# Nucleophilic Catalysis via Phosphine Conjugate Addition: Vinyl Sulfones as Reacting Partners in Catalytic Cross-Michael Cycloisomerization

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**Abstract:** Vinylsulfones serve as highly effective reacting partners in tributylphosphine catalyzed cross-Michael cycloisomerization. In all cases examined, the vinylsulfone moiety exclusively serves as the Michael acceptor to provide 5- and 6-membered ring products as single constitutional isomers in good to excellent yields.

**Keywords:** nucleophilic catalysis, vinyl sulfone, cycloisomerization, conjugate addition, phosphine

Despite the fact that enolates are among the most ubiquitous reactive intermediates employed in C-C bond formation, there are few catalytic methods for the regiospecific generation and capture of enolate nucleophiles. As part of a program in catalytic reaction development, the use of enones as precursors in tandem conjugate addition-electrophilic trapping is currently under investigation in our lab. Specifically, enone hydrometallation (1,4-reduction),<sup>1</sup> enone carbometallation (1,4-addition),<sup>2</sup> and phosphine conjugate addition (nucleophilic catalysis)<sup>3</sup> have been applied to the regiospecific generation of enolate nucleophiles, which are found to engage in subsequent additions to aldehydes,<sup>1a,c</sup> ketones,<sup>1d,e,2</sup> esters,<sup>2c</sup> nitriles,<sup>2c</sup> activated alkenes, 1a,b,3a,b Pd(II)-n-allyls3c and triarylbismuth(V) reagents.<sup>3d</sup> Indeed, through application of this simple enone-electrophile template, a family of catalytic transformations has emerged (Scheme 1).



Scheme 1

Perhaps the mildest and most operationally simple method for regiospecific enolate generation involves nucleo-

SYNTHESIS 2004, No. 15, pp 2579–2585 Advanced online publication: 26.08.2004 DOI: 10.1055/s-2004-831191; Art ID: M03204SS © Georg Thieme Verlag Stuttgart · New York philic catalysis via conjugate addition of *N*- and *P*nucleophiles. In addition to the Morita–Baylis–Hillman (MBH) reaction,<sup>4</sup> a surprisingly broad family of transformations has been achieved in accordance with this approach: the addition of oxygen nucleophiles to activated alkenes,<sup>5</sup> the internal redox isomerization of activated alkynes,<sup>6</sup> nucleophilic  $\alpha$ - and  $\gamma$ -additions to activated alkynes,<sup>7</sup> inter- and intramolecular [3+2] cycloadditions,<sup>8,9</sup> [4+2] cycloadditions,<sup>10</sup> cycloallylation of activated alkenes,<sup>11</sup> the coupling of allenic esters to activated alkenes,<sup>12</sup> the regiospecific substitution of MBH acetates,<sup>13</sup> and even Stetter-type condensations.<sup>14</sup>

Contributing to this growing subset of organocatalytic transformations, the present author and Roush concurrently reported an intramolecular variant of the phosphine catalyzed dimerization of activated alkenes.<sup>3a,15</sup> A related study was subsequently reported by Murphy.<sup>16</sup> Unlike the parent transformation,<sup>17</sup> the intramolecular process is amenable to cross-condensation, which has led to its use as a key bond formation in the total synthesis of complex natural products.<sup>18</sup> To extend the scope of this process, studies aimed at expanding the repertoire of reacting partners amenable to crossed cycloisomerization are ongoing. Here, inspired by the versatility of the sulfone moiety in organic syntheses,<sup>19</sup> we report the highly chemoselective cross-Michael cycloisomerization of vinylsulfones with appendant enone and enoate partners to afford cyclopentene and cyclohexene products (Scheme 2).





