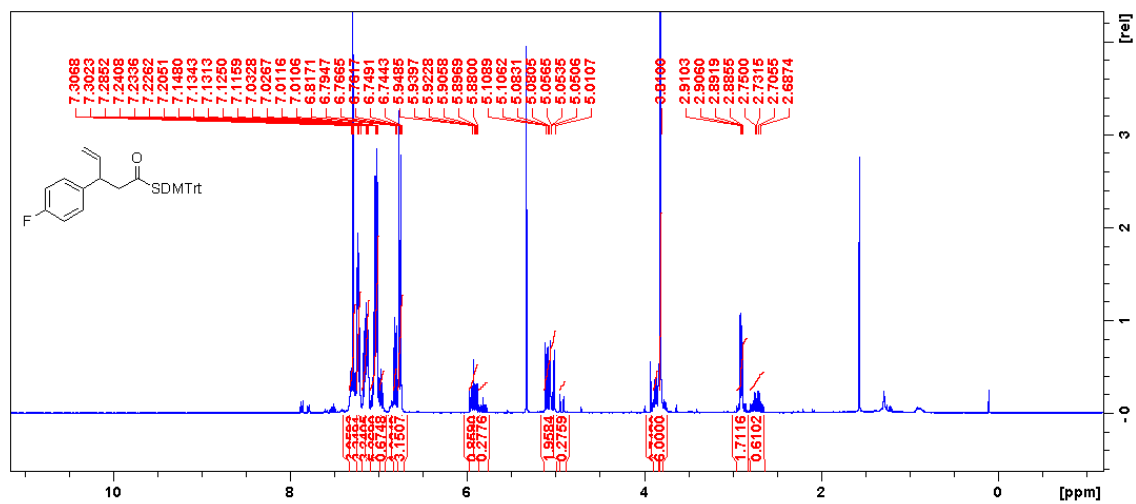


53 ^{13}C NMR (100 MHz, CDCl_3):

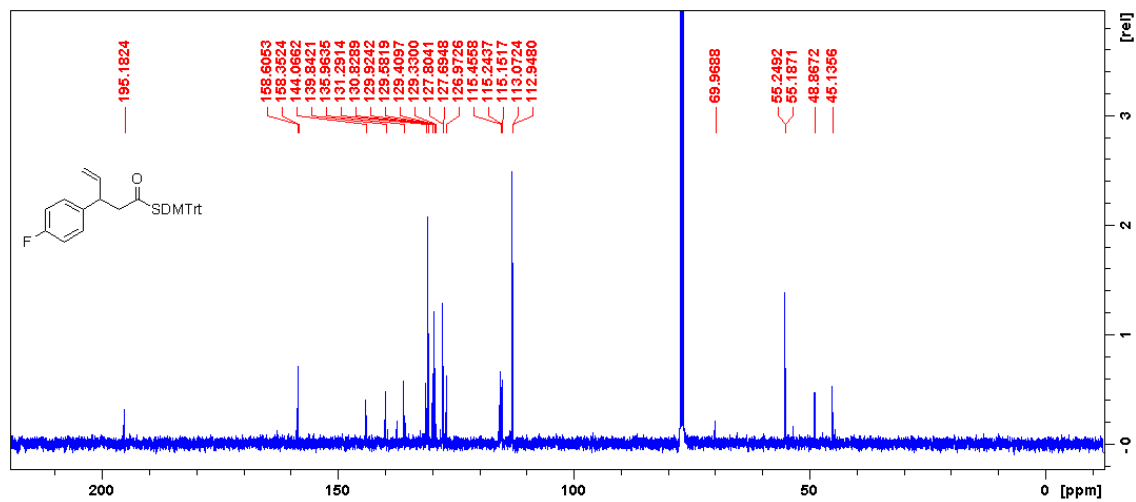


Supplementary Figure S17.

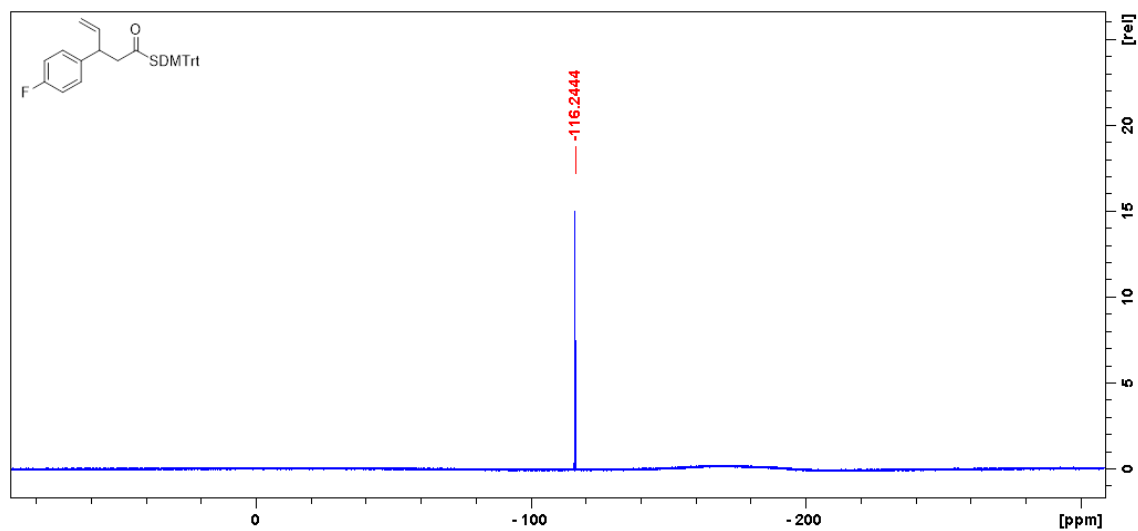
54 ^1H NMR (400 MHz, CDCl_3):



54 ^{13}C NMR (100 MHz, CDCl_3):

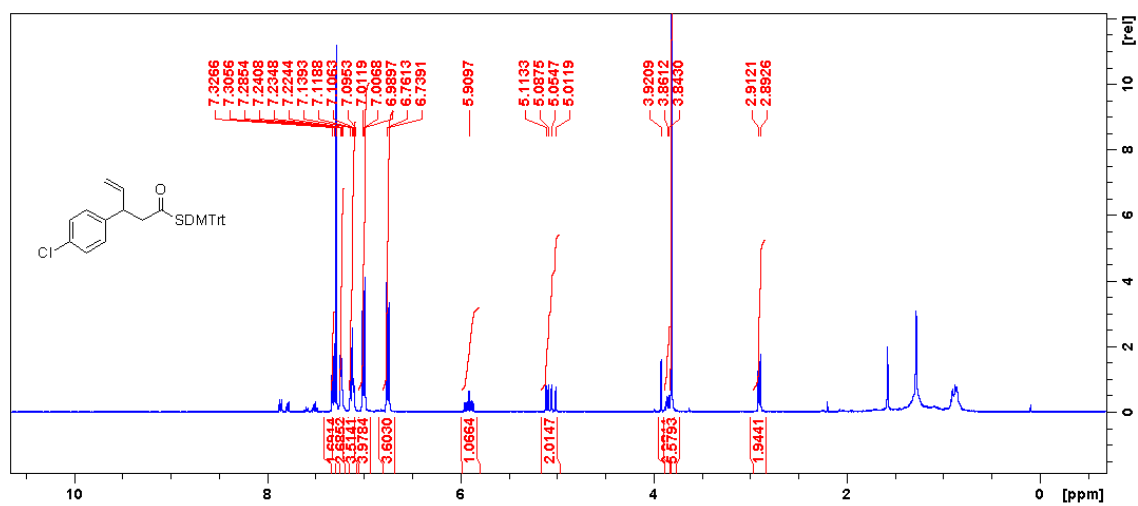


54 ^{19}F NMR (376 MHz, CDCl_3):

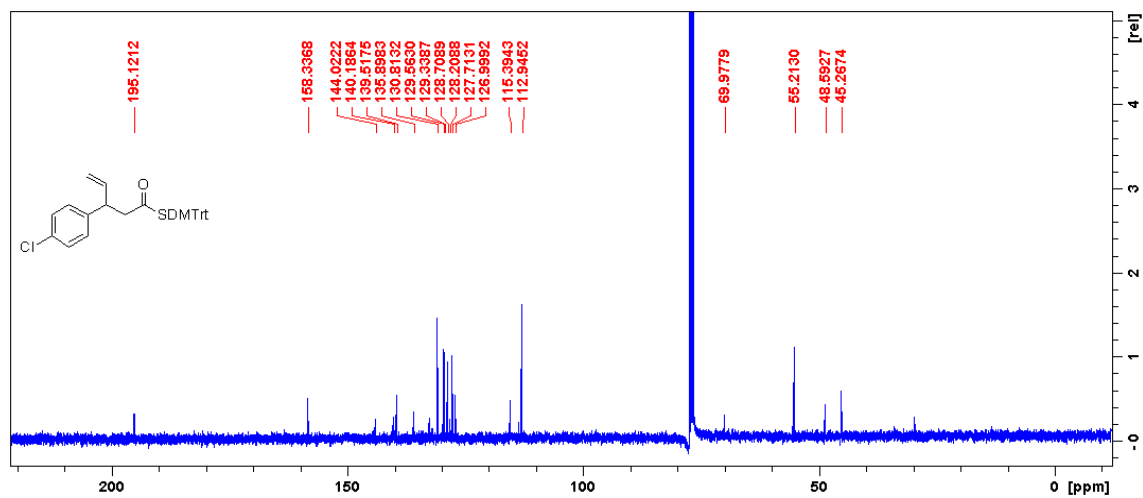


Supplementary Figure S18.

55 ^1H NMR (400 MHz, CDCl_3):

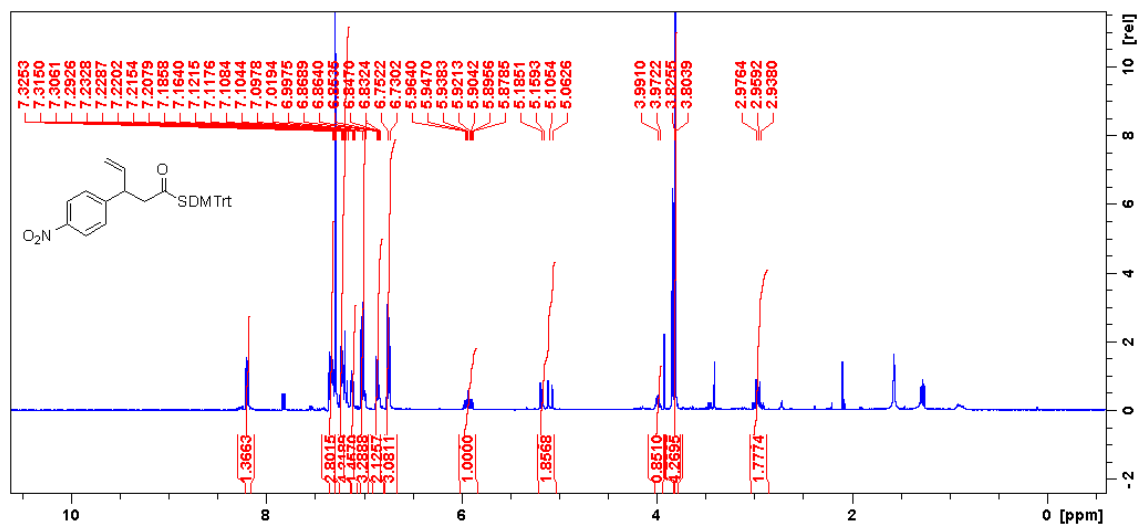


55 ^{13}C NMR (100 MHz, CDCl_3):

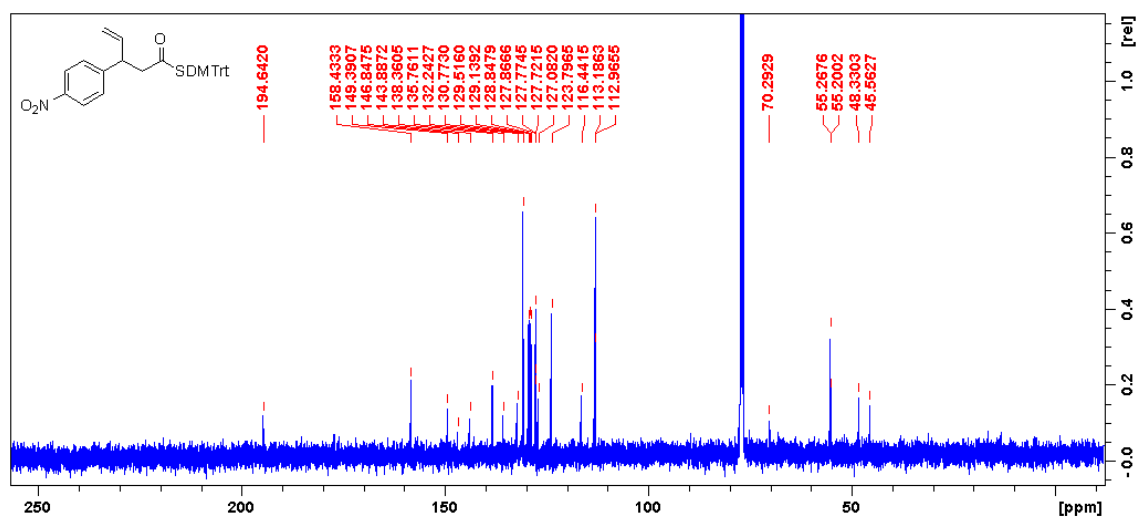


Supplementary Figure S19.

56 ^1H NMR (400 MHz, CDCl_3):

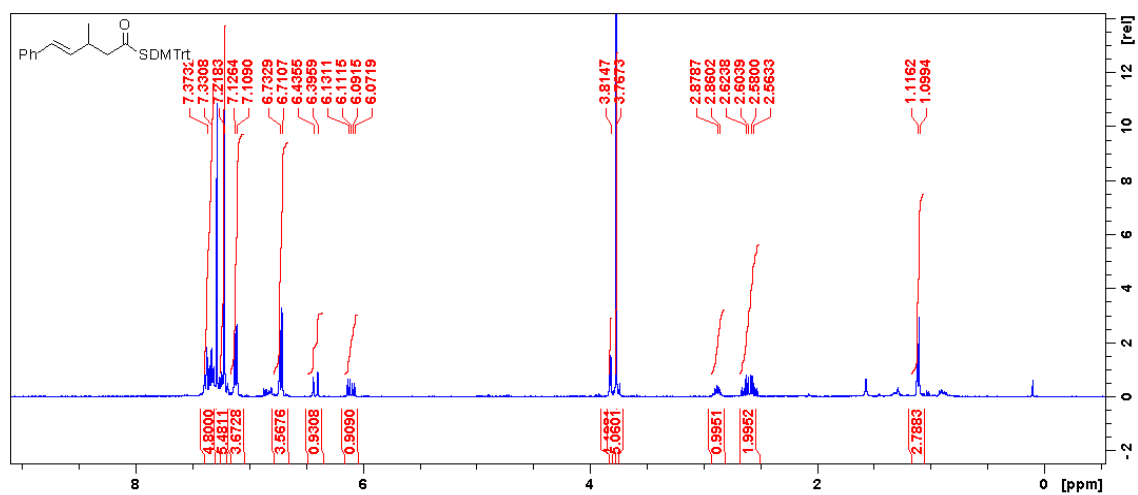


56 ^{13}C NMR (100 MHz, CDCl_3):

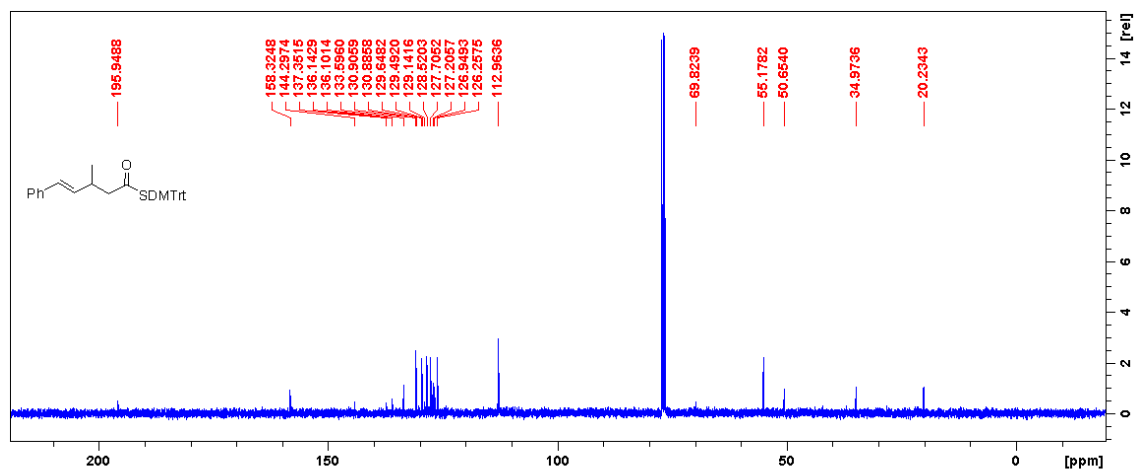


Supplementary Figure S20.

57 ^1H NMR (400 MHz, CDCl_3):

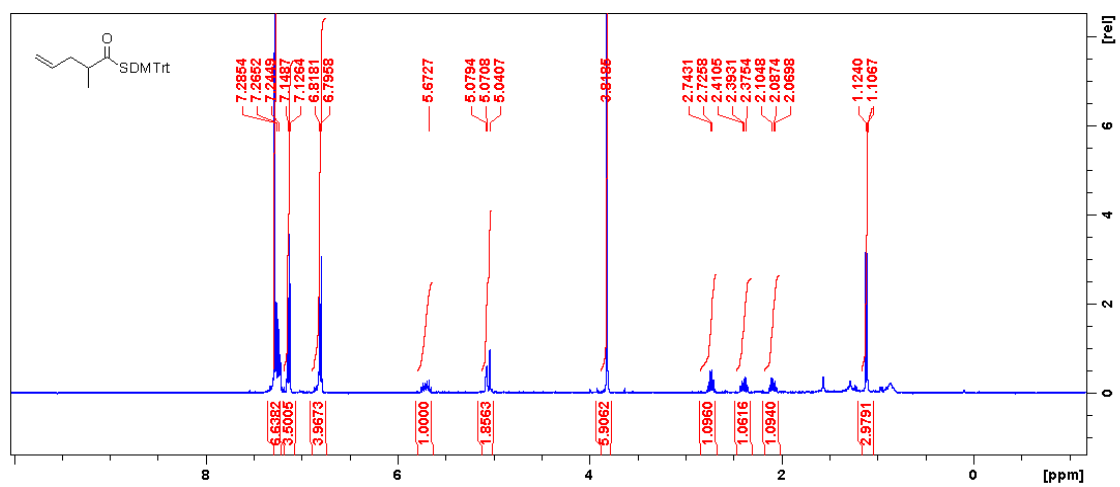


57 ^{13}C NMR (100 MHz, CDCl_3):

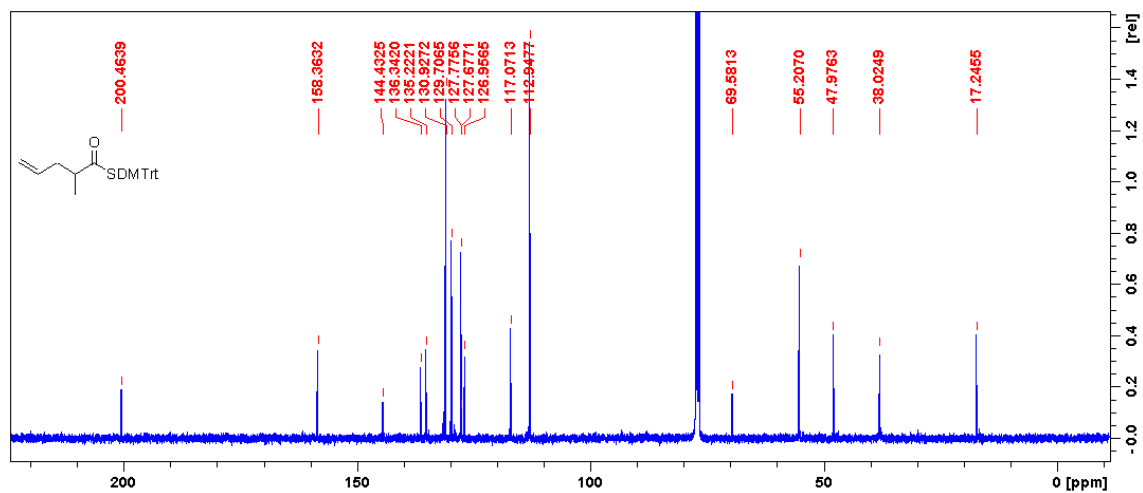


Supplementary Figure S21.