Initial studies focused on the identification of a concise and modular synthetic route to the sulfone containing cycloisomerization substrates. Among methods for the introduction of vinyl sulfones,<sup>20</sup> the indicated *para*nitrophenylsulfone-based Wittig–Horner–Wadsworth– Emmons reagent **A** proved to be most versatile,<sup>21</sup> enabling access to sulfone containing substrates **6a–12a** in good overall yields from the corresponding aldehydes. The *para*-nitrophenylsulfonyl moiety is required as the parent phenylsulfone derivatives do not engage in cyclization. Using the Wittig-Horner-Wadsworth-Emmons reagent A, the previously reported thioenoate-containing aldehydes 1 and 2 provide 6a and 7a in 89% and 90% yields, respectively. In the case of the nitrogen-tethered substrate 8a, initial introduction of the vinyl sulfone moiety occurs in 65% yield to afford, after acidic hydrolysis, the aldehyde 3. Exposure of 3 to the thiol acetic ester based Wittig-Horner reagent EtSCOCHPPh<sub>3</sub><sup>22</sup> affords 8a in 81% yield. Finally, olefination of 4-pentenal and 5-hexenal using Wittig-Horner-Wadsworth-Emmons reagent A provides the olefinic vinylsulfones 4 and 5 in 91% and 93% yields, respectively. Cross metathesis<sup>23</sup> of the terminal alkenes 4 and 5 using the second generation Grubbs catalyst with phenyl vinyl ketone (PVK) provides substrates 9a and 10a in 57% and 59% yields, respectively. Similarly, through the use of methyl vinyl ketone (MVK), substrates **11a** and **12a** are obtained in 64% and 68% yields, respectively (Scheme 3).

With substrates **6a–12a** in hand, conditions for phosphine catalyzed cross-Michael cycloisomerization were explored. As previously observed, the ideal choice of temperature and reaction solvent was highly substrate dependent. Indeed, for the vinyl sulfone containing substrates **6a–12a**, optimal reaction conditions were unique for each substrate. However, upon identification of suitable conditions, the cycloisomerization products **6b–12b** were produced in good to excellent yields using 10–20 mol% of tributylphosphine as catalyst. In each case, the vinylsulfone moiety serves as the electrophilic partner in

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Ana Liza Luis received a B.S. in Chemistry from the University of Texas at San Antonio and an M.S. in

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were not observed (Table 1).

°C.

Texas at Austin and an NIH predoctoral fellow.



Michael J. Krische received a B.S. in Chemistry from the University of California at Berkeley under the tutelage of Professor H. Rapoport as a Presidents Undergraduate Fellow. whereupon he was granted a Fulbright Fellowship for study in Europe. Dr. Krische received his Ph.D. in Chemistry from Stanford University for studies performed with Professor B. M. Trost as a Peter Veatch Fellow,

and then pursued post-doctoral studies with Jean-Marie Lehn at the Université Louis Pasteur as an NIH Post-Doctoral Fellow where he was granted the title of Maître de Conference, Collége de France. Dr. Krische joined the faculty at the University of Texas at Austin in Fall 1999, where he has established a program of research combining the topics catalytic reaction development, asymmetric synthesis, self-assembly and materials chemistry. Selected honors and awards include the Camille Dreyfus Teacher Scholar Award (2003), the Alfred P. Sloan Research Fellowship (2003), the Cottrell Scholar Award (2002), the Frasch Foundation Award in Chemistry (2002), the Eli Lilly Grantee for Untenured Faculty (2002), and the National Science Foundation-CAREER Award (2000).



Scheme 3 Preparation of cross-Michael cycloisomerization sub-

strates 6a-12a. Reagents and conditions: (a) A, n-BuLi, THF, -78 °C

to 25 °C. (b) 50% aq TFA, 25 °C. (c) EtSCOCHPPh<sub>3</sub>, THF, 66 °C. (d) **A**, LHMDS, THF, -78 °C to 25 °C. (e) PVK, 5 mol% Grubbs II cata-

lyst, CH<sub>2</sub>Cl<sub>2</sub>, 40 °C. (f) MVK, 5 mol% Grubbs II catalyst, CH<sub>2</sub>Cl<sub>2</sub>, 40

the cyclization. Isomeric products derived via direct addi-

tion of tributylphosphine to the vinylsulfone moiety fol-

lowed by cyclization onto the appendant enone or enoate

Entry	Substrate	Product	$PBu_3 (mol\%)$	T (°C)	Solvent	Isolated Yield (%)
1	Ets SO <sub>2</sub> Ar	EtS SO <sub>2</sub> Ar	10	50	t-AmylOH <sup>c</sup>	89
2	6a Ets	6b Ets SO <sub>2</sub> Ar	10	25	MeCN	86
3	7a	7b	20	130	t-AmylOH	76
4	8a Ph	8b Ph SO <sub>2</sub> Ar	10	50	EtOAc	97
5	9a Ph	9b Ph	10	25	Acetone	74
6	10a $H_{3}C$ SO <sub>2</sub> Ar	$10b$ $H_{3C} - SO_{2}Ar$	20	82	t-BuOH	84
7	11a $H_{3C}$ $SO_{2}Ar$	$\mathbf{11b}$ $\mathbf{H}_{3}\mathbf{C} \xrightarrow{O} SO_{2}Ar$	20	60	t-AmylOH <sup>c</sup>	80
	12a	12b				

Table 1 Phosphine-Catalyzed Cross-Cycloisomerization of Substrates 6a-12aa-c

<sup>a</sup> Procedure: To a solution of substrate (100 mol%) in the indicated solvent (0.2 M) under an atmosphere of Ar was added tributylphosphine (10–20 mol%). The reaction was allowed to stir at the indicated temperature until consumption of the starting material was observed, at which point the solvent was removed under reduced pressure and the resulting oil was purified using flash chromatography (SiO<sub>2</sub>: hexane–EtOAc) to provide cyclized products.

<sup>b</sup> Ar = p-nitrophenyl.

<sup>c</sup> Reactions were performed at a concentration of 0.1 M.

In summation, *p*-nitrophenyl substituted vinylsulfones serve as highly effective reacting partners in phosphine catalyzed cross-Michael cycloisomerization. For all substrates examined, good to excellent yields of 5- and 6membered ring products were obtained using 10–20 mol% tributylphosphine. Moreover, as the vinylsulfone moiety exclusively serves as the Michael acceptor, cyclized products appear as single constitutional isomers. Future studies will be devoted to the development of related catalytic transformations, including enantioselective variants of the reactions described herein.

All experiments involving water-sensitive compounds were conducted under an atmosphere of Ar. Anhydrous solvents were transferred by an oven-dried syringe. Flasks were flame-dried and cooled under a stream of  $N_2$ . THF was distilled over sodium-benzophenone. Dichloromethane was distilled from calcium hydride. Compounds 1 and 2 were prepared according to known literature procedure.<sup>24</sup> Analytical TLC was carried out using 0.2 mm commercial silica gel plates (DC-Fertigplatten Krieselgel 60 F254). Preparative column chromatography employing silica gel was performed according to the method of Still.25 Solvents for chromatography are listed in volume/volume ratios. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer. HRMS were obtained on a Micromass ZAB-2E and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion [M+1] or a suitable fragment ion. <sup>1</sup>H NMR spectra were recorded in CDCl<sub>3</sub> at 300 MHz using a Varian spectrometer. Chemical shifts are reported in delta ( $\delta$ ) units, ppm downfield from TMS. Coupling constants are reported in Hz. <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> at 75 MHz using a Varian spectrometer. Chemical shifts are reported in delta ( $\delta$ ) units, ppm relative to the center of the triplet at 77.0 ppm for CDCl<sub>3</sub>. <sup>13</sup>C NMR spectra were routinely run with broadbrand decoupling.

#### Synthesis of 4 and 5; General Procedure

To a stirred solution of (4-nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (5.60 g, 18.1 mmol, 100 mol%) in THF (0.2 M) under Ar at -78 °C was added lithium hexamethyldisilazide (18.1 mL, 1.0 M in THF, 100 mol%). The solution was allowed to stir at -78 °C for 1 h, at which point aldehyde (23.8 mol, 130 mol%) in CH<sub>2</sub>Cl<sub>2</sub> (1.6 M) was added. The reaction was allowed to warm to r.t. over a period of 1 h. The reaction mixture was poured into a solution of sat. NH<sub>4</sub>Cl, and the aqueous layer was extracted with Et<sub>2</sub>O (3 × 150 mL). The organic extracts were combined, washed with brine, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The resulting residue was subjected to chromatographic purification [SiO<sub>2</sub>: hexane–EtOAc (9:1)] to afford compounds **4** and **5** as yellow oils.

#### **1-(Hexa-1,5-diene-1-sulfonyl)-4-nitro-benzene (4)** Yield: 91%.

FTIR (film): 3056, 2986, 2686, 2305, 1639, 1607, 1535, 1422, 1351, 1266, 1149, 1087, 1013, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.34 (d, *J* = 9.7 Hz, 2 H), 8.04 (d, *J* = 10.7 Hz, 2 H), 7.06 (dt, *J* = 15.1, 6.6 Hz, 1 H), 6.32 (d, *J* = 15.1 Hz, 1 H), 5.70 (m, 1 H), 4.9 (m, 2 H), 2.36 (q, *J* = 6.5 Hz, 2 H), 2.21 (m, 2 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 149.1, 136.0, 129.6, 128.9, 124.4, 116.3, 31.3, 30.7.