58 ^1H NMR (400 MHz, CDCl_3):

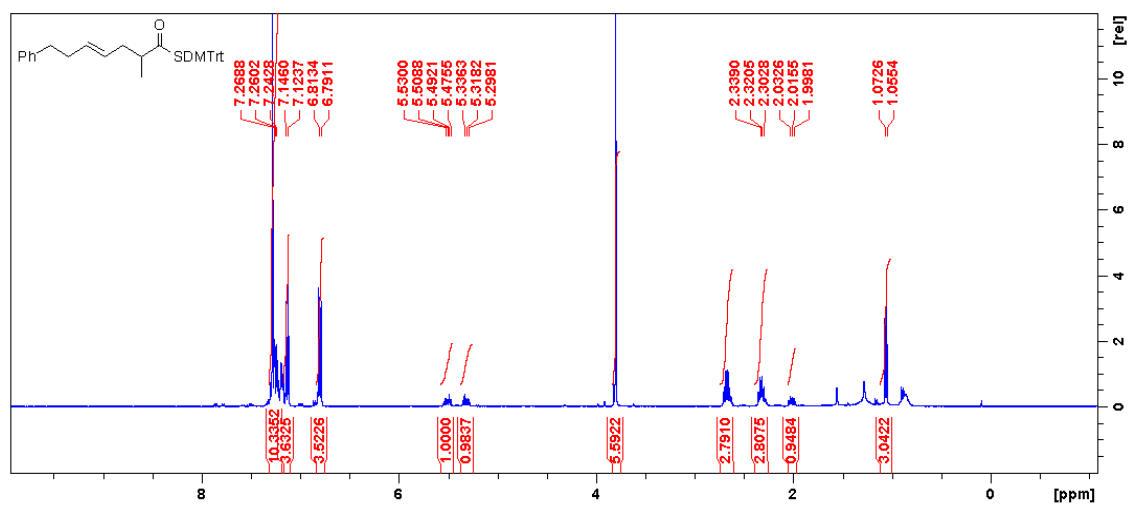


58 ^{13}C NMR (100 MHz, CDCl_3):

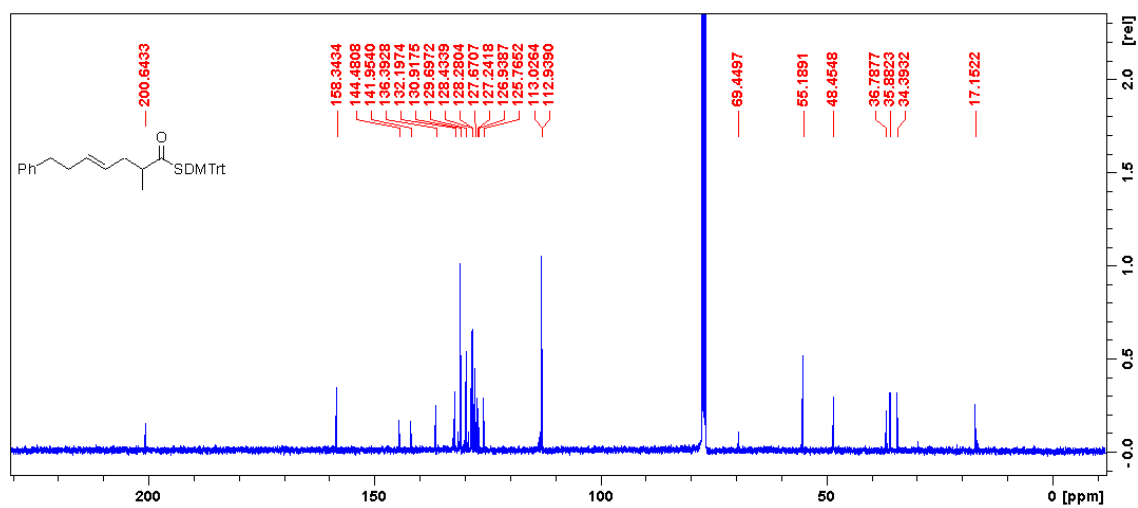


Supplementary Figure S22.

59 ^1H NMR (400 MHz, CDCl_3):

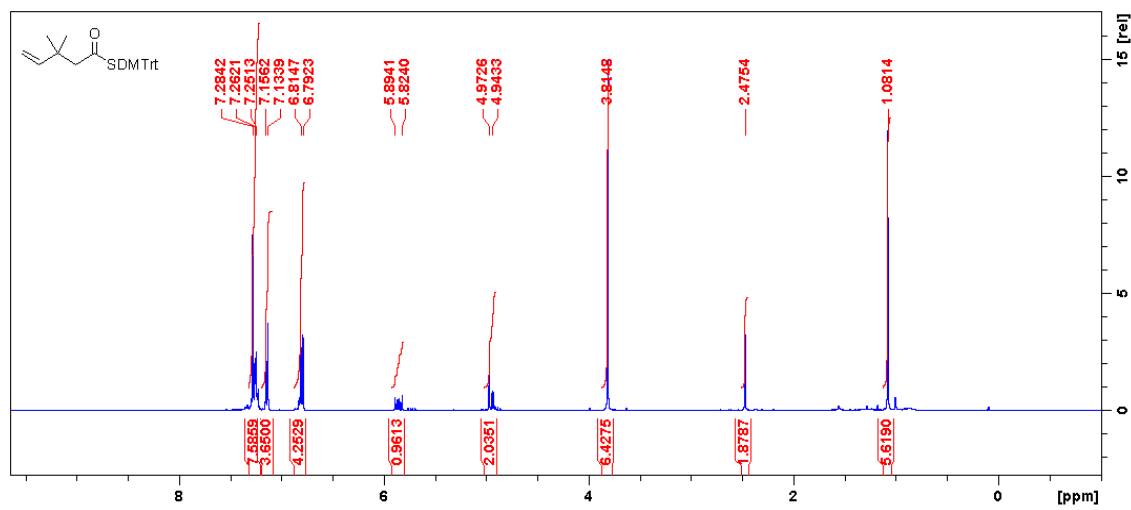


59 ^{13}C NMR (100 MHz, CDCl_3):

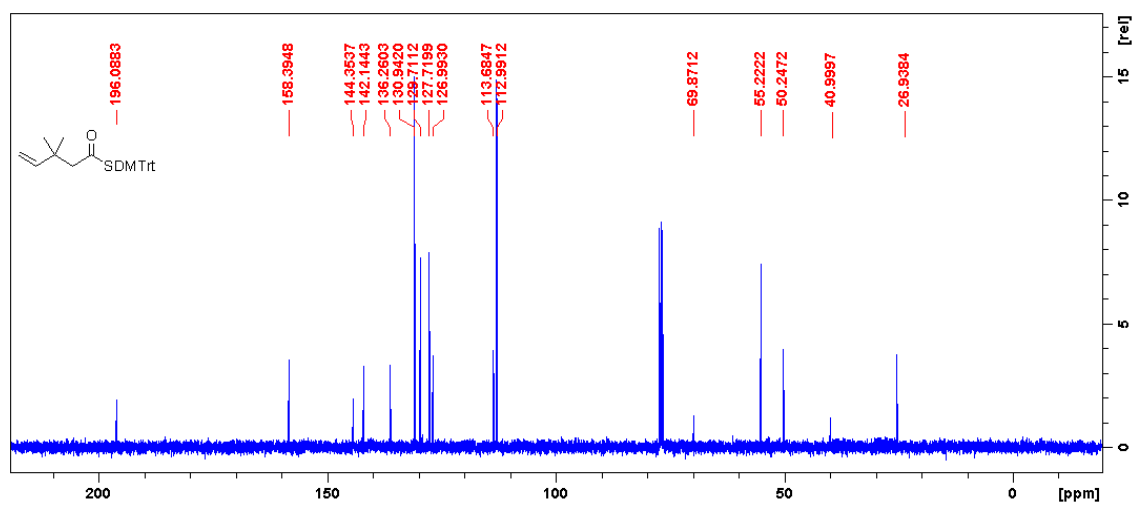


Supplementary Figure S23.

60 ^1H NMR (400 MHz, CDCl_3):

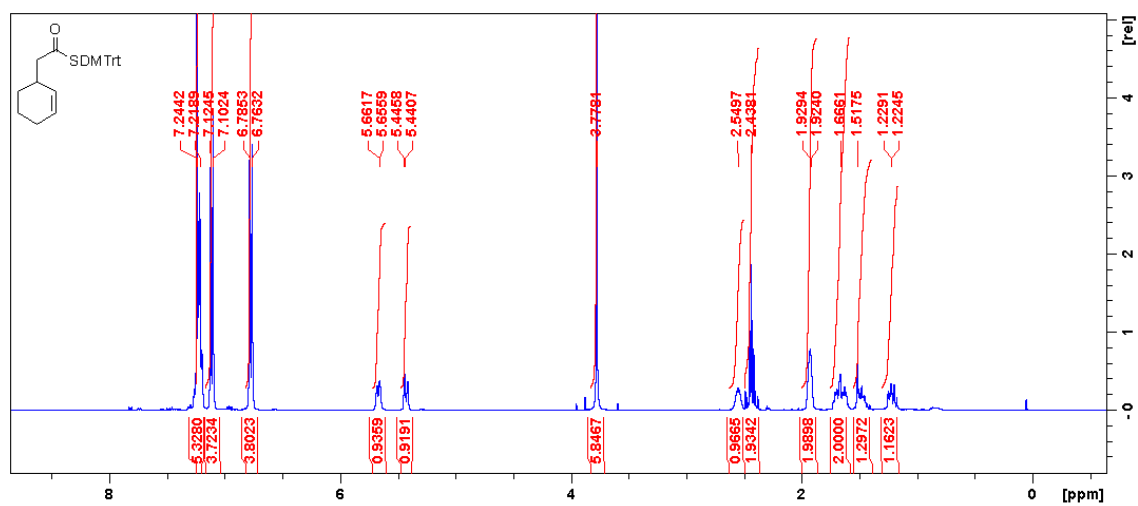


60 ^{13}C NMR (100 MHz, CDCl_3):

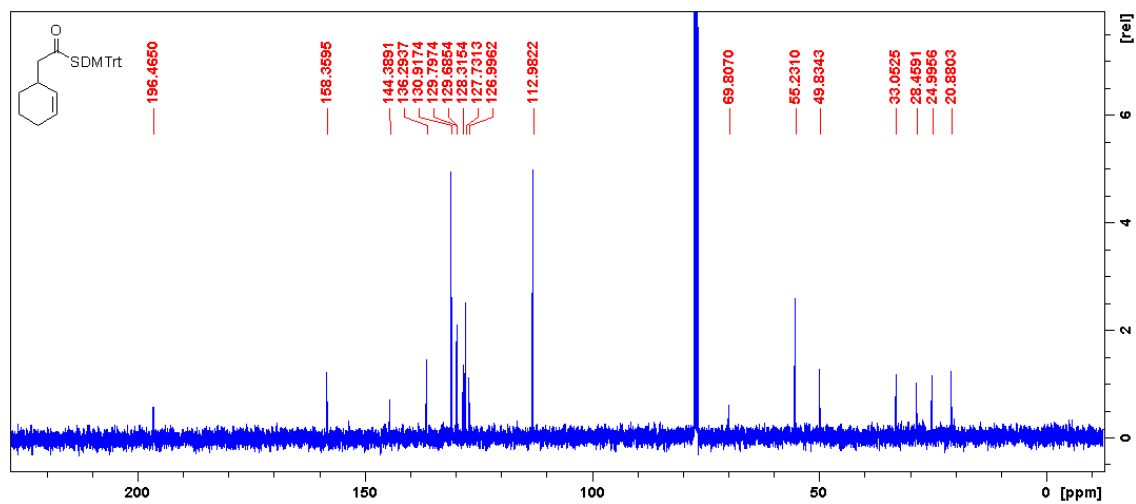


Supplementary Figure S24.

61 ^1H NMR (400 MHz, CDCl_3):

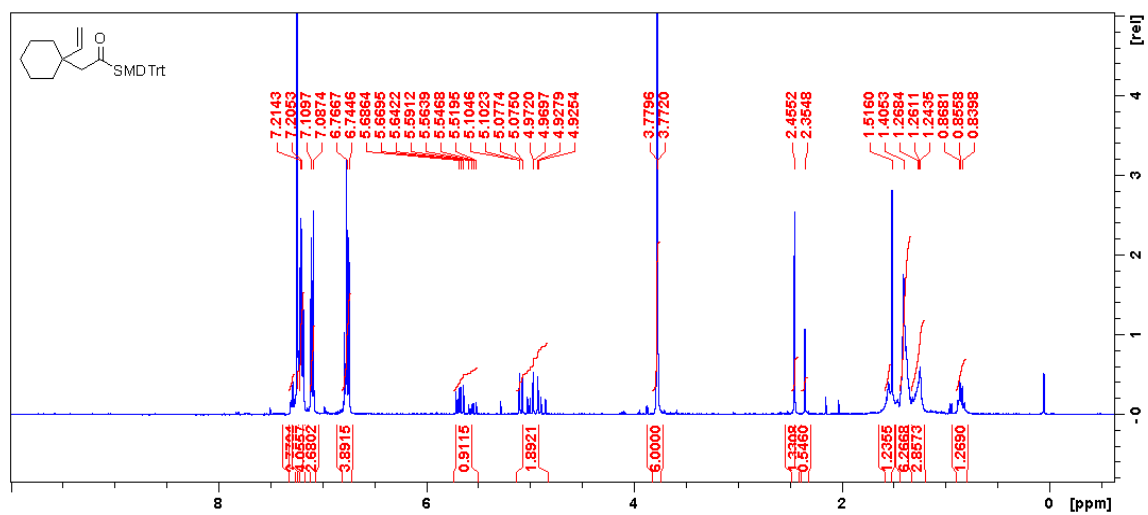


61 ^{13}C NMR (100 MHz, CDCl_3):

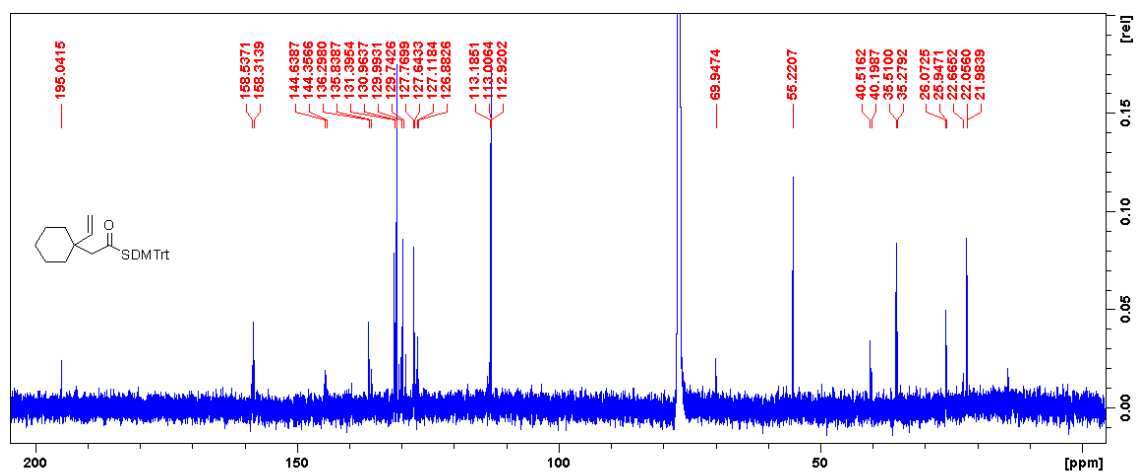


Supplementary Figure S25.

62 ^1H NMR (400 MHz, CDCl_3):

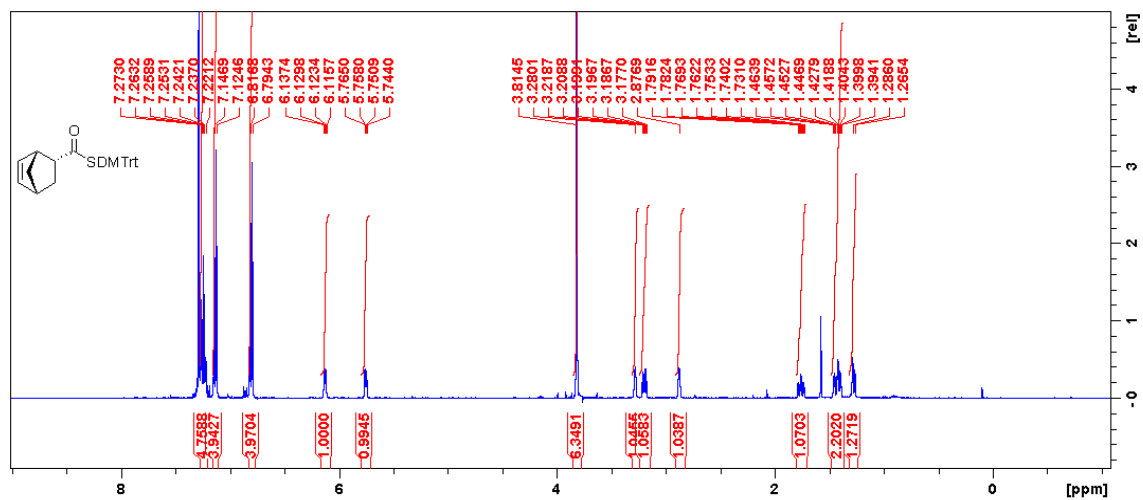


62 ^{13}C NMR (100 MHz, CDCl_3):

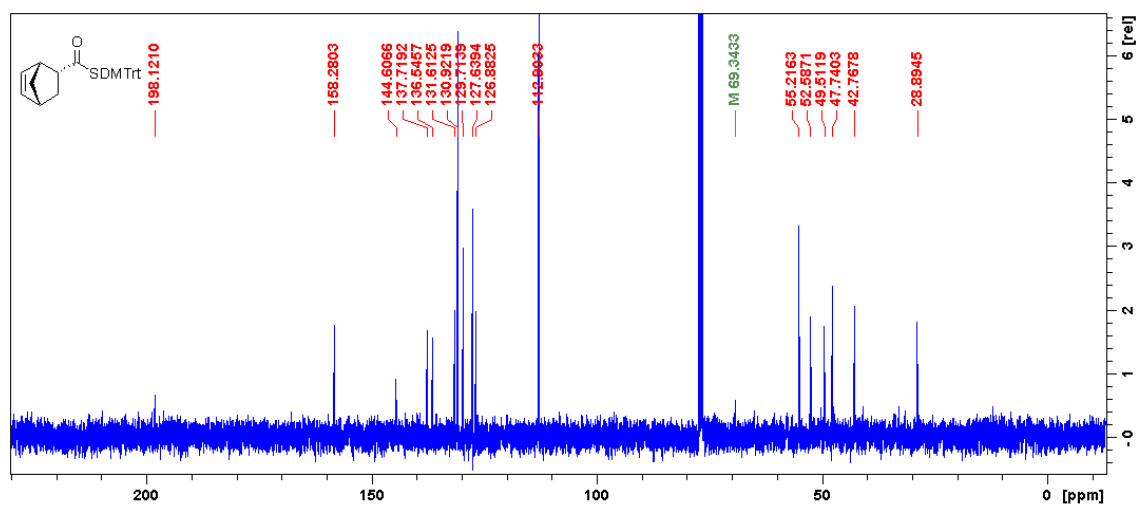


Supplementary Figure S26.

63 ^1H NMR (400 MHz, CDCl_3):

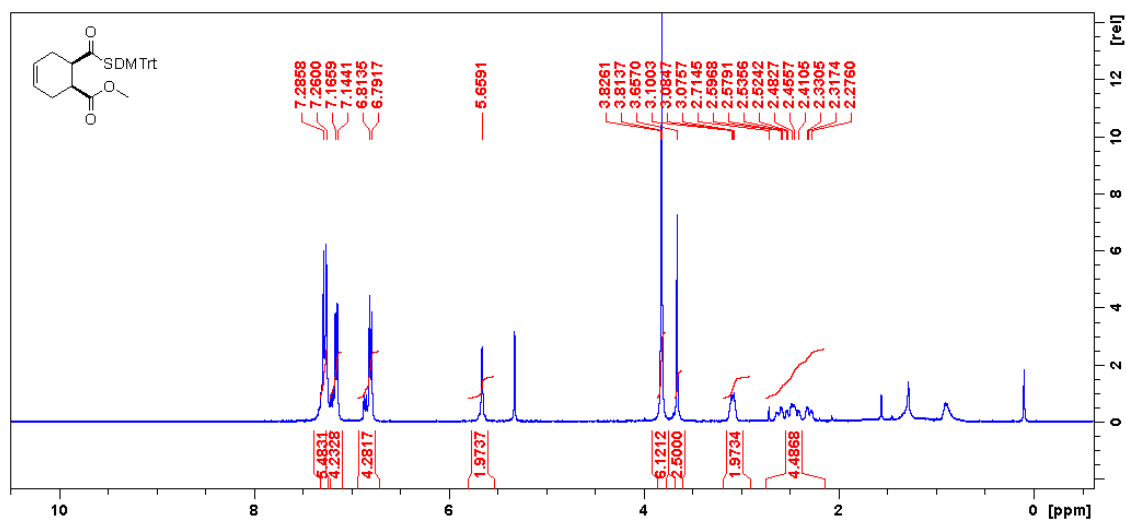


63 ^{13}C NMR (100 MHz, CDCl_3):

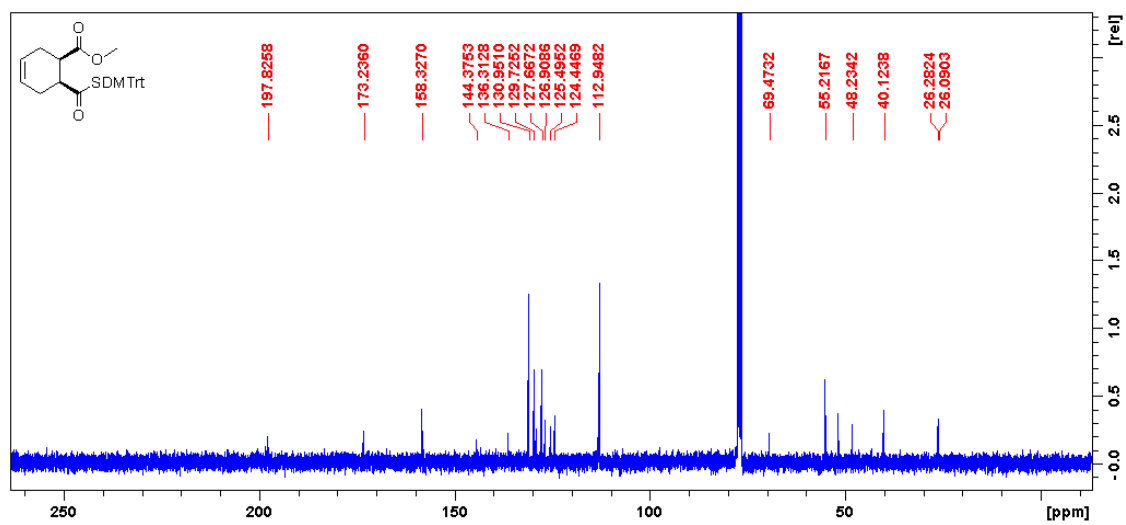


Supplementary Figure S27.

64 ^1H NMR (400 MHz, CDCl_3):

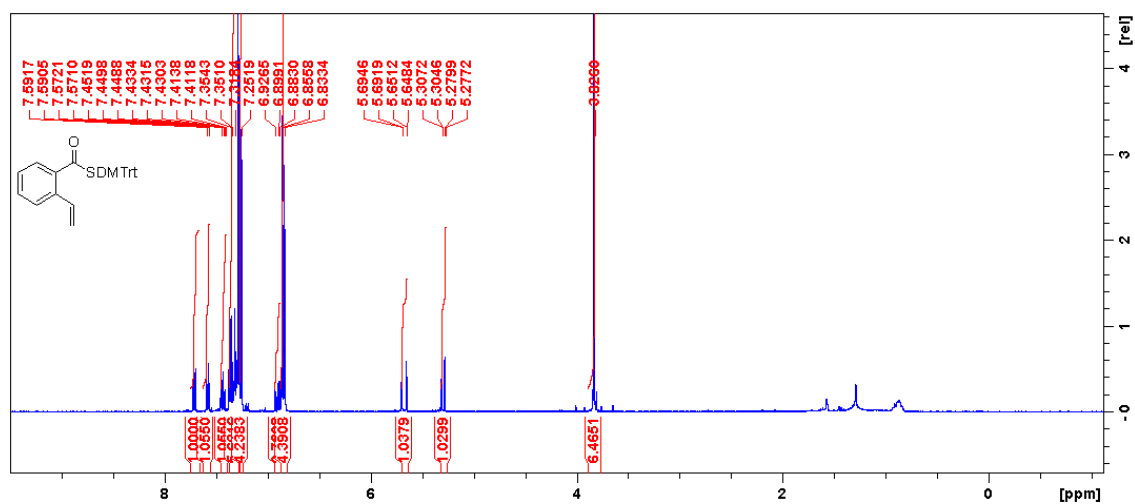


64 ^{13}C NMR (100 MHz, CDCl_3):

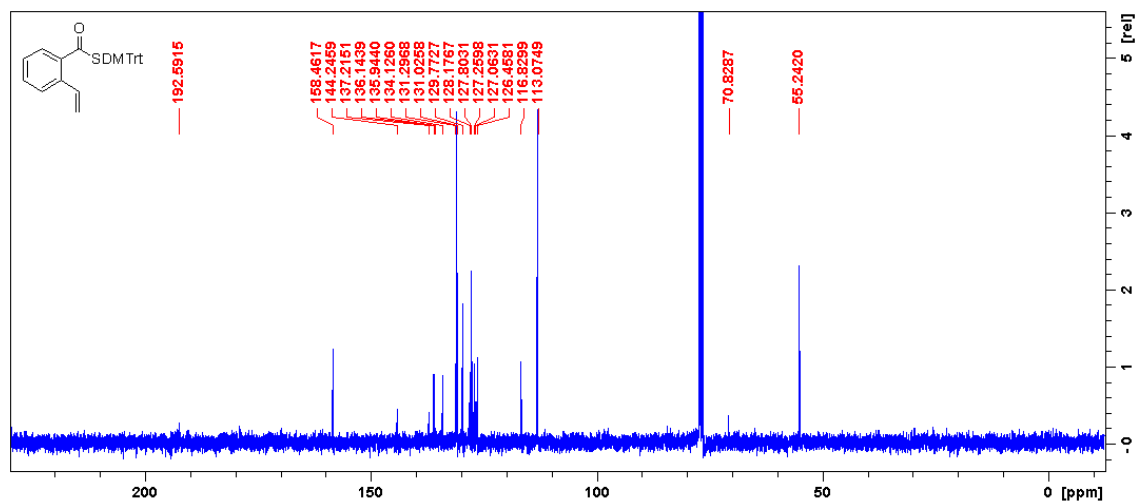


Supplementary Figure S28.

65 ^1H NMR (400 MHz, CDCl_3):

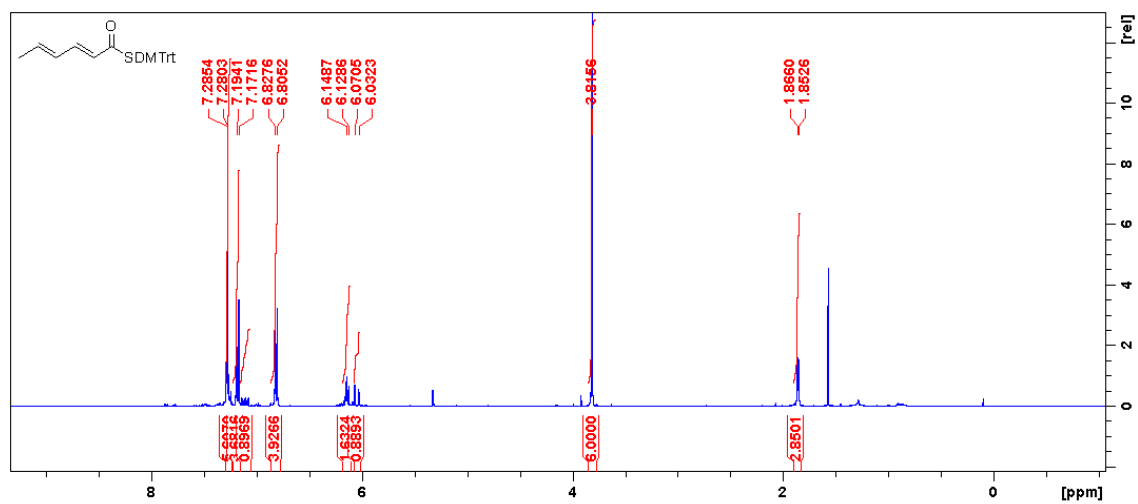


65 ^{13}C NMR (100 MHz, CDCl_3):

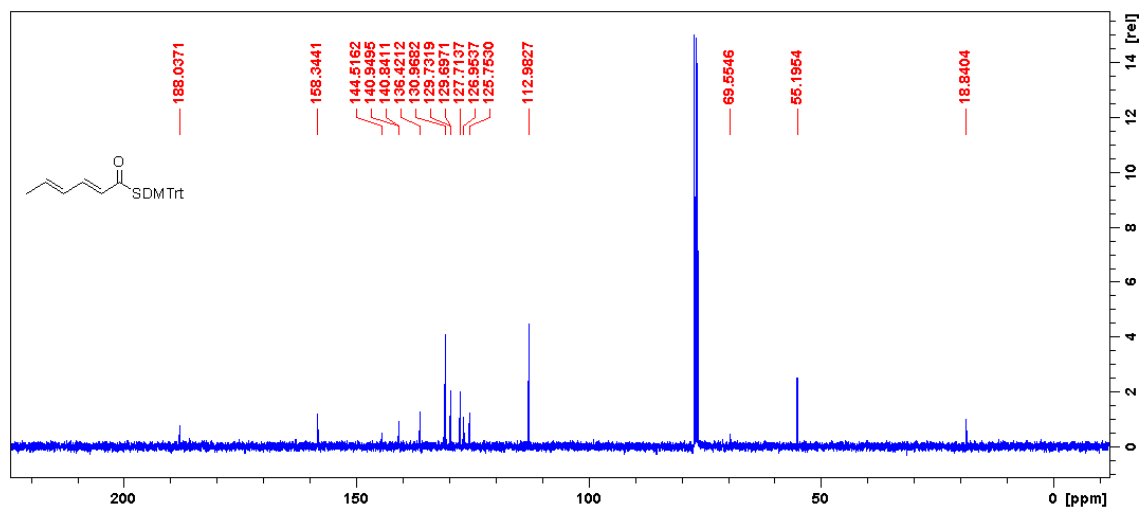


Supplementary Figure S29.

66 ^1H NMR (400 MHz, CDCl_3):

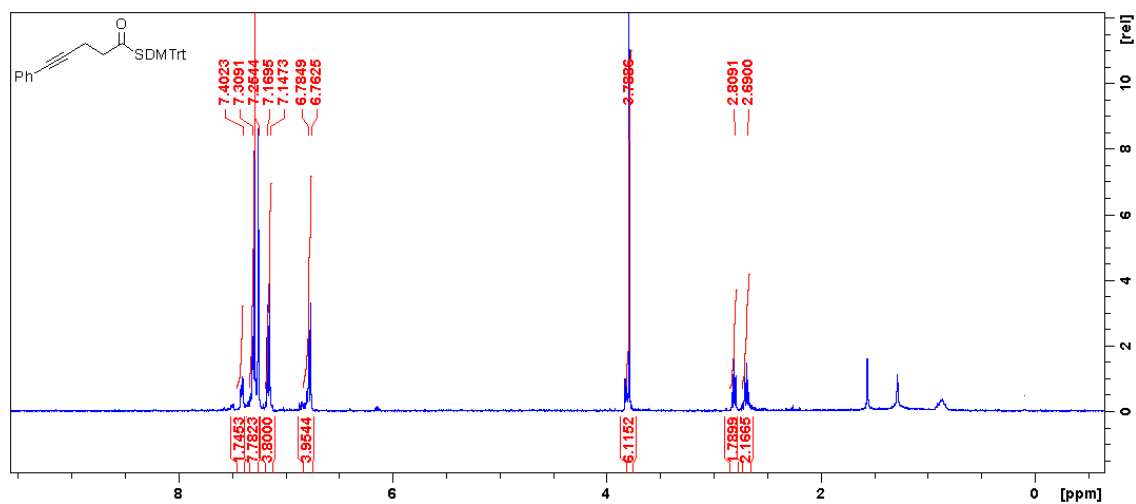


66 ^{13}C NMR (100 MHz, CDCl_3):

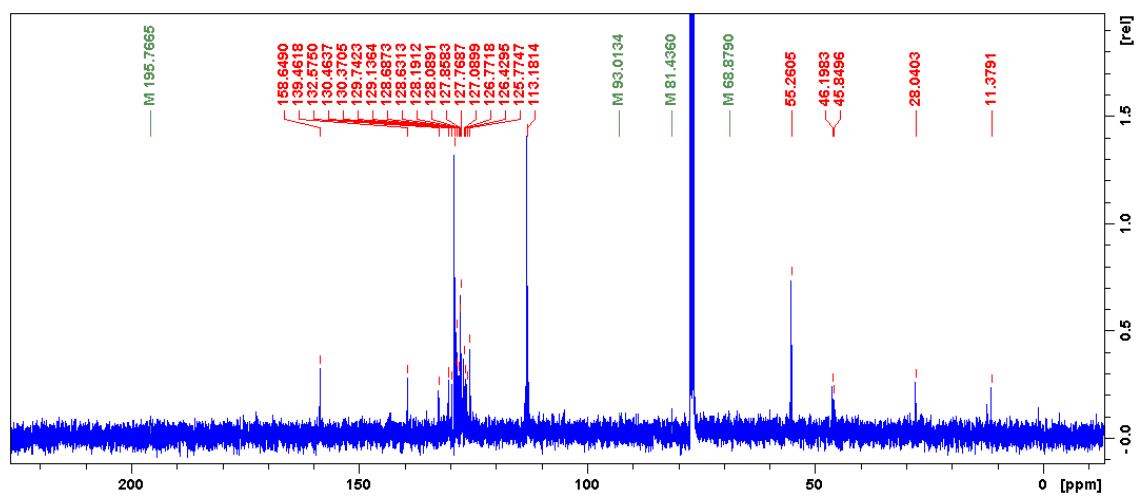


Supplementary Figure S30.

67 ^1H NMR (400 MHz, CDCl_3):

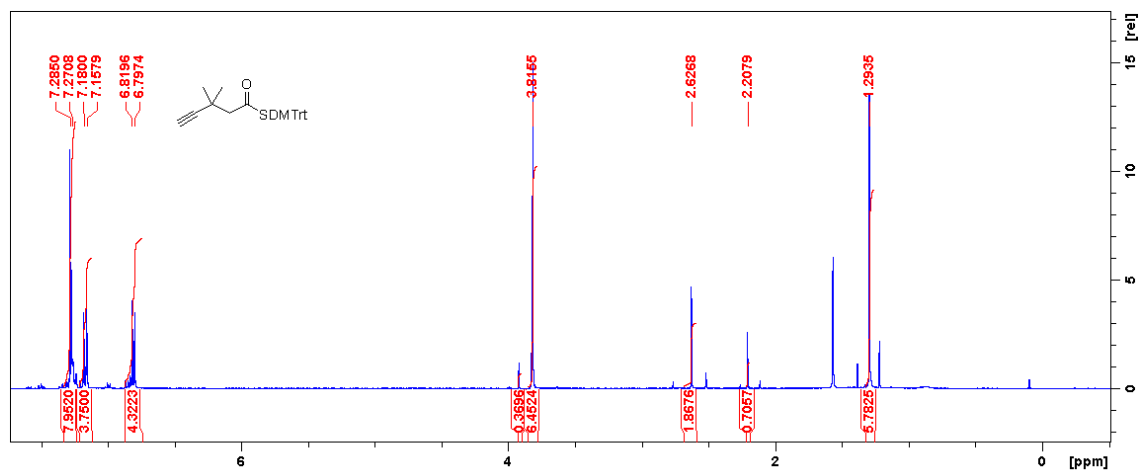


68 ^{13}C NMR (100 MHz, CDCl_3):

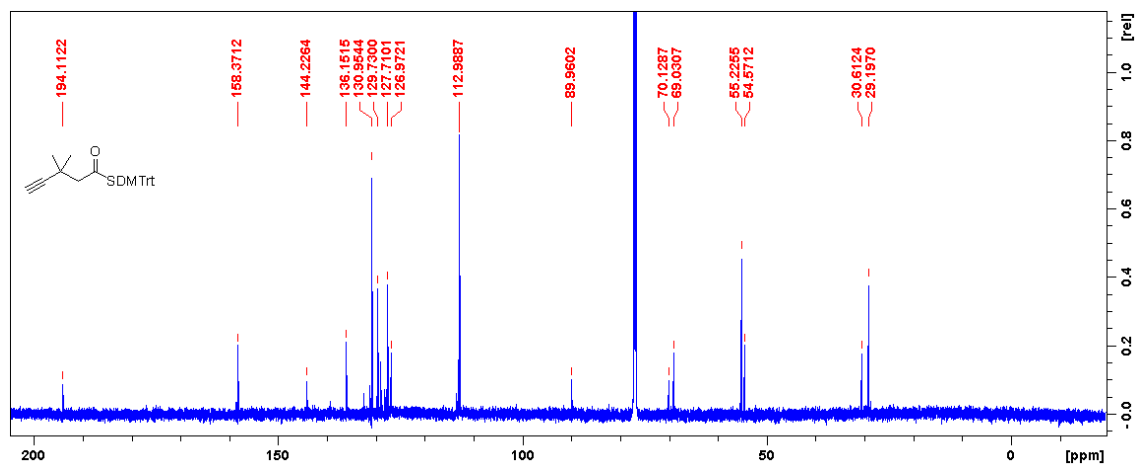


Supplementary Figure S32.

69 ^1H NMR (400 MHz, CDCl_3):

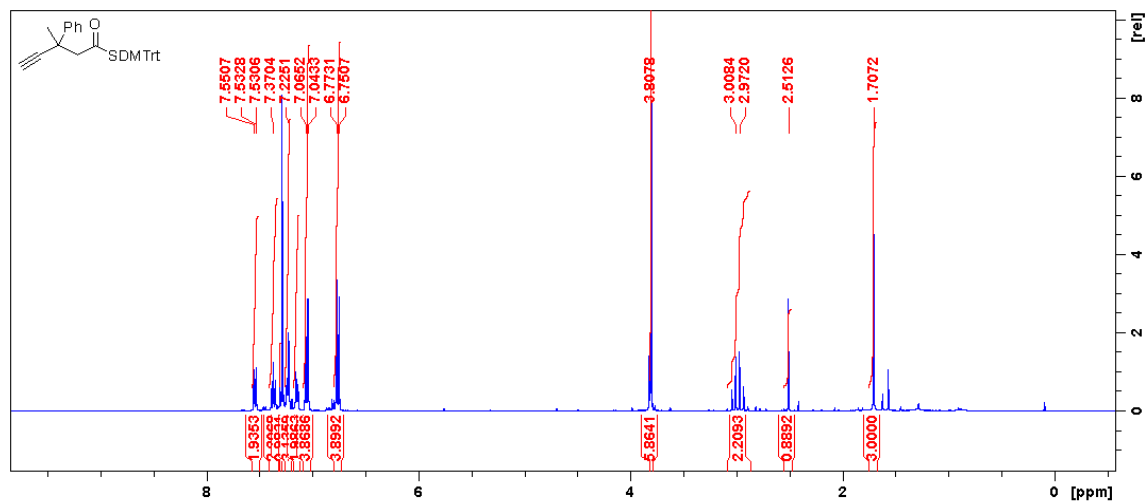


69 ^{13}C NMR (100 MHz, CDCl_3):

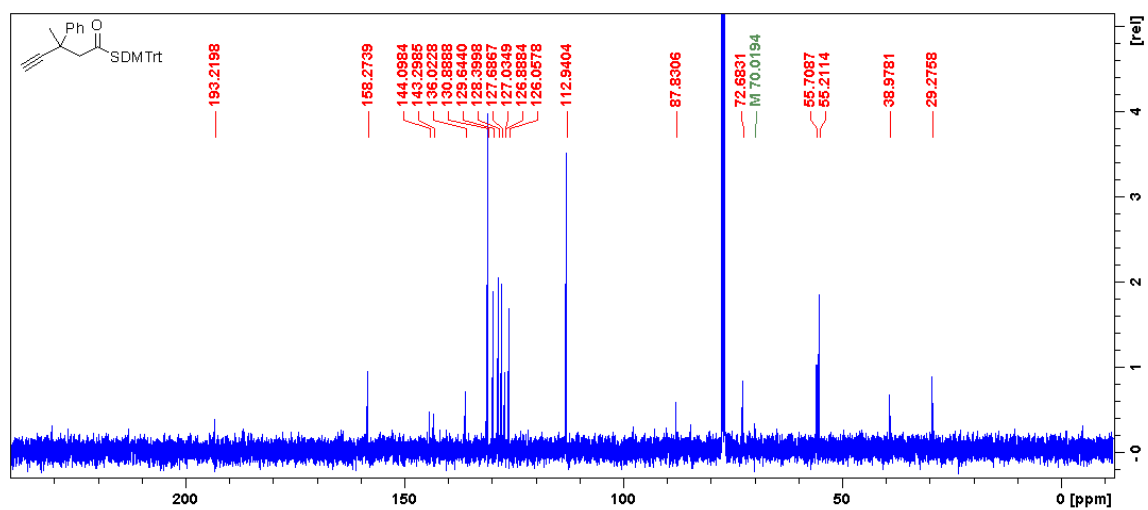


Supplementary Figure S33.

70 ^1H NMR (400 MHz, CDCl_3):

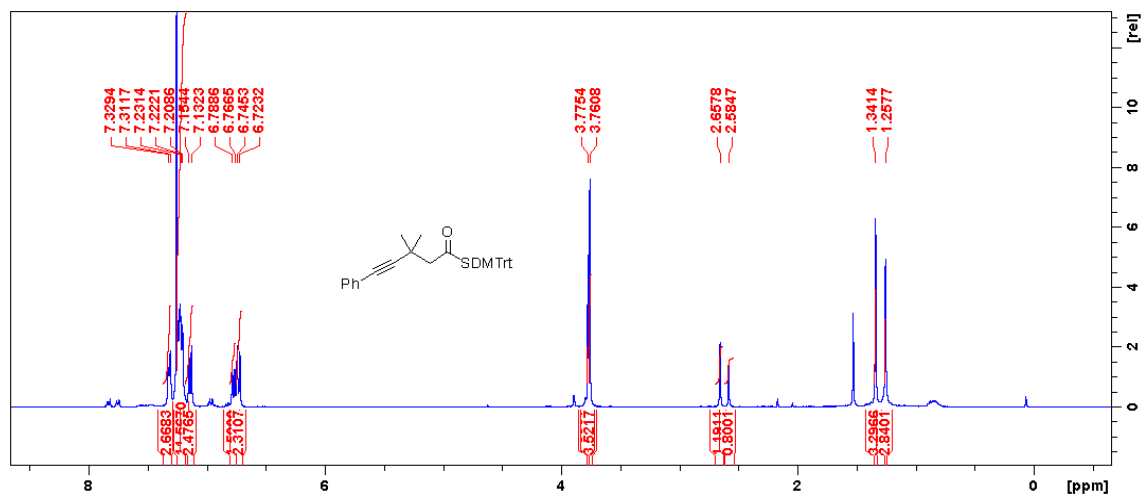


70 ^{13}C NMR (100 MHz, CDCl_3):

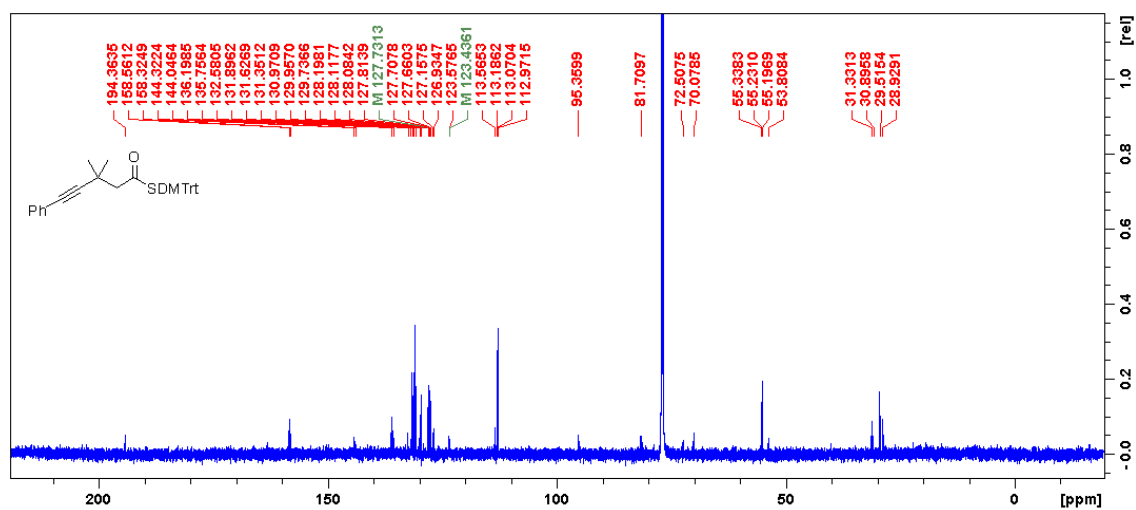


Supplementary Figure S34.