HRMS: m/z [M + 1] calcd for C<sub>12</sub>H<sub>14</sub>NO<sub>4</sub>S: 268.0648; found: 268.0644.

#### **1-(Hepta-1,5-diene-1-sulfonyl)-4-nitro-benzene (5)** Yield: 93%.

FTIR (film): 3056, 2986, 2686, 2305, 1639, 1607, 1535, 1422, 1351, 1266, 1148, 1086, 1013, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.35 (d, *J* = 8.9 Hz, 2 H), 8.04 (d, *J* = 9.0 Hz, 2 H), 7.06 (dt, *J* = 15.1, 6.8 Hz, 1 H), 6.31 (d, *J* = 15.1 Hz, 1 H), 5.71 (m, 1 H), 4.96 (m, 2 H), 2.27 (q, *J* = 7.3 Hz, 2 H), 2.05 (q, *J* = 7.1 Hz, 2 H), 1.56 (qt, *J* = 7.4 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 149.7, 146.5, 137.2, 129.4, 128.9, 124.4, 115.6, 32.8, 26.5.

HRMS: m/z [M + 1] calcd for C<sub>13</sub>H<sub>16</sub>NO<sub>4</sub>S: 282.0798; found: 282.0800.

#### Synthesis of Substrates 6a and 7a; General Procedure

To (4-nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (3.06 g, 9.90 mmol, 100 mol%) in THF (0.20 M) under Ar at -78 °C was added *n*-BuLi (4.0 mL, 2.5 M in THF, 100 mol%) dropwise. After 1 h, **1** or **2** (10.39 mmol, 105 mol%) was added in THF (0.7 M) dropwise. Reaction was allowed to warm to r.t. over a period of 1 h and poured into a solution of sat. aq NH<sub>4</sub>Cl. The aqueous layer was extracted with three portions of Et<sub>2</sub>O and the combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>), filtered and concentrated under vacuum. The resulting residue was subjected to chromatographic purification [SiO<sub>2</sub>: hexane–EtOAc (9:1)] to afford compounds **6a** and **7a** as white solids.

# 7-(4-Nitro-benzenesulfonyl)-hepta-2,6-dienethioic Acid S-Ethyl Ester (6a)

Yield: 89%; mp 78-79 °C.

FTIR (film): 3055, 2987, 2685, 2305, 1667, 1631, 1535, 1422, 1350, 1265, 1149, 1086, 972, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.33 (d, *J* = 9.2 Hz, 2 H), 8.01 (d, *J* = 8.5 Hz, 2 H), 7.02 (dt, *J* = 15.0, 6.6 Hz, 1 H), 6.70 (dt, *J* = 15.7, 6.6 Hz, 1 H), 6.34 (d, *J* = 15.4 Hz, 1 H), 6.03 (d, *J* = 15.4 Hz, 1 H),

2.88 (q, *J* = 7.5 Hz, 2 H), 2.45 (q, *J* = 6.9 Hz, 2 H), 2.37 (q, *J* = 6.9 Hz, 2 H), 1.22 (t, *J* = 7.52 Hz, 3 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 189.4, 150.4, 147.6, 146.1, 141.3, 130.4, 129.8, 128.9, 124.5, 29.7, 29.6, 23.1, 14.6.

HRMS: m/z [M + 1] calcd for C<sub>14</sub>H<sub>16</sub>NO<sub>5</sub>S: 356.0633; found: 356.0626.

# 8-(4-Nitro-benzenesulfonyl)-octa-3,8-dienethioic Acid S-Ethyl Ester (7a)

Yield: 90%; mp 81-82 °C.

FTIR (film): 3055, 2987, 2685, 2305, 1667, 1631, 1535, 1422, 1350, 1265, 1149, 1086, 972, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta = 8.35$  (d, J = 8.55 Hz, 2 H), 8.04 (d, J = 8.89 Hz, 2 H), 7.04 (dt, J = 15.0, 6.75 Hz, 1 H), 6.75 (dt, J = 15.7, 7.01 Hz, 1 H), 6.32 (d, J = 15.0 Hz, 1 H), 6.03 (d, J = 15.7 Hz, 1 H), 2.89 (q, J = 7.41 Hz, 2 H), 2.28 (q, J = 6.84 Hz, 2 H), 2.19 (q, J = 7.18 Hz, 2 H), 1.64 (qt, J = 7.61 Hz, 2 H), 1.23 (t, J = 7.35 Hz, 3 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 189.7, 150.4, 148.6, 146.2, 142.8, 129.8, 129.5, 128.9, 124.5, 31.1, 30.8, 25.7, 23.1, 14.7.