71 ^1H NMR (400 MHz, CDCl_3):

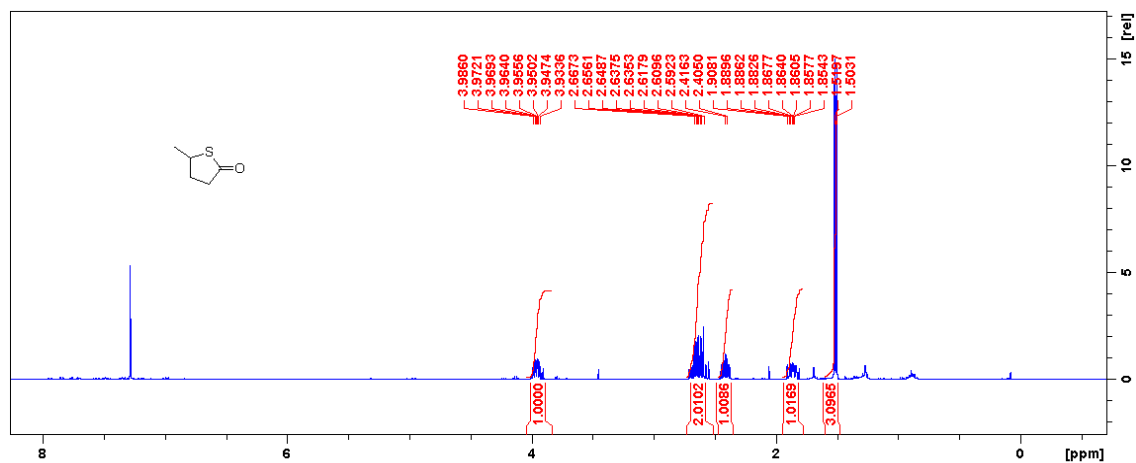


71 ^{13}C NMR (100 MHz, CDCl_3):

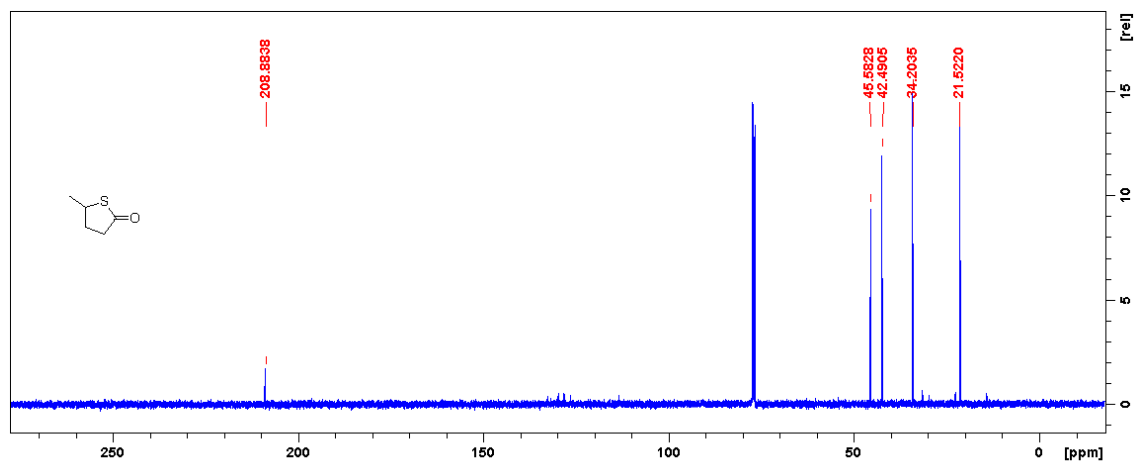


Supplementary Figure S35.

1a ^1H NMR (400 MHz, CDCl_3):

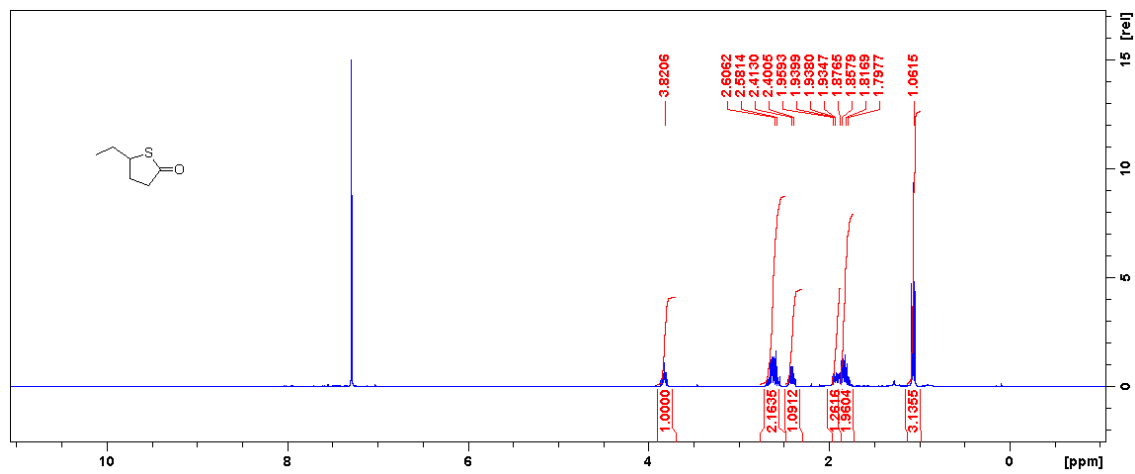


1a ^{13}C NMR (100 MHz, CDCl_3):

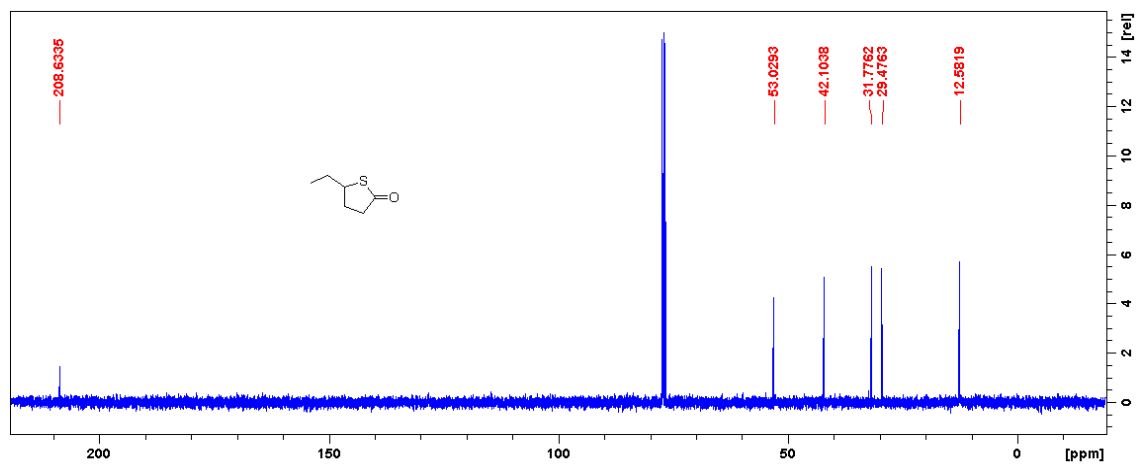


Supplementary Figure S36.

1b ^1H NMR (400 MHz, CDCl_3):

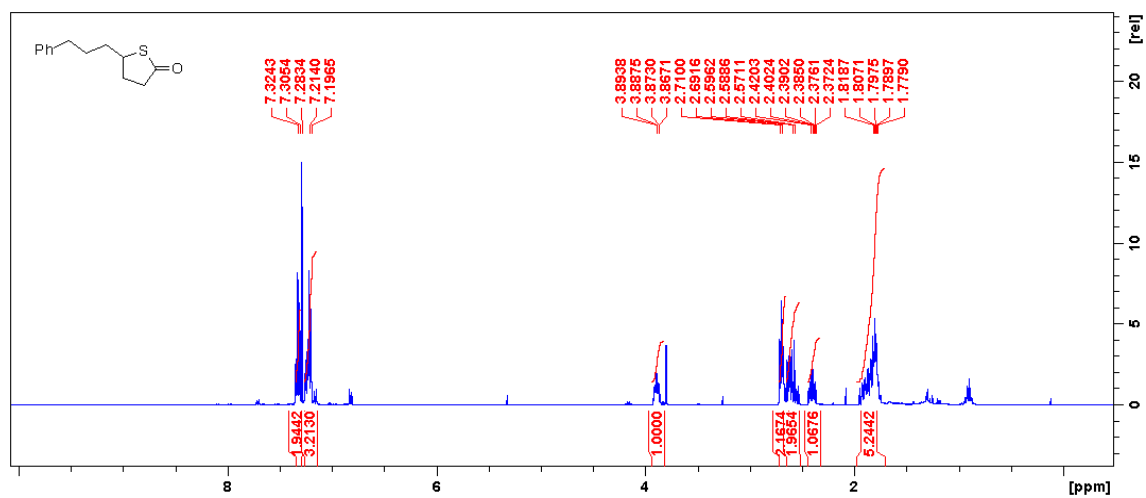


1b ^{13}C NMR (100 MHz, CDCl_3):

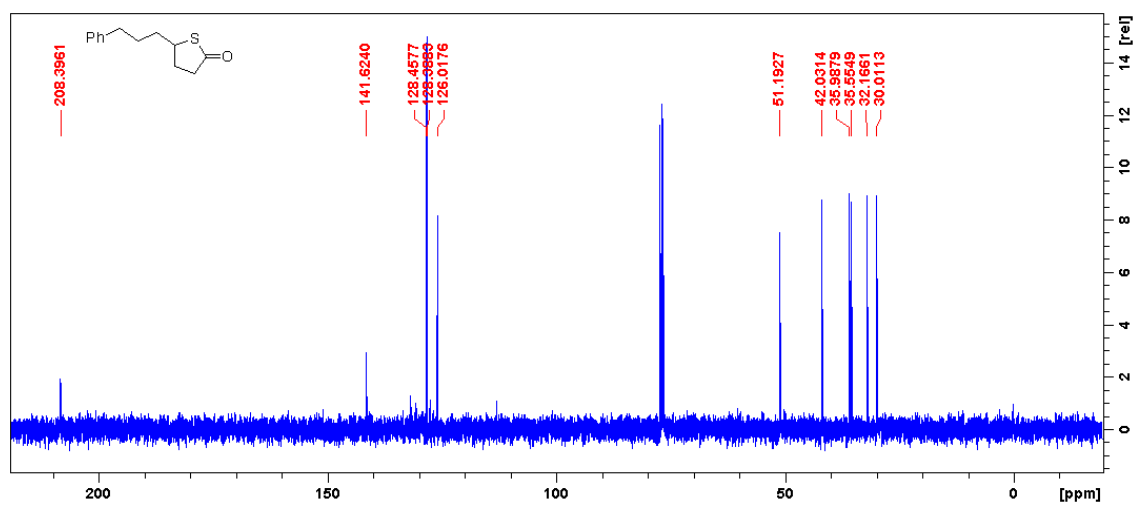


Supplementary Figure S37.

1c ^1H NMR (400 MHz, CDCl_3):

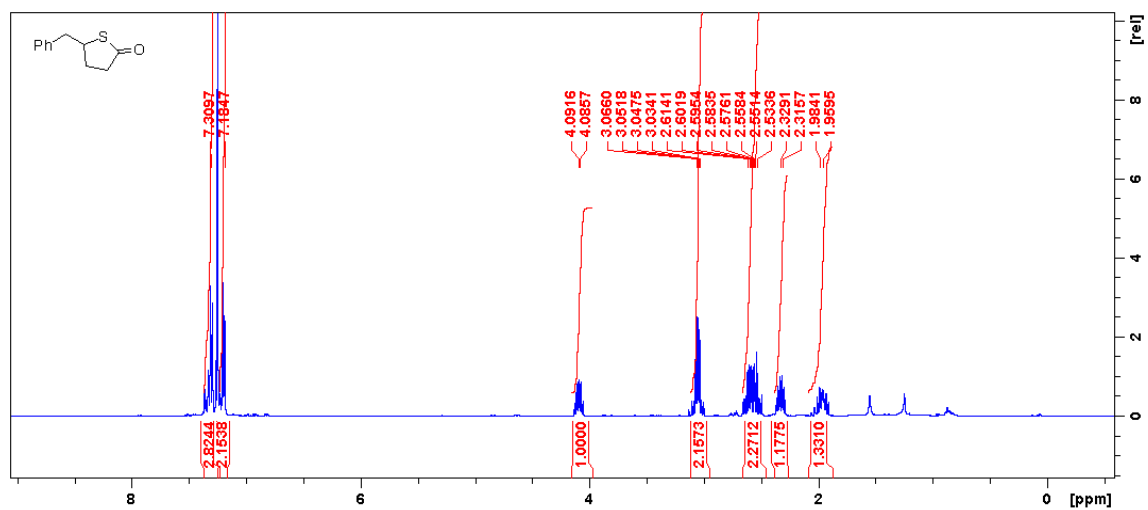


1c ^{13}C NMR (100 MHz, CDCl_3):

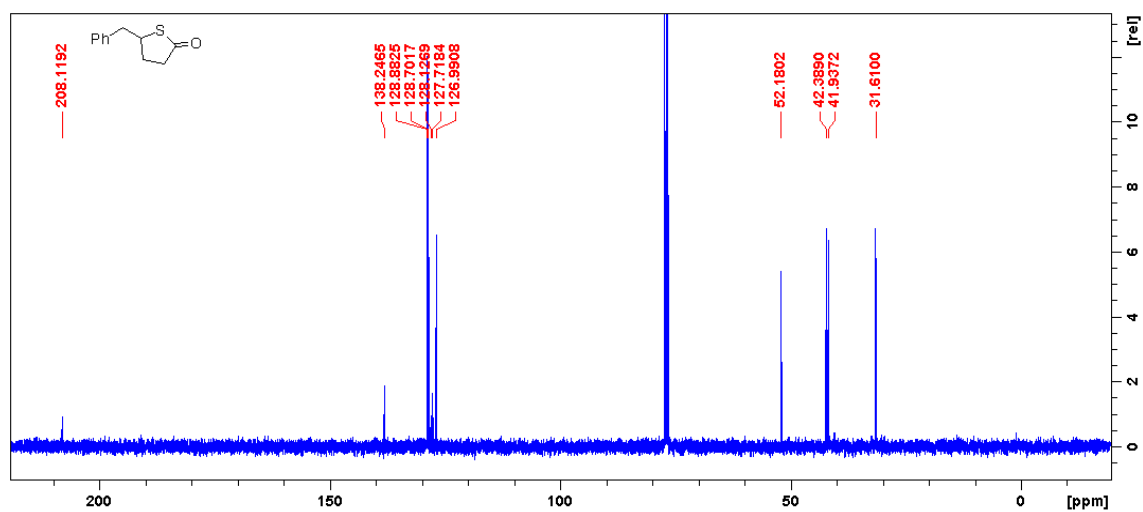


Supplementary Figure S38.

1d ^1H NMR (400 MHz, CDCl_3):

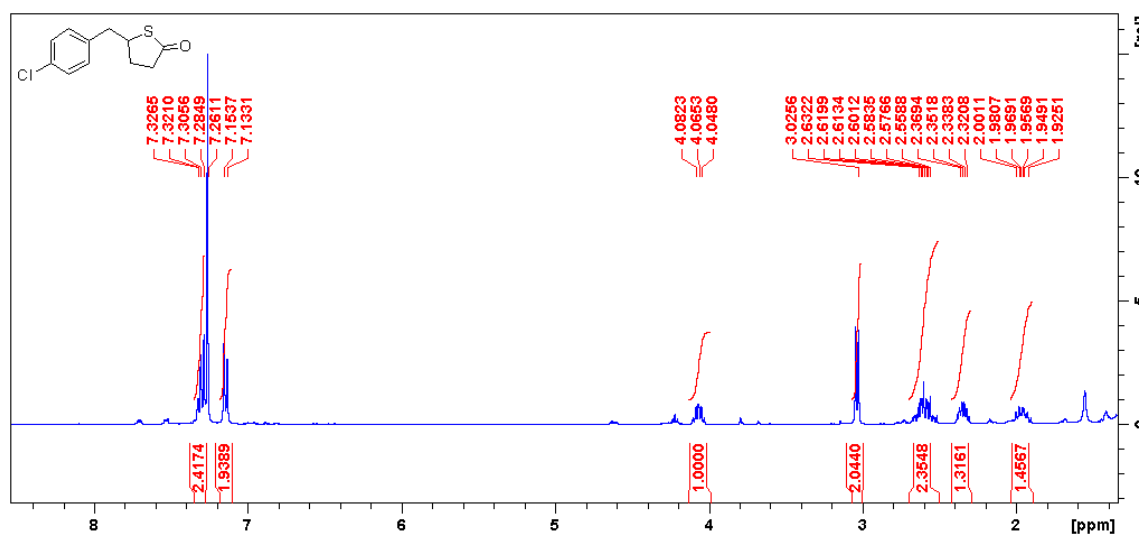


1d ^{13}C NMR (100 MHz, CDCl_3):

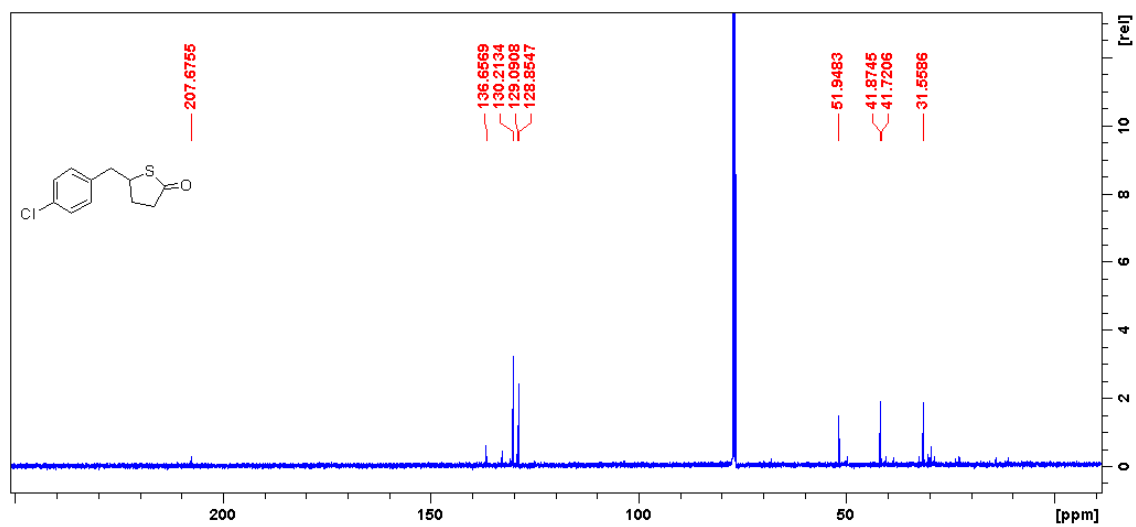


Supplementary Figure S39.

1e ^1H NMR (400 MHz, CDCl_3):

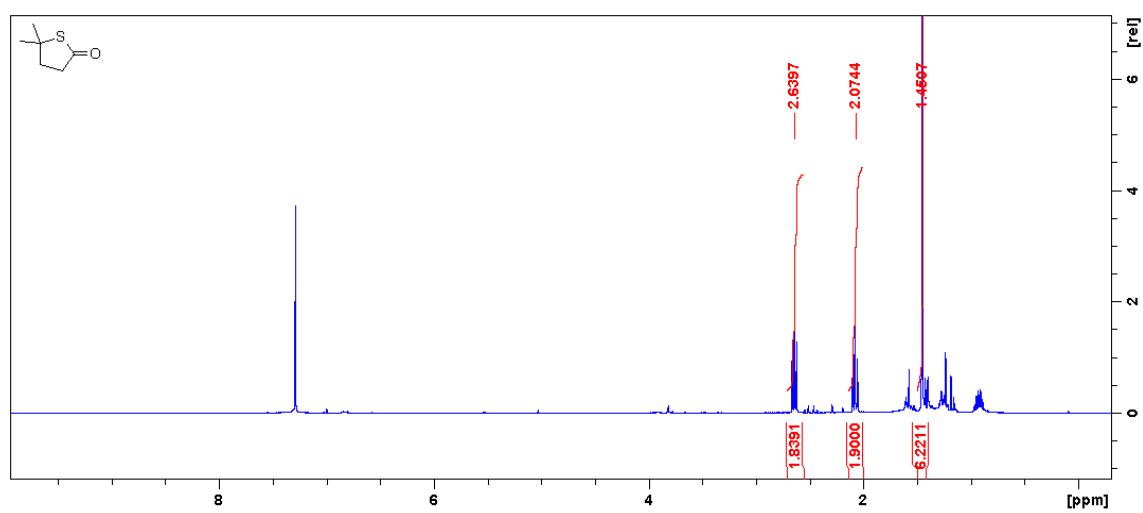


1e ^{13}C NMR (100 MHz, CDCl_3):

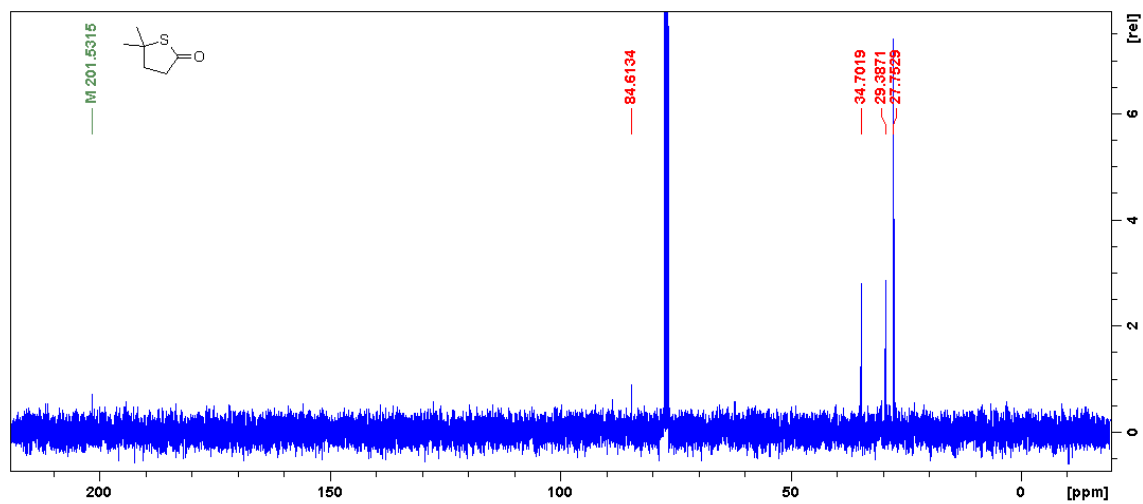


Supplementary Figure S40.

1f ^1H NMR (400 MHz, CDCl_3):

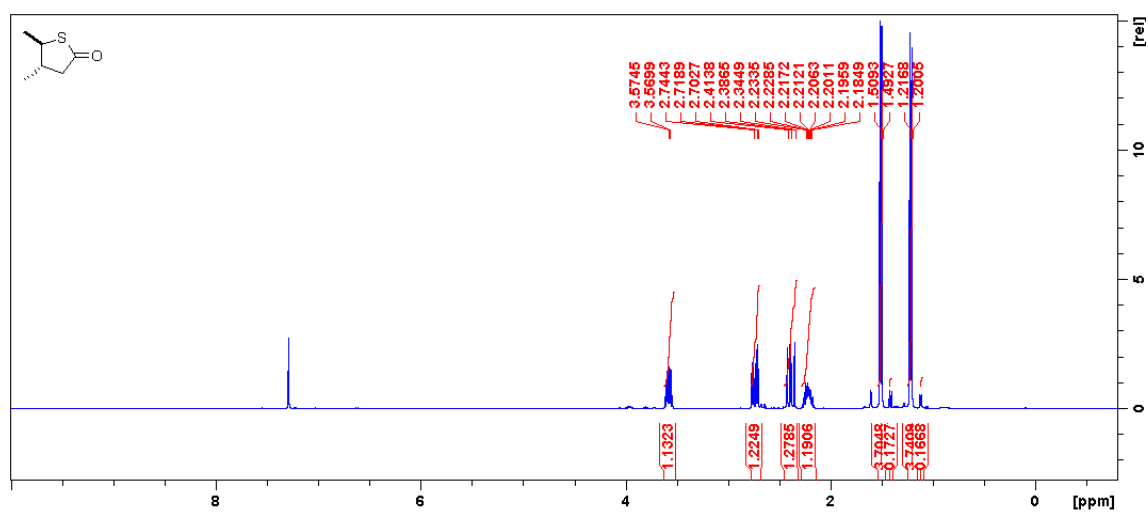


1f ^{13}C NMR (100 MHz, CDCl_3):

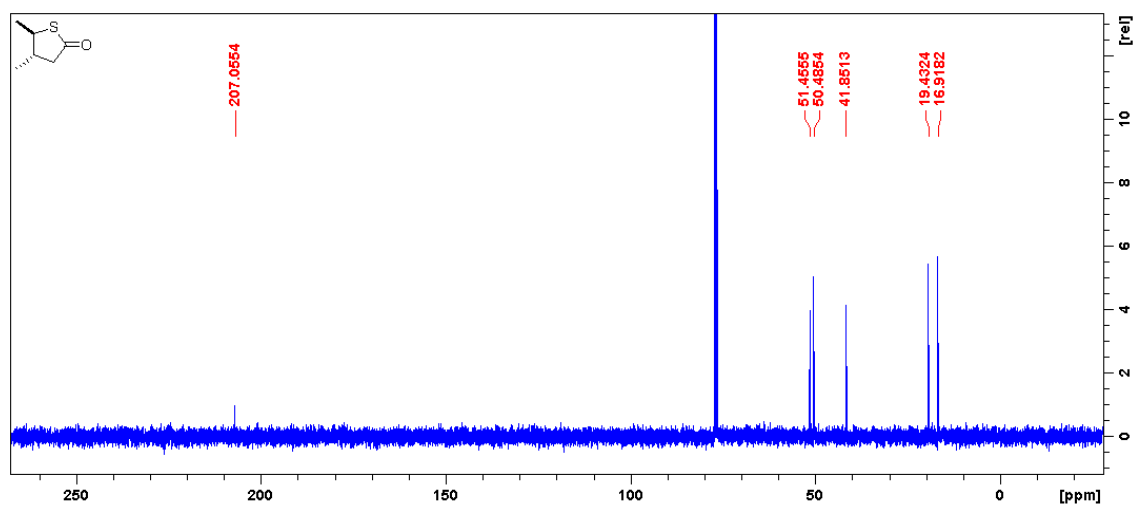


Supplementary Figure S41.

1g ^1H NMR (400 MHz, CDCl_3):

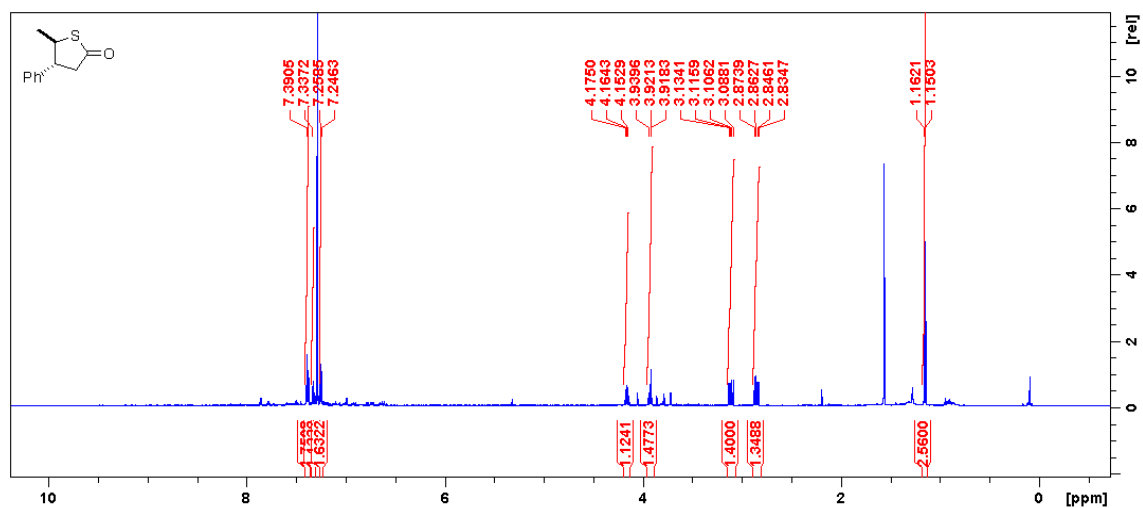


1g ^{13}C NMR (100 MHz, CDCl_3):

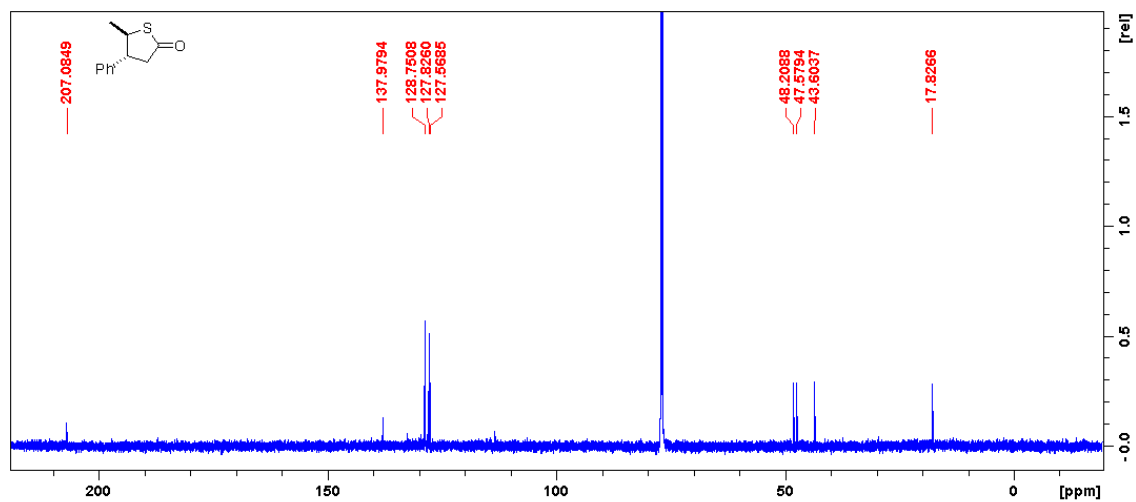


Supplementary Figure S42.

1h ^1H NMR (400 MHz, CDCl_3):

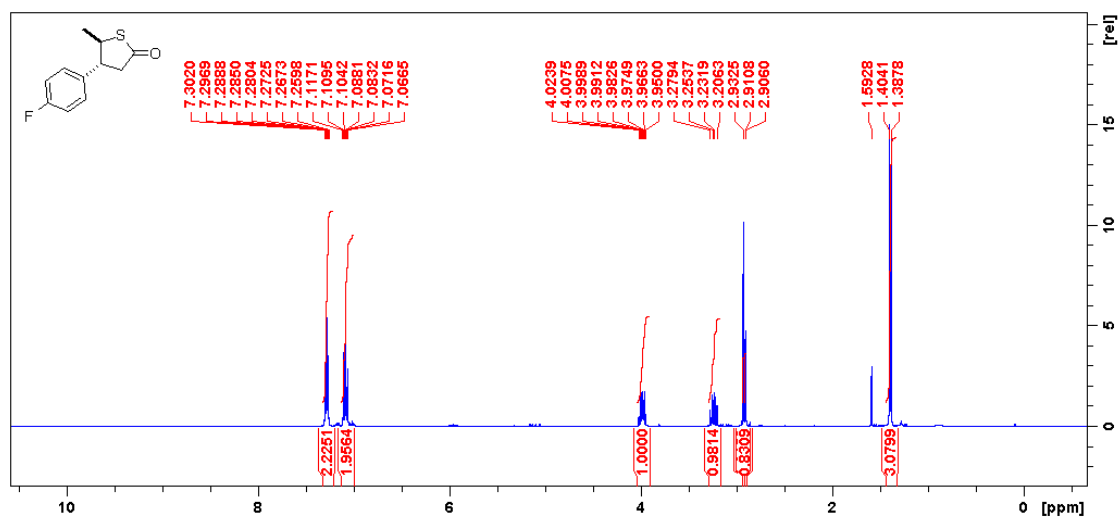


1h ^{13}C NMR (100 MHz, CDCl_3):

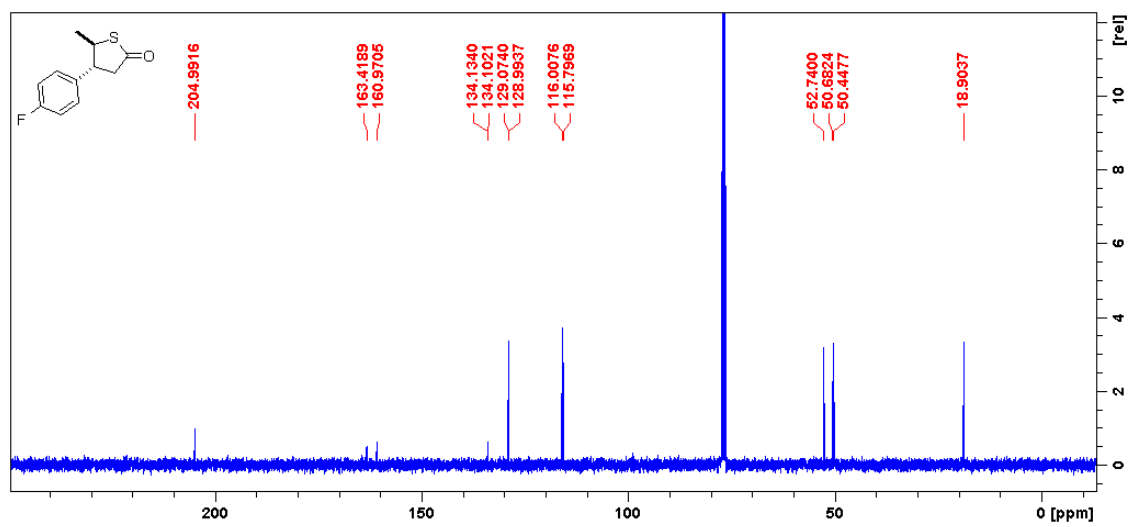


Supplementary Figure S43.

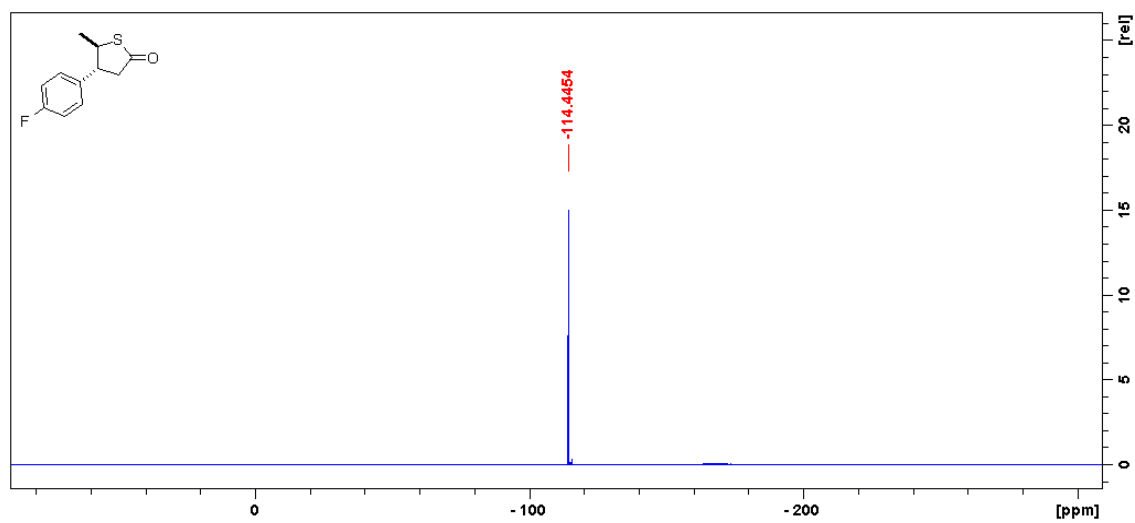
1i ^1H NMR (400 MHz, CDCl_3):



1i ^{13}C NMR (100 MHz, CDCl_3):

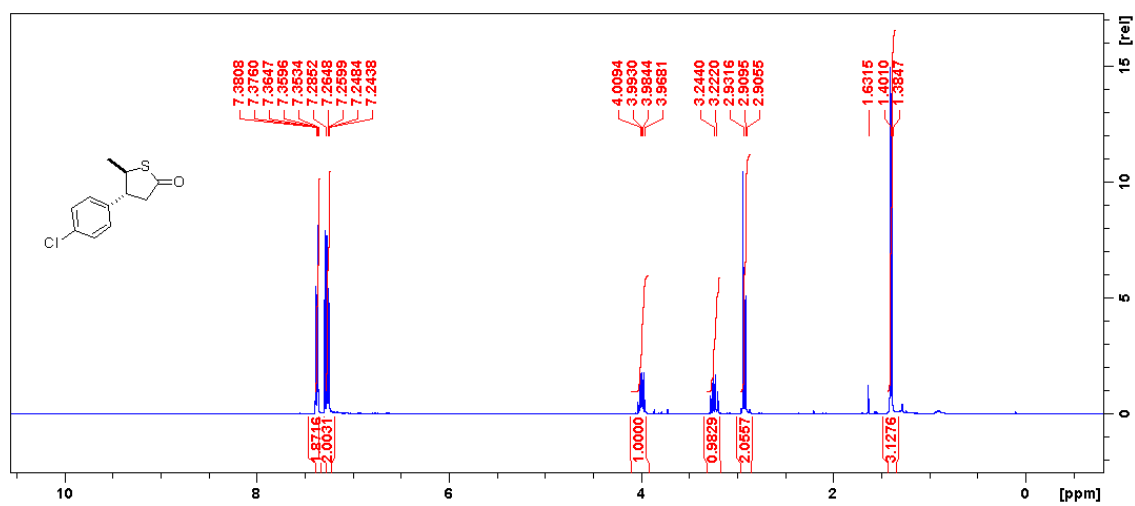


1i ^{19}F NMR (376 MHz, CDCl_3):

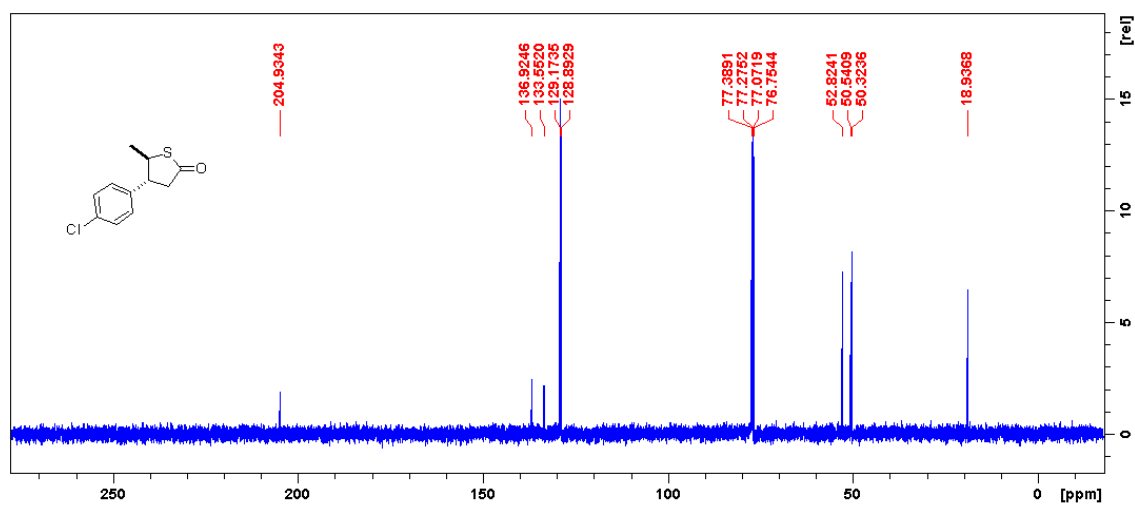


Supplementary Figure S44.

1j ¹H NMR (400 MHz, CDCl₃):

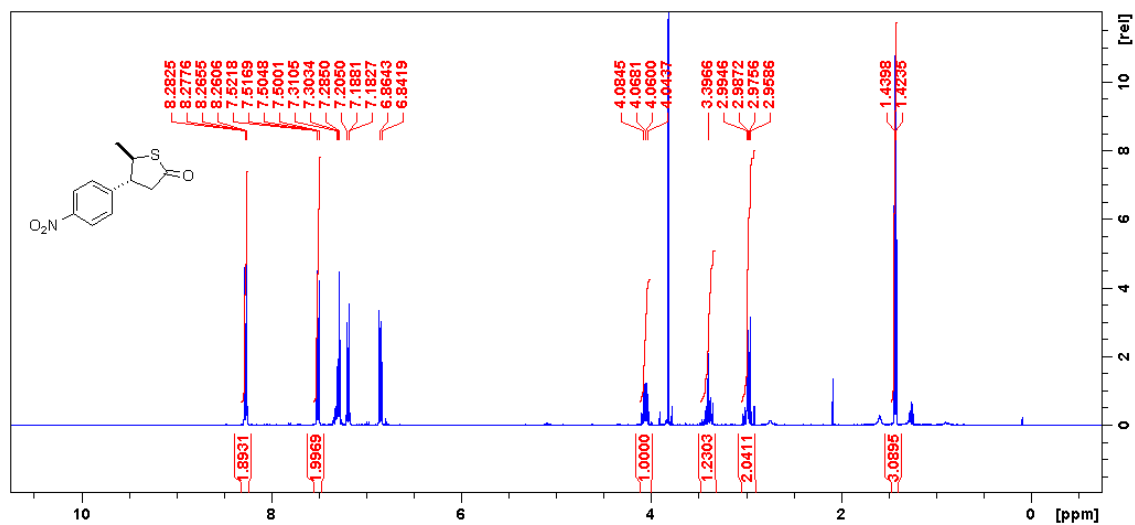


1j ¹³C NMR (100 MHz, CDCl₃):

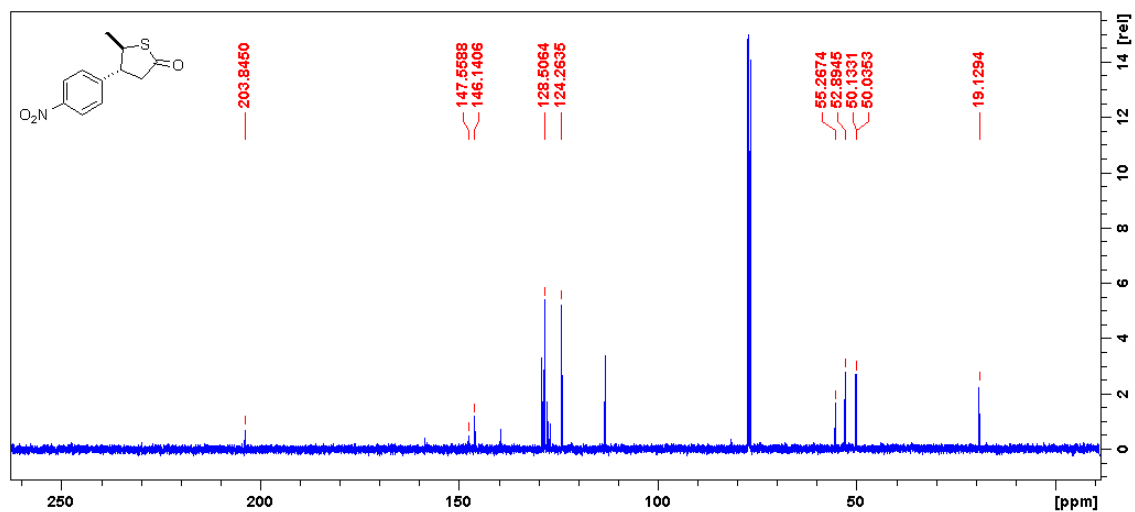


Supplementary Figure S44.