HRMS: m/z [M + 1] calcd for C<sub>15</sub>H<sub>18</sub>NO<sub>5</sub>S: 370.0781; found: 370.0783.

#### 4-{[3-(4-Nitro-benzenesulfonyl)-allyl]-(toluene-4-sulfonyl)-amino}-but-2-enethioic Acid S-Ethyl Ester (8a)

To a stirred solution of (4-nitro-benzenesulfonylmethyl)-phosphonic acid dimethyl ester (1.43 g, 4.62 mmol, 100 mol%) in THF (36 mL, 0.15 M) at -78 °C under an atmosphere of Ar was added n-BuLi (1.85 mL, 2.5 M in hexanes, 100 mol%). The solution was stirred at -78 °C for 1 h, at which point N-(2,2-diethoxy-ethyl)-4methyl-N-(2-oxo-ethyl)-benzenesulfonamide (1.50 g, 4.62 mmol, 100 mol%) in THF (12 mL) was added dropwise. The reaction was allowed to warm to r.t. over a period of 45 min. The reaction mixture was then poured into a solution of sat. aq NH<sub>4</sub>Cl. The aqueous layer was extracted with  $Et_2O$  (3 × 150 mL). The organic extracts were combined, washed with brine, dried (MgSO<sub>4</sub>) and concentrated under reduced pressure. The resulting residue was subjected to chromatographic purification [SiO<sub>2</sub>: hexane-EtOAc (9:1)] to afford N-(2,2-diethoxy-ethyl)-4-methyl-N-[3-(4-nitro-benzenesulfonyl)allyl]-benzenesulfonamide (1.54 g, 3.01 mol) as a yellow oil in 65% yield.

To a solution of N-(2,2-diethoxy-ethyl)-4-methyl-N-[3-(4-nitrobenzenesulfonyl)-allyl]-benzenesulfonamide (1.50 g, 2.93 mmol, 100 mol%) in CH<sub>2</sub>Cl<sub>2</sub> (9.0 mL, 0.33M) at 0 °C was added dropwise an 50% aq solution of trifluoroacetic acid (3.0 mL). Reaction was allowed to stir at ambient temperature for 24 h, at which point the reaction mixture was filtered and the solid dried under vacuum to give 4-methyl-N-[3-(4-nitro-benzenesulfonyl)-allyl]-N-(2-oxo-ethyl)-benzenesulfonamide (**3**; 1.02 g, 2.34 mol) as a white solid in 80% yield.

To a solution of 4-methyl-*N*-[3-(4-nitro-benzenesulfonyl)-allyl]-*N*-(2-oxo-ethyl)-benzenesulfonamide (1.00 g, 2.28 mol, 100 mol%) in THF (24 mL, 0.1 M) was added (triphenyl- $\lambda^5$ -phosphanylidene)-thioacetic acid *S*-ethyl ester (1.20g, 3.42 mmol, 150 mol%). The reaction mixture was heated to reflux and was allowed to stir overnight. Upon cooling, the reaction mixture was concentrated under vacuum and the resulting residue was subjected to chromatographic purification [SiO<sub>2</sub>: hexane–EtOAc (9:1)] to provide **8a** (0.970 g, 1.85 mmol) as a white solid in 81% yield; mp 134–136 °C.

FTIR (film): 3055, 2987, 2685, 2305, 1670, 1631, 1536, 1422, 1350, 1265, 1163, 1152, 1086, 972, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.37 (d, *J* = 8.8 Hz, 2 H), 8.03 (d, *J* = 8.8 Hz, 2 H), 7.62 (d, *J* = 8.2 Hz, 2 H), 7.29 (d, *J* = 7.8 Hz, 2 H),

6.92 (dt, J = 15.0, 4.9 Hz, 1 H), 6.52 (d, J = 15.0 Hz, 1 H), 6.42 (dt, J = 15.4, 5.9 Hz, 1 H), 5.97 (d, J = 15.4 Hz, 1 H), 3.94 (d, J = 4.7 Hz, 2 H), 3.88 (d, J = 6.1 Hz, 2 H), 2.89 (q, J = 7.4 Hz, 2 H), 2.40 (s, 3 H), 1.23 (t, J = 7.4 Hz, 3 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 188.8, 150.6, 145.4, 144.5, 143.2, 136.1, 135.5, 131.8, 131.2, 130.1, 129.1, 127.1, 124.6, 49.1, 47.7, 23.3, 21.5, 14.5.