1k (PhCO₂Me contaminant) ¹H NMR (400 MHz, CDCl₃):

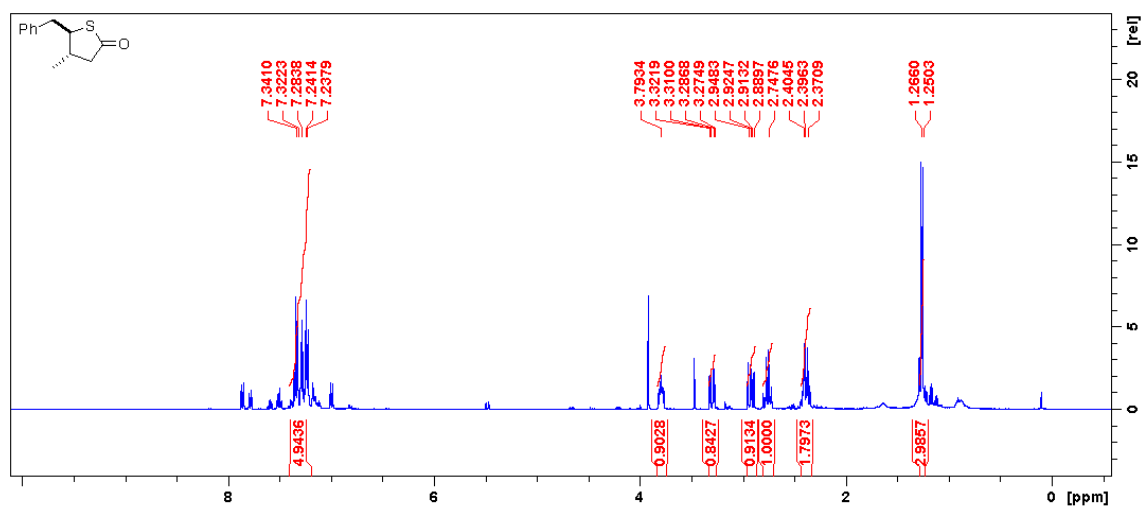


1k (PhCO₂Me contaminant) ¹³C NMR (100 MHz, CDCl₃):

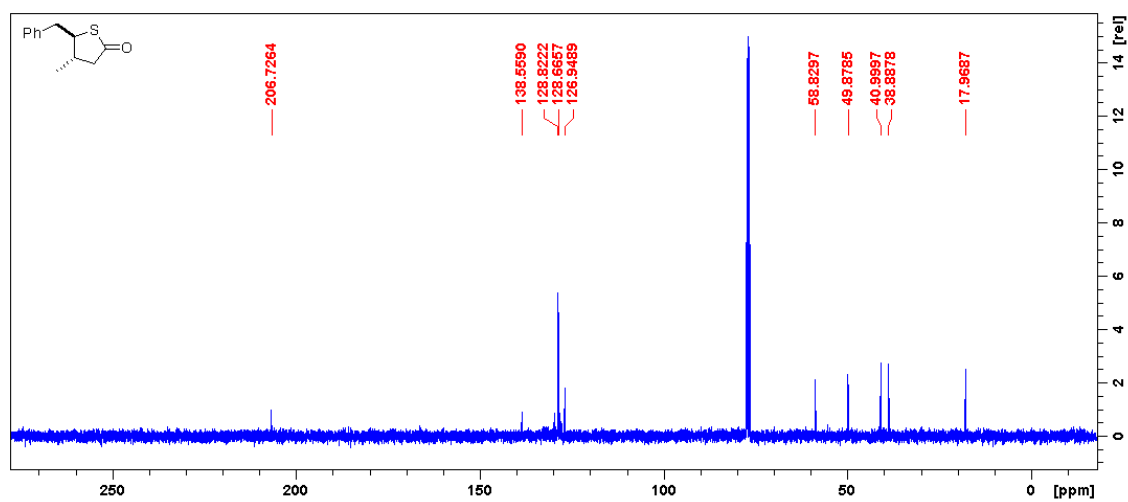


Supplementary Figure S45.

11 ^1H NMR (400 MHz, CDCl_3):

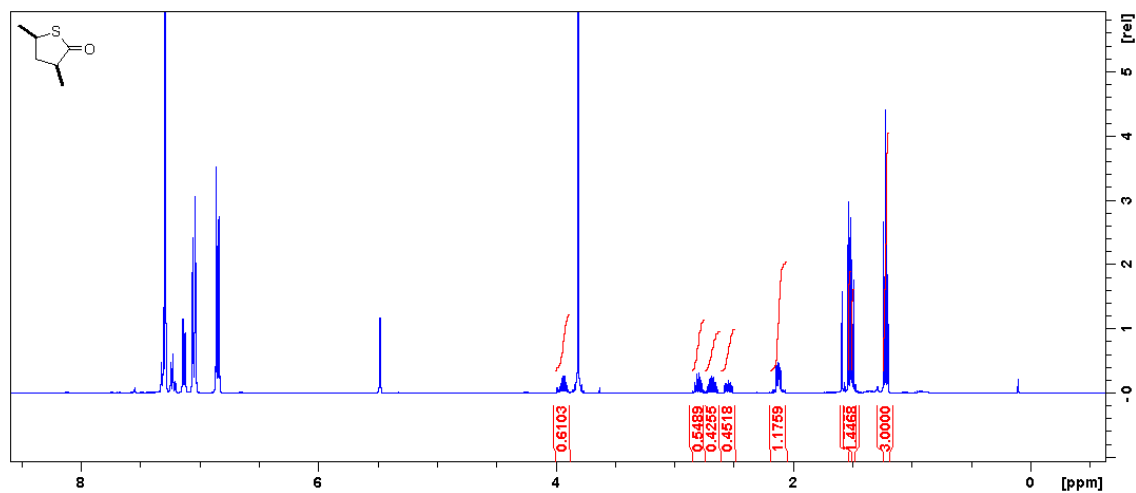


11 ^{13}C NMR (100 MHz, CDCl_3):

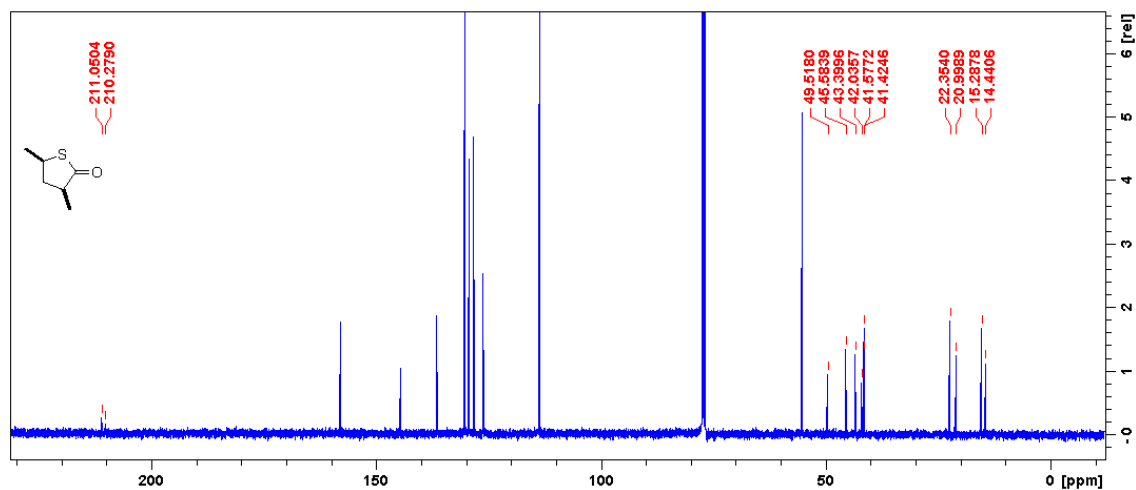


Supplementary Figure S46.

1m (DMTrtH contaminant) ^1H NMR (400 MHz, CDCl_3):

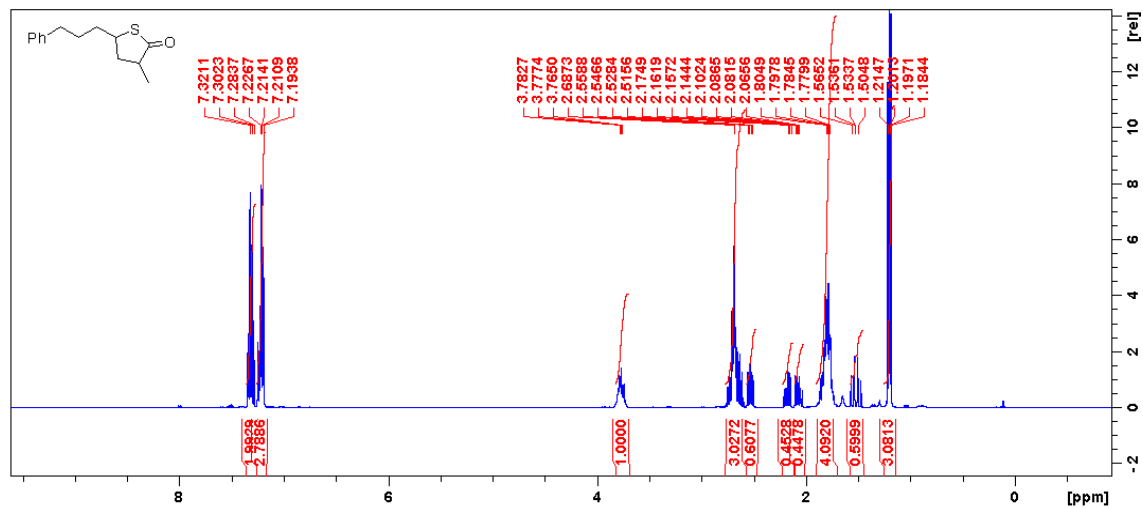


1m (DMTrtH contaminant) ^{13}C NMR (100 MHz, CDCl_3):

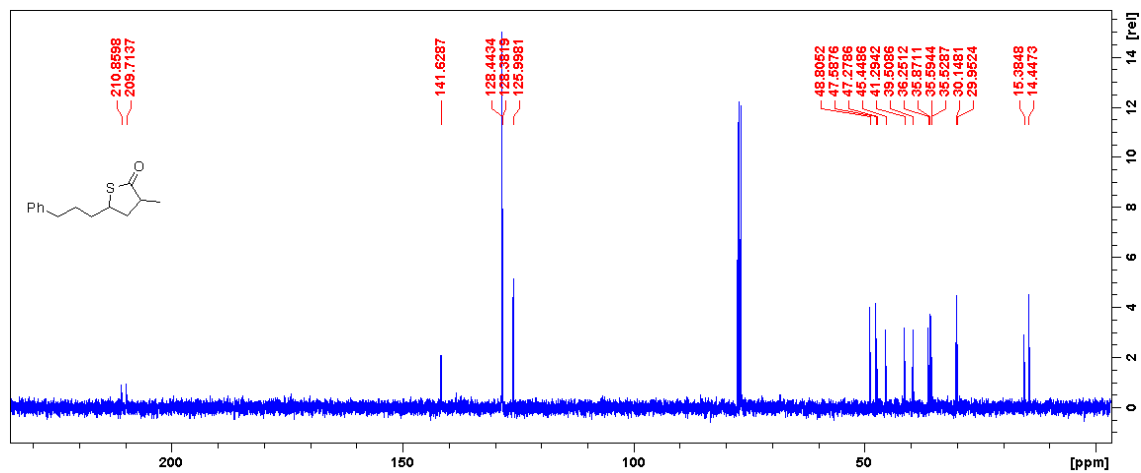


Supplementary Figure S47.

1n ^1H NMR (400 MHz, CDCl_3):

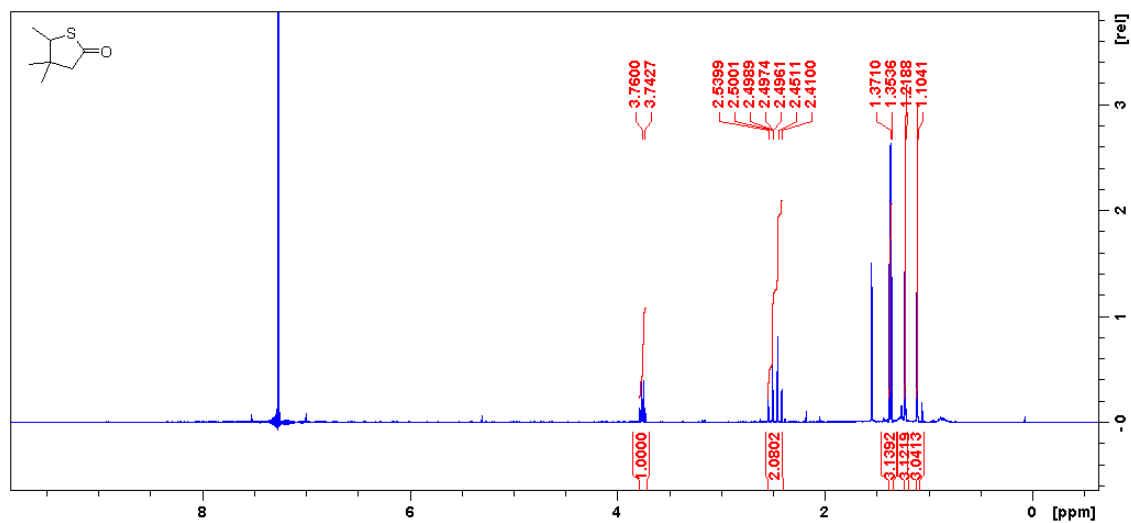


1n ^{13}C NMR (100 MHz, CDCl_3):

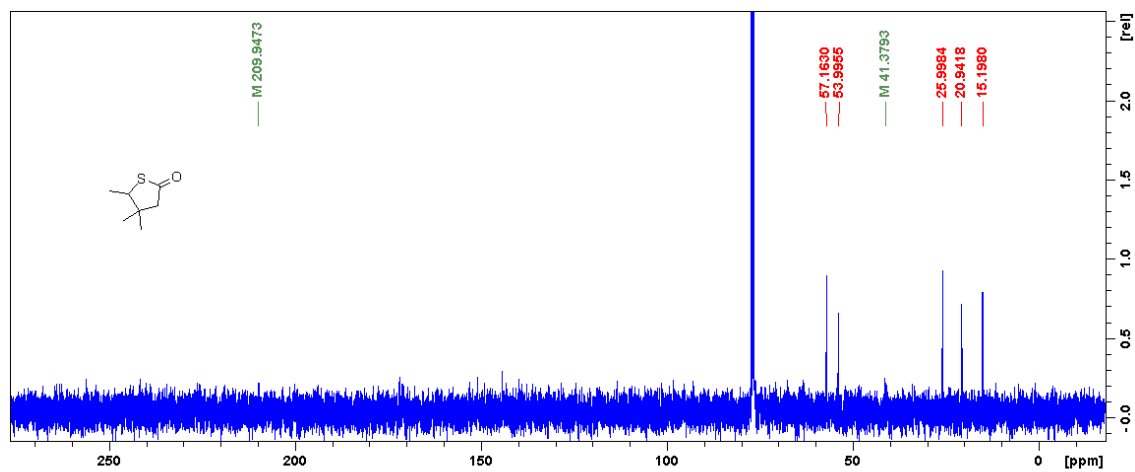


Supplementary Figure S48.

1o ^1H NMR (400 MHz, CDCl_3):

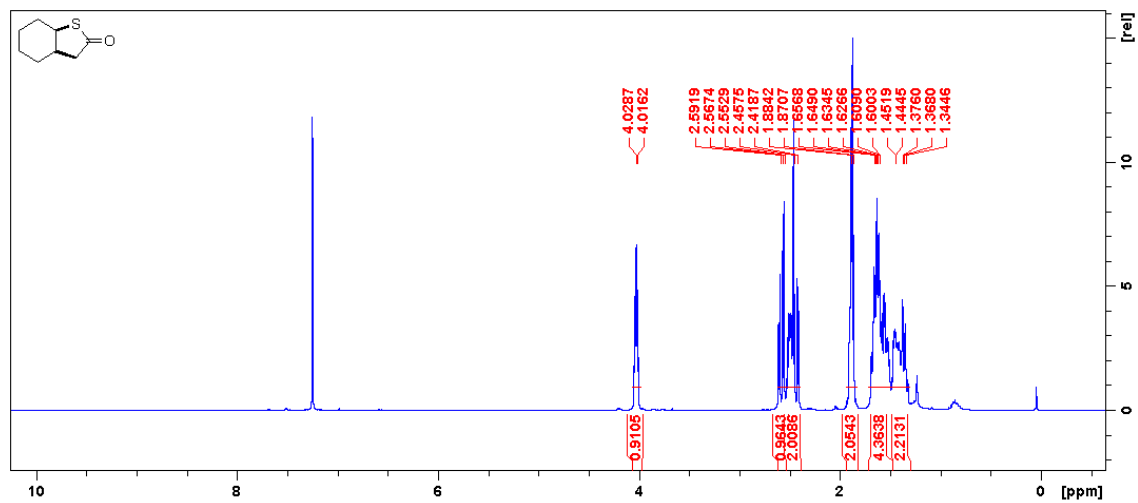


1o ^{13}C NMR (100 MHz, CDCl_3):

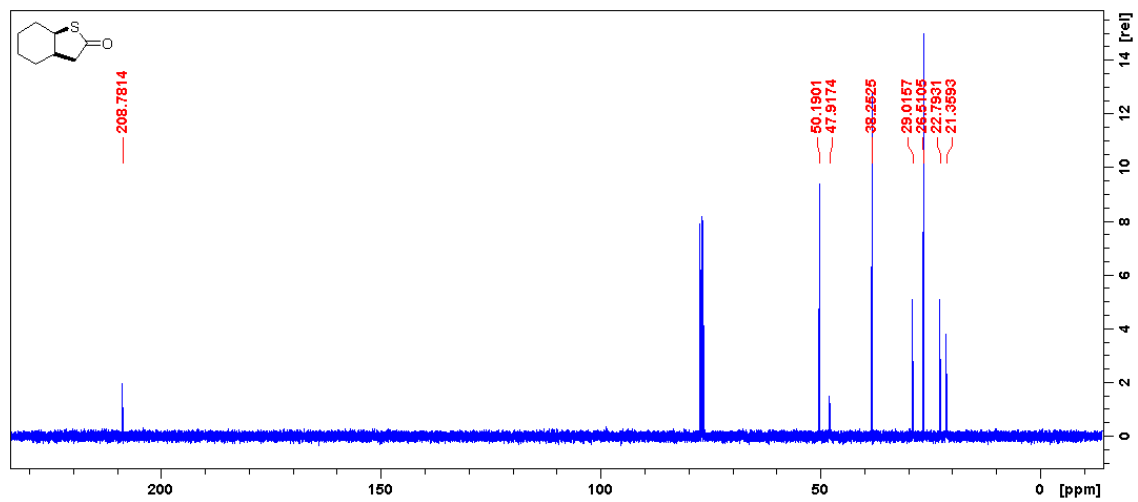


Supplementary Figure S49.

1p ^1H NMR (400 MHz, CDCl_3):

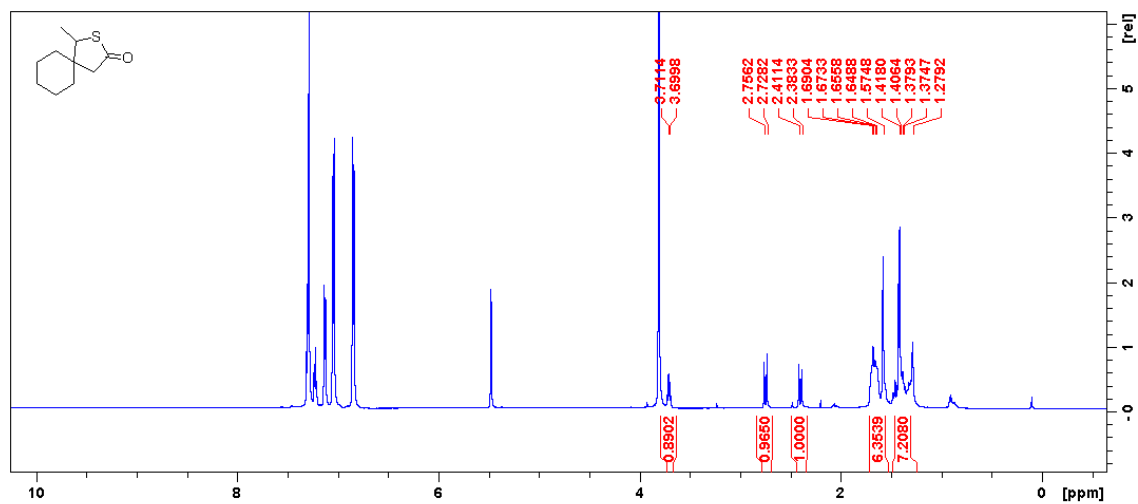


1p ^{13}C NMR (100 MHz, CDCl_3):

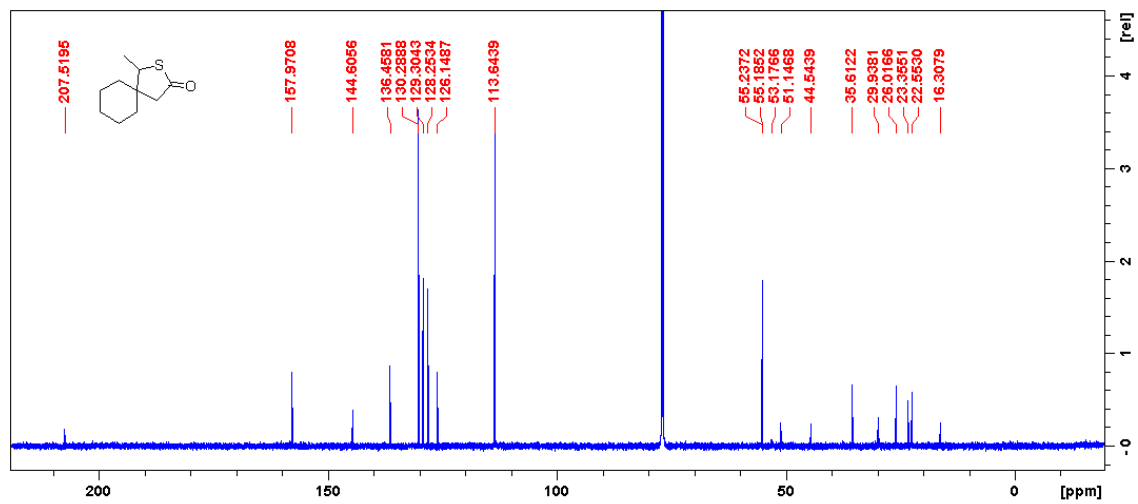


Supplementary Figure S50.

1q (DMTrtH contaminant) ^1H NMR (600 MHz, CDCl_3):

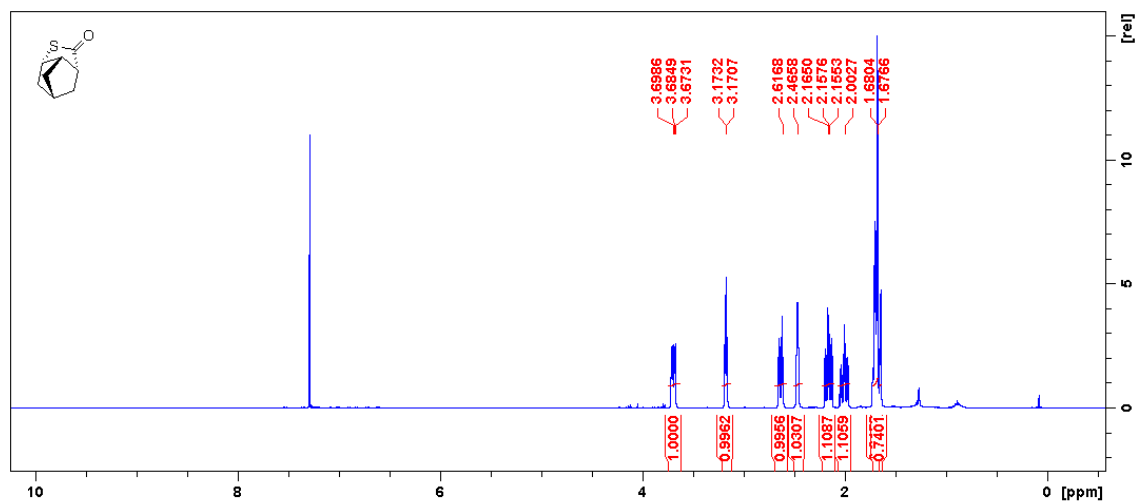


1q (DMTrtH contaminant) ^{13}C NMR (150 MHz, CDCl_3):

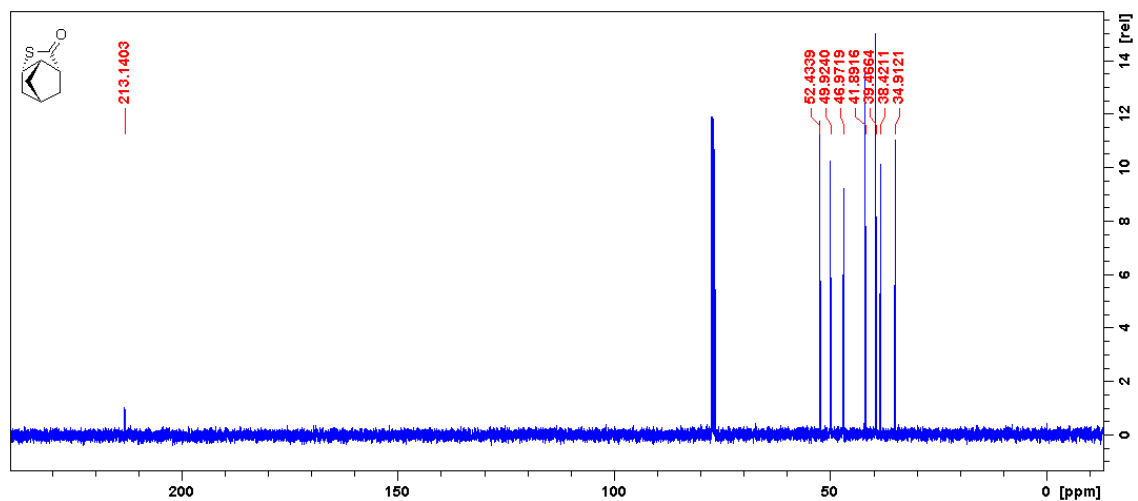


Supplementary Figure S51.

1r ^1H NMR (600 MHz, CDCl_3):

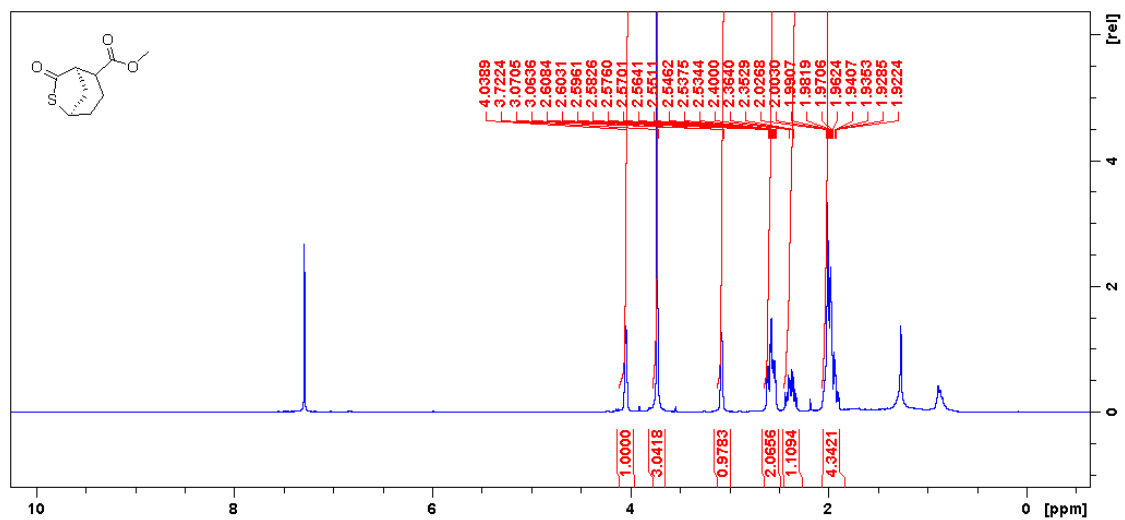


1r ^{13}C NMR (150 MHz, CDCl_3):

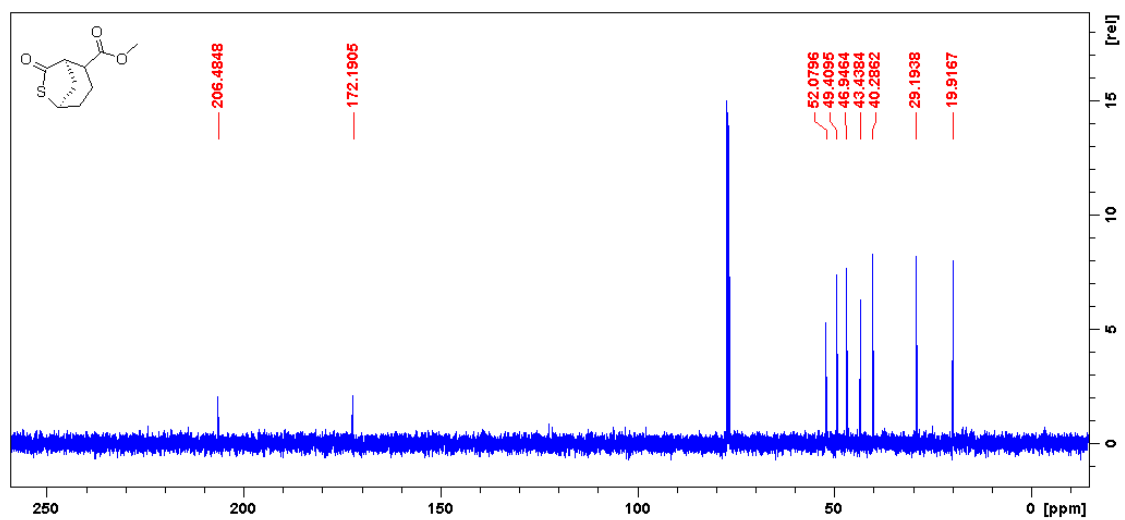


Supplementary Figure S52.

1s ^1H NMR (600 MHz, CDCl_3):

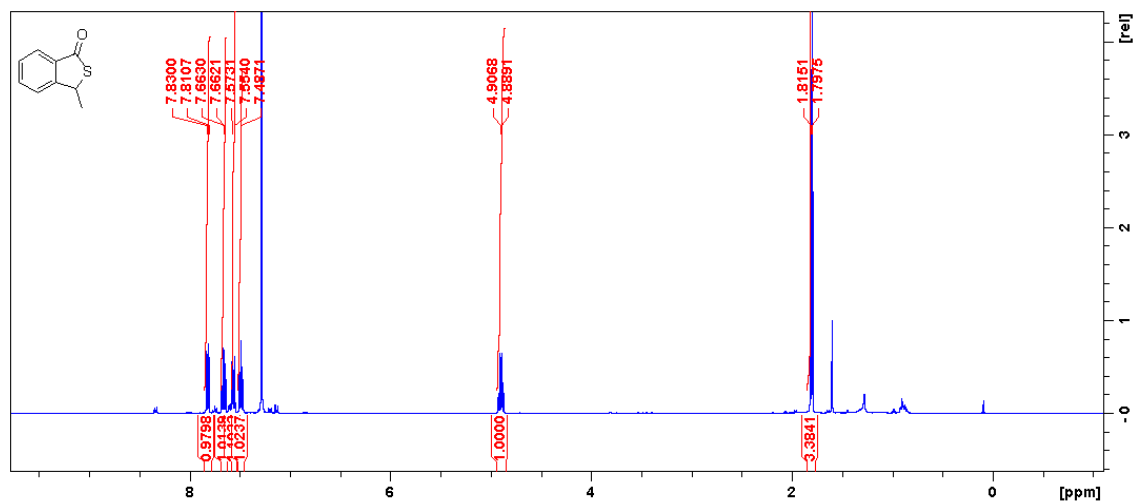


1s ^{13}C NMR (150 MHz, CDCl_3):

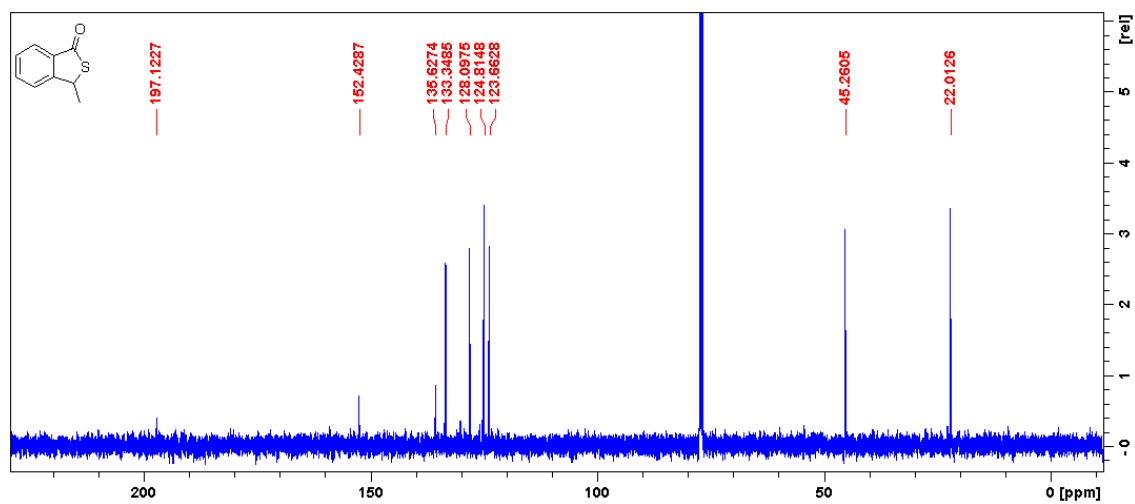


Supplementary Figure S53.

1t ^1H NMR (600 MHz, CDCl_3):

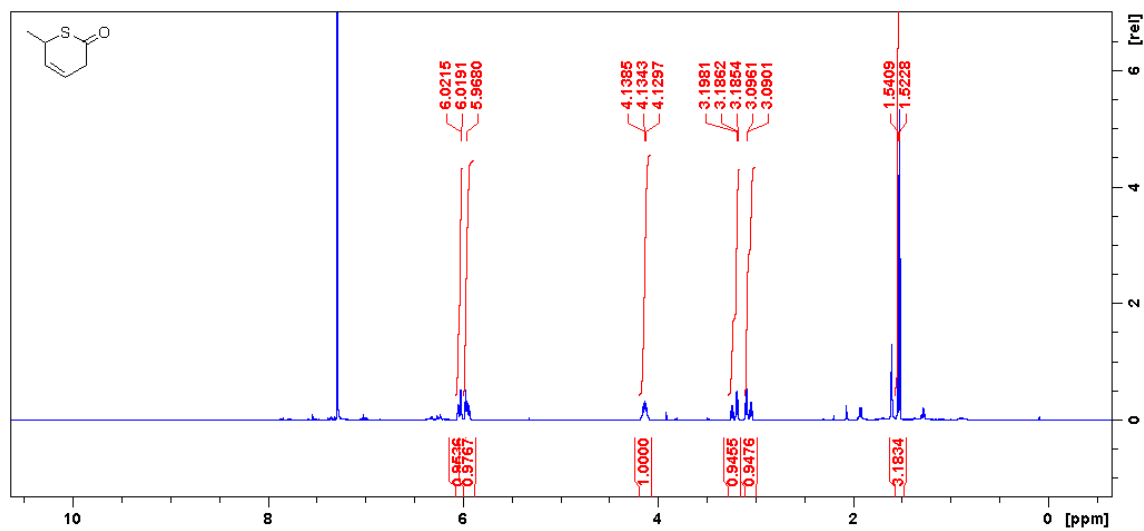


1t ^{13}C NMR (150 MHz, CDCl_3):

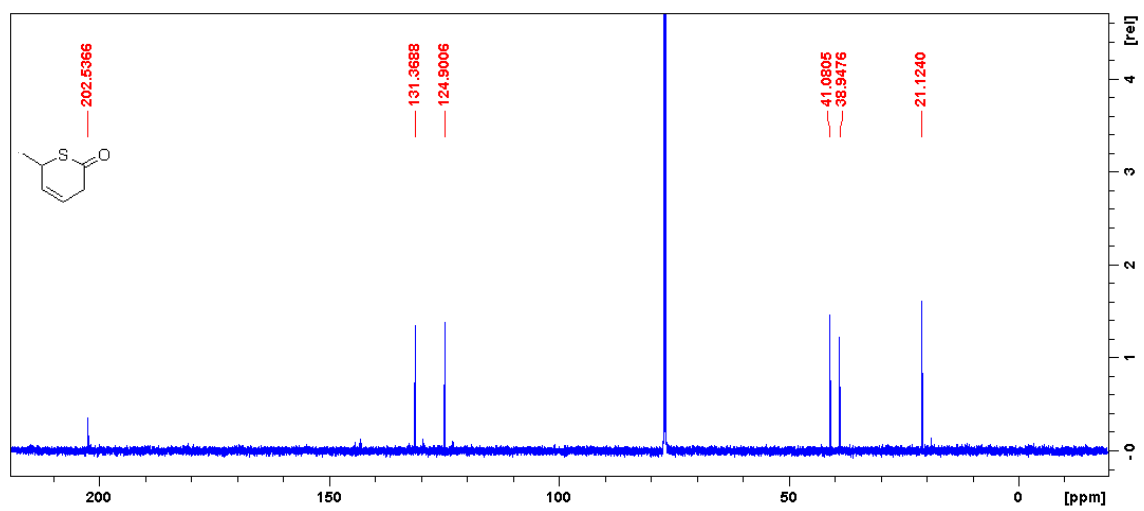


Supplementary Figure S54.

1u ^1H NMR (600 MHz, CDCl_3):

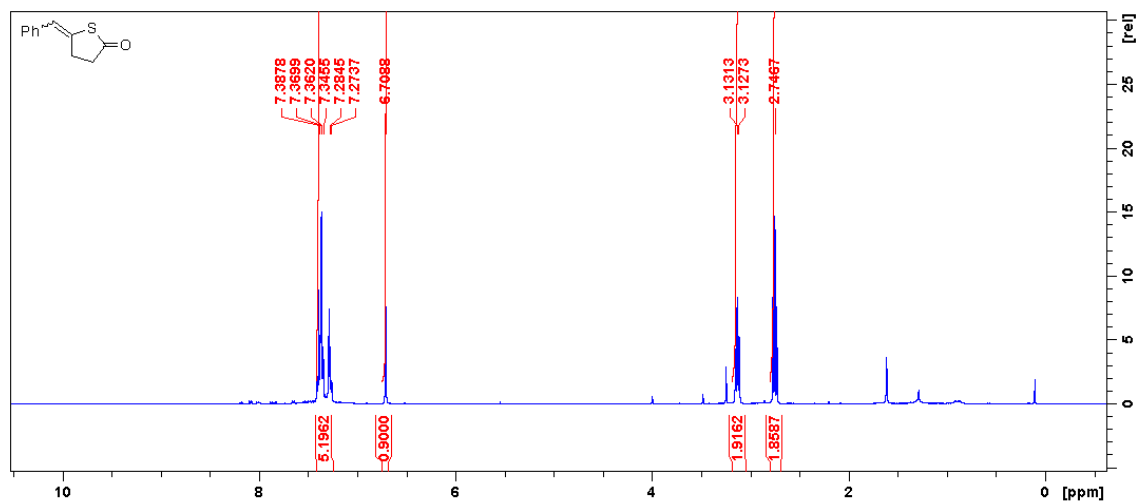


1u ^{13}C NMR (150 MHz, CDCl_3):

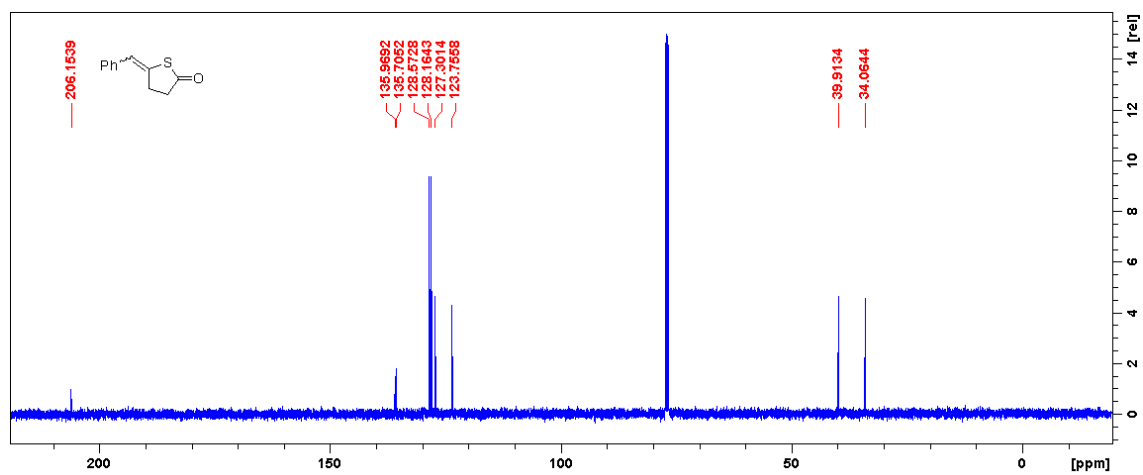


Supplementary Figure S55.

2a ¹H NMR (400 MHz, CDCl₃):

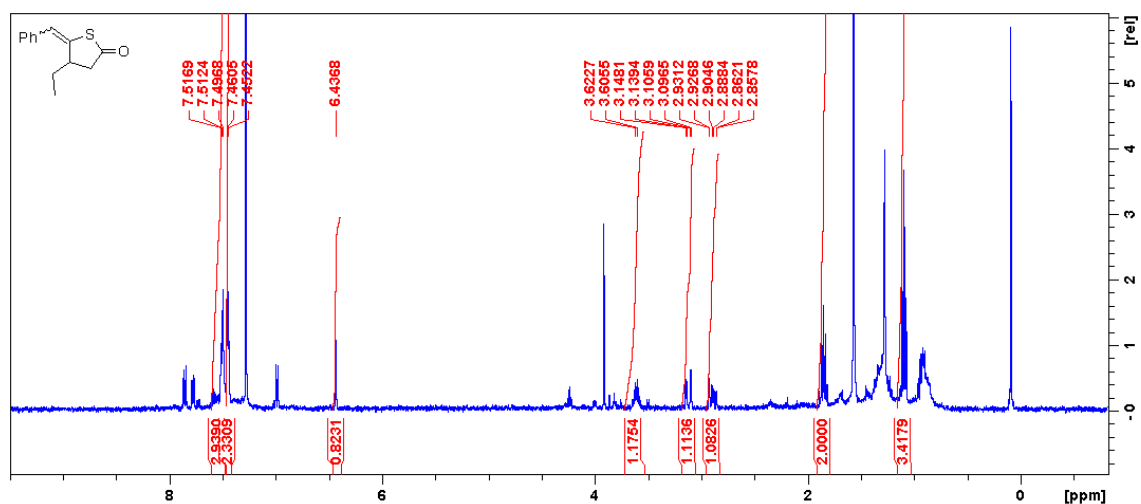


2a ¹³C NMR (100 MHz, CDCl₃):

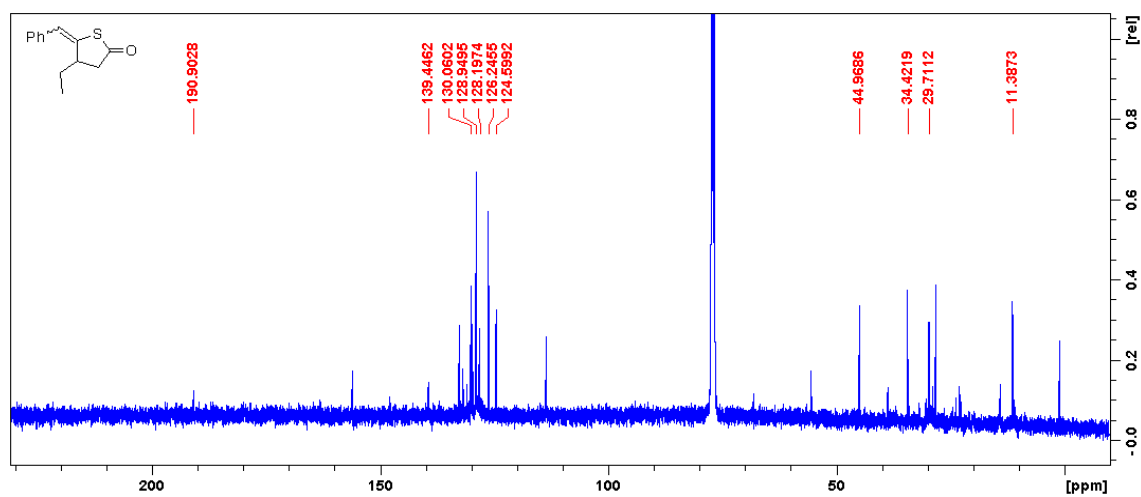


Supplementary Figure S56.

2b (traces of DMTrtH contaminant) ^1H NMR (400 MHz, CDCl_3):

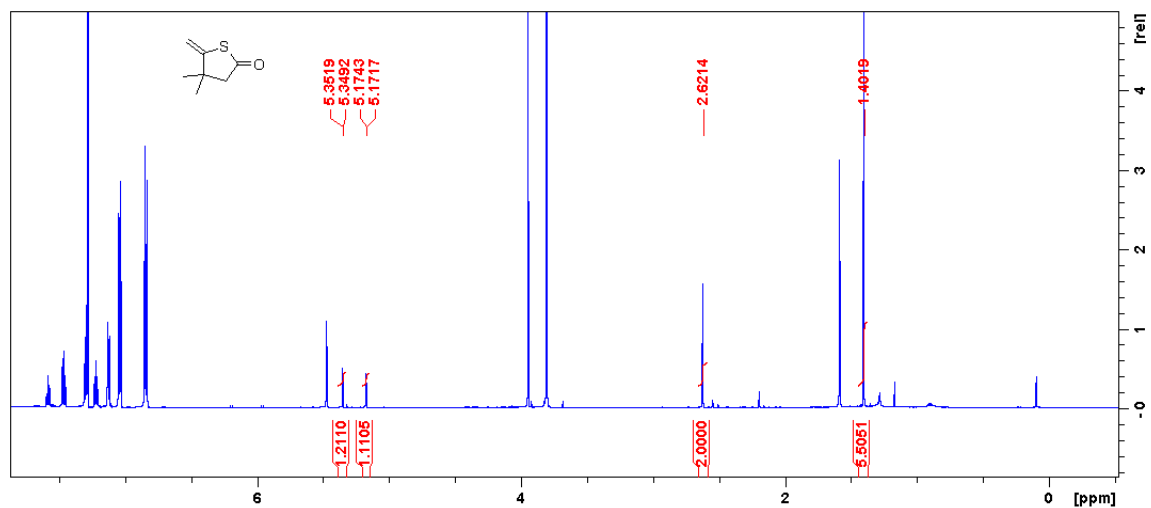


2b (traces of DMTrtH contaminant) ^{13}C NMR (100 MHz, CDCl_3):

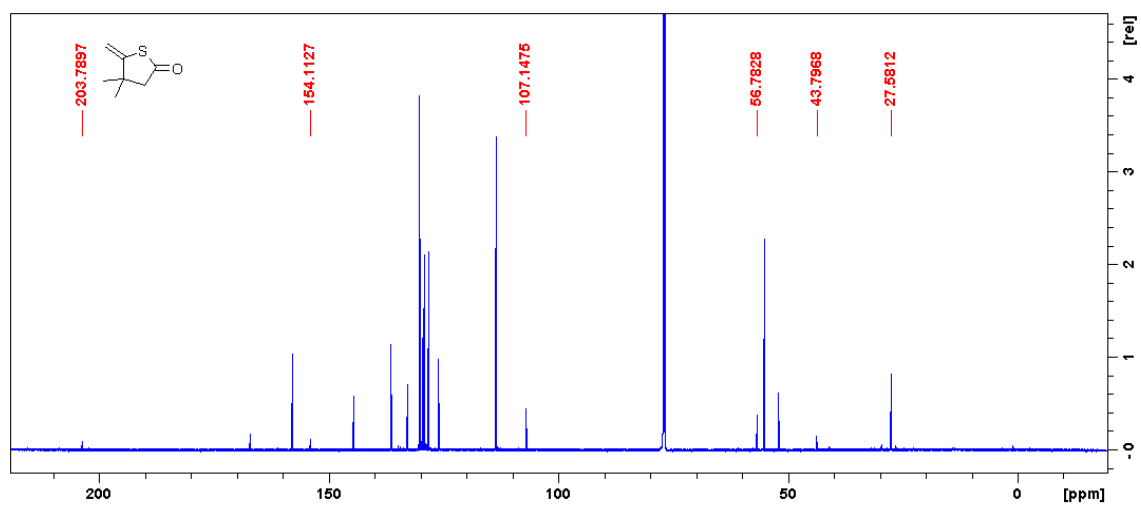


Supplementary Figure S57.

2c (DMTrtH contaminant) ^1H NMR (400 MHz, CDCl_3):

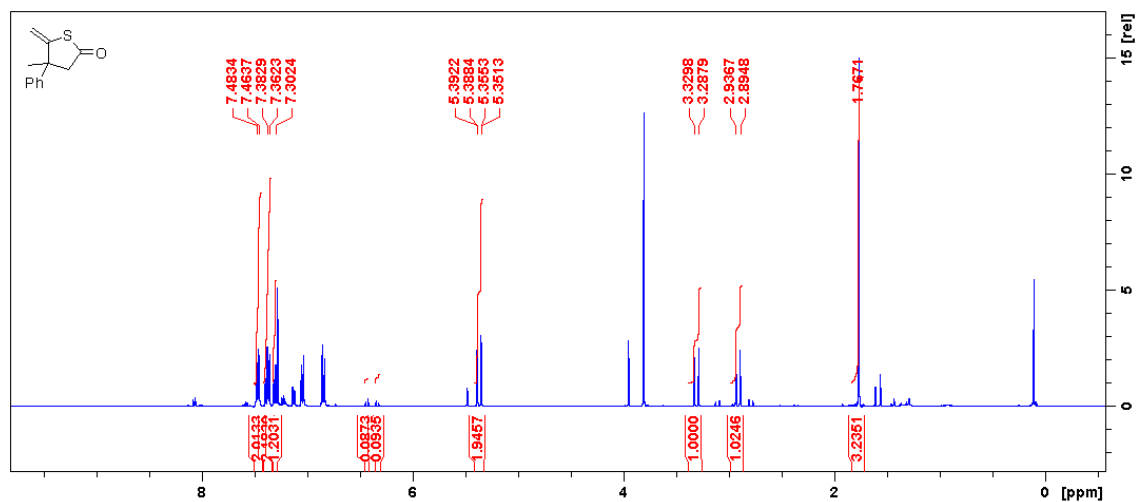


2c (DMTrtH contaminant) ^{13}C NMR (150 MHz, CDCl_3):

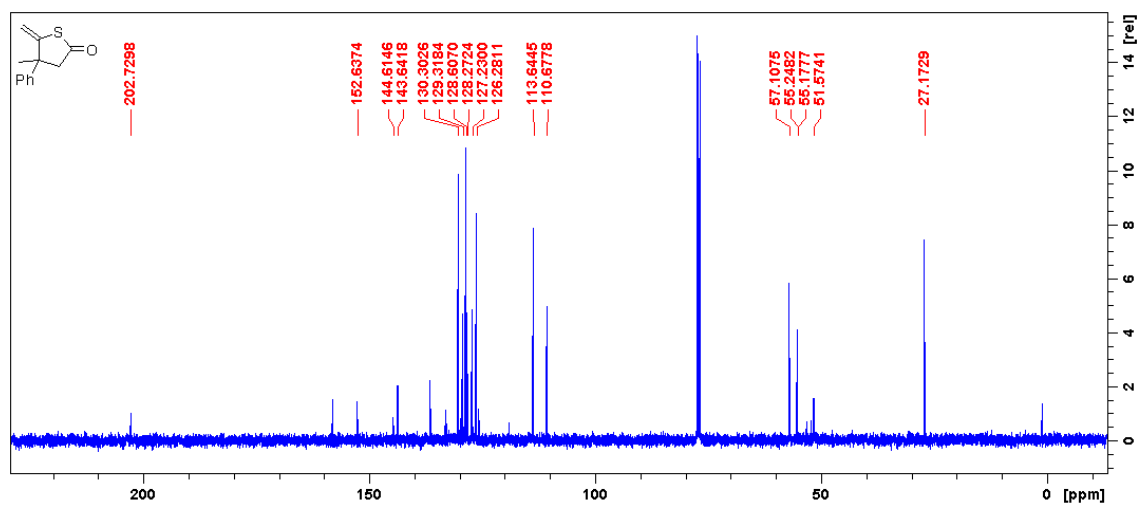


Supplementary Figure S58.

2d *exo* (DMTrtH contaminant) ^1H NMR (400 MHz, CDCl_3):

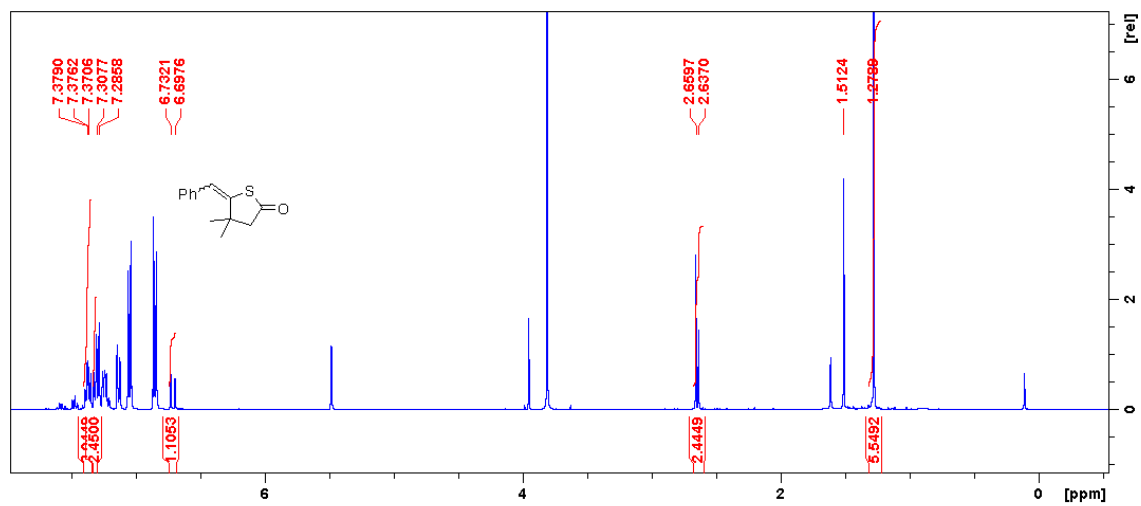


2d *exo* (DMTrtH contaminant) ^{13}C NMR (100 MHz, CDCl_3):

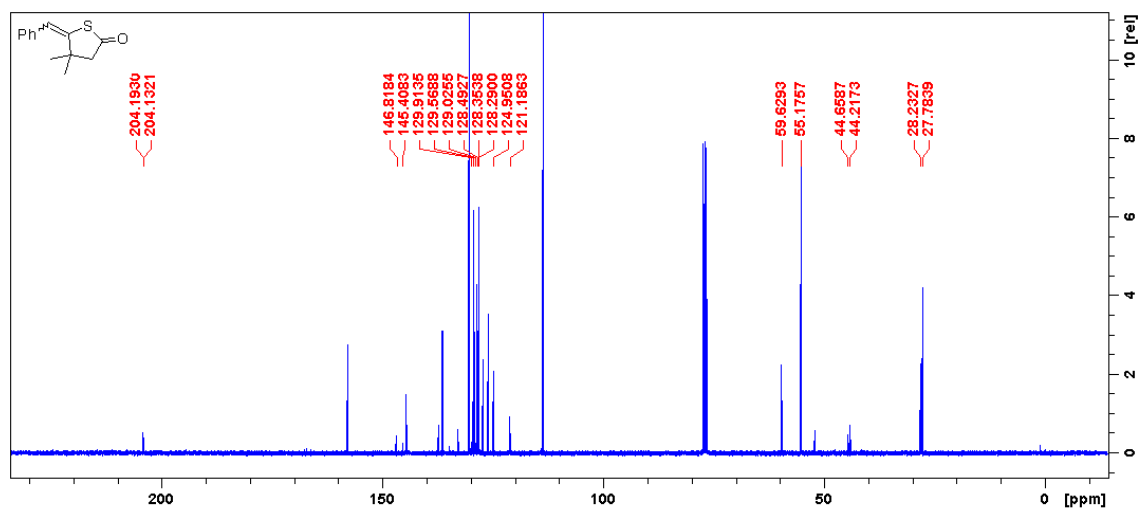


Supplementary Figure S59.

2e *exo* ^1H NMR (400 MHz, CDCl_3):

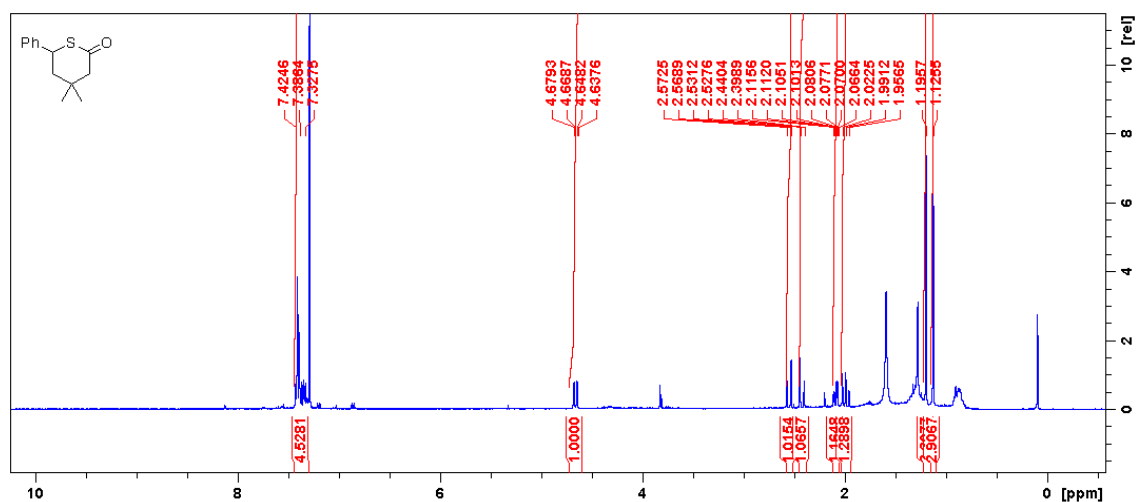


2e *exo* ^{13}C NMR (100 MHz, CDCl_3):

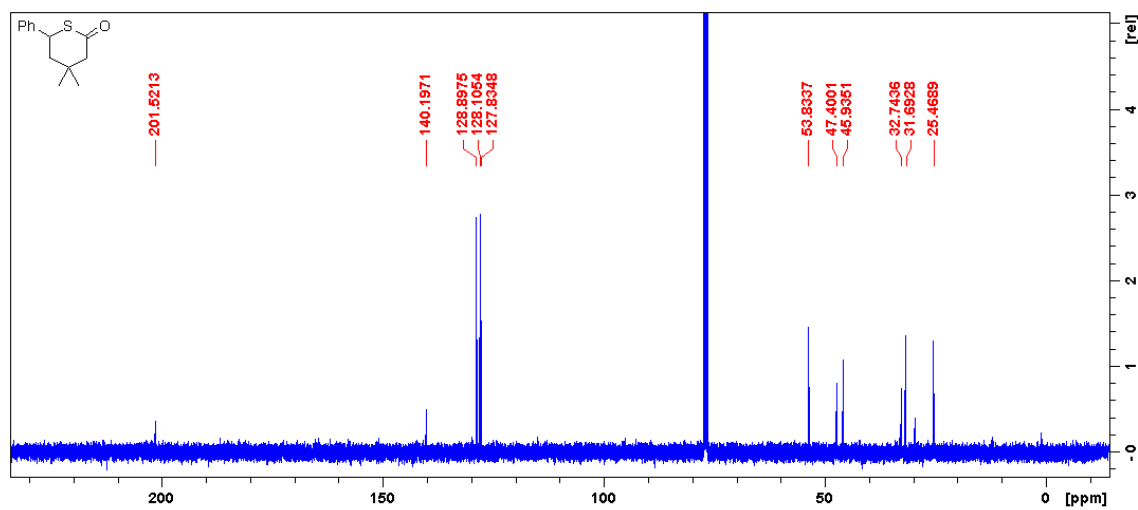


Supplementary Figure S60.

2e endo ^1H NMR (400 MHz, CDCl_3):



2e endo ^{13}C NMR (100 MHz, CDCl_3):



11. References

1. G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw, K. I. Goldberg, *Organometallics* **2010**, *29*, 2176–2179.
2. C. Qin, H. M. L Davies, *J. Am. Chem. Soc.* **2013**, *135*, 14516–14519.
3. T. Šmejkal, B. Breit, *Angew. Chem. Int. Ed.* **2008**, *47*, 311-315.
4. M. Lafrance, M. Roggen, E. M. Carreira, *Angew. Chem. Int. Ed.* **2012**, *51*, 3470-3473.
5. G. L. Hoang, Z.-D. Yang, S. M. Smith, R. Pal, J. L. Miska, D. E. Pérez, L. S. W. Pelter, X. C. Zeng, J. M. Takacs, *Org. Lett.* **2015**, *17*, 940-943.
6. H. Ito, H. Kuroi, H. Ding, T. Taguchi, *J. Am. Chem. Soc.* **1998**, *120*, 6623-6624.
7. S. M. Smith, N. C. Thacker, J. M. Takacs, *J. Am. Chem. Soc.* **2008**, *130*, 3734-3735.
8. Q. Liu, L. Wu, H. Jiao, X. Fang, R. Jackstell, M. Beller, *Angew. Chem. Int. Ed.* **2013**, *52*, 8064-8068.
9. Y. Kawamata, T. Hashimoto, K. Maruoka, *J. Am. Chem. Soc.* **2016**, *138*, 5206-5209.
10. S. F. Musolino, O. S. Ojo, N. J. Westwood, J. E. Taylor, A. D. Smith, *Chem. Eur. J.* **2016**, *22*, 18916-18922.
11. J. D. Griffin, C. L. Cavanaugh, D. A. Nicewicz, *Angew. Chem. Int. Ed.* **2017**, *56*, 2097-2100.
12. A. Fernández-Mateos, P. Herrero Teijón, L. Mateos Burón, R. Rabanedo Clemente, R. Rubio González, *J. Org. Chem.* **2007**, *72*, 9973-9982.
13. L. Zhou, C. K. Tan, X. Jiang, F. Chen, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2010**, *132*, 15474-15476.
14. T. Ito, L. E. Overman, J. Wang, *J. Am. Chem. Soc.* **2010**, *132*, 3272-3273.
15. R. Appel, R. Loos, H. Mayr, *J. Am. Chem. Soc.* **2009**, *131*, 704-714.
16. S. S. M. Spoehrle, T. H. West, J. E. Taylor, A. M. Z. Slawin, A. D. Smith, *J. Am. Chem. Soc.* **2017**, *139*, 11895-11902.
17. D. A. Devalankar, P. U. Karabal, A. Sudalai, *Org. Biomol. Chem.* **2013**, *11*, 1280-1285.
18. A. Bouziane, M. Hérou, B. Carboni, F. Carreaux, B. Demerseman, C. Bruneau, J.-L. Renaud, *Chem. Eur. J.* **2008**, *14*, 5630-5637.
19. K. Miyata, H. Kutsuna, S. Kawakami, M. Kitamura, *Angew. Chem. Int. Ed.* **2011**, *50*, 4649-4653.
20. P.-F. Li, H.-L. Wang, J. Qu, *J. Org. Chem.* **2014**, *79*, 3955-3962.
21. T. N. T. Nguyen, N. O. Thiel, F. Pape, J.-F. Teichert, *Org. Lett.* **2016**, *18*, 2455-2458.
22. P. Dai, T. K. Trullinger, X. Liu, P. H. Dussault, *J. Org. Chem.* **2006**, *71*, 2283-2292.
23. M.-B. Li, H. Li, J. Wang, C.-R. Liu, S.-K. Tian, *Chem. Commun.* **2013**, *49*, 8190-8192.
24. C. Piemontesi, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2016**, *138*, 11148-11151.
25. A. Christopher, D. Brandes, S. Kelly, T. Minehan, *Org. Lett.* **2006**, *8*, 451-454.
26. R. S. Huber, G. B. Jones, *J. Org. Chem.* **1992**, *57*, 5778-5780.
27. R. J. Comito, F. G. Finelli, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2013**, *135*, 9358-9361.
28. W. Li, K. D. Moeller, *J. Am. Chem. Soc.* **1996**, *118*, 10106-10112.
29. S. H. Youk, S. H. Oh, H. S. Rho, J. E. Lee, J. W. Lee, C. E. Song, *Chem. Commun.* **2009**, 2220-2222.
30. J.-i. Ito, K. Fujii, H. Nishiyama, *Chem. Eur. J.* **2013**, *19*, 601-605.
31. J. D. Trenkle, T. F. Jamison, *Angew. Chem. Int. Ed.* **2009**, *48*, 5366-5368.
32. S. W. Smith, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 12645-12647.
33. B. M. Trost, J. T. Masters, B. R. Taft, J.-P. Lumb, *Chem. Sci.* **2016**, *7*, 6217-6231.
34. V. I. Tararov, A. Korostylev, G. König, A. Börner, *Synth. Commun.* **2006**, *36*, 187-191.
35. A. G. Cameron, D. W. Knight, *Tetrahedron Lett.* **1985**, *26*, 3503-3506.
36. A. R. Mohite, R. G. Bhat, *Org. Lett.* **2013**, *15*, 4564-4567.

37. S. Ahmar, E. Fillion, *Org. Lett.* **2014**, *16*, 5748-5751.
38. C. Møller, M. S. Plesset, *Phys. Rev.* **1934**, *46*, 618-622.
39. A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648-5652.
40. C. T. Lee, W. T. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.
41. C. Adamo, V. Barone, *J. Chem. Phys.* **1998**, *108*, 664-675.
42. T. Yanai, D. P. Tew, N. C. Handy, *Chem. Phys. Lett.* **2004**, *393*, 51-57.
43. J.-D. Chai, M. Head-Gordon, *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615-6620.
44. Y. Zhao, D. Truhlar, *Theor. Chem. Acc.* **2008**, *120*, 215-241.
45. H. S. Yu, X. He, S. L. Li, D. G. Truhlar, *Chem. Sci.* **2016**, *7*, 5032-5051.
46. M. J. Frisch, J. A. Pople, J. S. Binkley, *J. Chem. Phys.* **1984**, *80*, 3265-3269.
47. A. E. Reed, L. A. Curtiss, F. Weinhold, *Chem. Rev.* **1988**, *88*, 899-926.
48. E. D. Glendening, F. Weinhold, *J. Comput. Chem.* **1998**, *19*, 593-609.
49. E. D. Glendening, J. K. Badenhop, F. Weinhold, *J. Comput. Chem.* **1998**, *19*, 628-646.