HRMS: m/z [M + 1] calcd for  $C_{22}H_{25}N_2O_7S_3$ : 525.0836; found: 525.0824.

#### Synthesis of Substrates 9a-12a; General Procedure

To a solution of tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidine]ruthenium(IV) dichloride (72.8 mg, 0.0858 mmol, 3 mol%) in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) under an atmosphere of Ar was added **1** or **2** (2.86 mmol, 100 mol%) in anhyd CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and phenyl vinyl ketone or methyl vinyl ketone (3.56 mmol, 124 mol%). The reaction mixture was heated to reflux for 12 h, at which point it was allowed to cool to r.t. The reaction mixture was stirred open to the air for 20 min and concentrated under vacuum. The resulting residue was subjected to chromatographic purification [SiO<sub>2</sub>: hexane–EtOAc (8:2)] to afford the title compounds **9a–12a** as yellow crystalline solids (**9a** and **10a**) and white crystalline solids (**11a** and **12a**).

# 7-(4-Nitro-benzenesulfonyl)-1-phenyl-hepta-2,6-diene-1-one (9a)

Yield: 57%; mp 60-61 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.25 (d, *J* = 8.9 Hz, 2 H), 8.00 (d, *J* = 8.9 Hz, 2 H), 7.86 (d, *J* = 8.2 Hz, 2 H), 7.55 (dt, *J* = 7.3, 1.4 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 7.08 (m, 1 H), 6.87 (m, 2 H), 6.38 (d, *J* = 15.0 Hz, 1 H), 2.52 (t, *J* = 2.7 Hz, 4 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 189.8, 150.4, 147.8, 146.1, 145.8, 137.3, 133.0, 130.5, 128.9, 128.6, 128.4, 127.0, 124.5, 30.4, 30.0.

HRMS: m/z [M + 1] calcd for C<sub>19</sub>H<sub>18</sub>NO<sub>5</sub>S: 372.0904; found: 372.0906.

# 8-(4-Nitro-benzenesulfonyl)-1-phenyl-octa-2,7-diene-1-one (10a)

Yield: 59%; mp 63-65 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896  $\rm cm^{-1}.$ 

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 8.33 (d, J = 8.9 Hz, 2 H), 8.04 (d, J = 8.9 Hz, 2 H), 7.87 (d, J = 8.9 Hz, 2 H), 7.53 (dt, J = 7.3, 1.20 Hz, 1 H), 7.43 (t, J = 7.5 Hz, 2 H), 7.08 (dt, J = 15.0, 6.8 Hz, 1 H), 6.95 (dt, J = 15.4, 6.7 Hz, 1 H), 6.86 (d, J = 15.4 Hz, 1 H), 6.35 (m, 1 H), 2.33 (q, J = 6.8 Hz, 4 H), 1.70 (qt, J = 7.4 Hz, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 190.3, 150.4, 148.7, 147.5, 146.2, 137.5, 132.8, 129.8, 128.9, 128.5, 128.4, 126.6, 124.4, 124.4, 31.8, 30.9, 25.9.

HRMS: m/z [M + 1] calcd for C<sub>20</sub>H<sub>20</sub>NO<sub>5</sub>S: 386.1068; found: 386.1062.

#### **8-(4-Nitro-benzenesulfonyl)-octa-3,7-diene-2-one (11a)** Yield: 64%; mp 78–79 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1675, 1628, 1535, 1422, 1351, 1265, 1149, 1086, 979, 896  $\rm cm^{-1}.$ 

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.3 (d, *J* = 7.9 Hz, 2 H), 8.03 (d, *J* = 7.8 Hz, 2 H), 7.05 (dt, *J* = 14.9, 6.2 Hz, 1 H), 6.67 (dt, *J* = 15.9, 6.4 Hz, 1 H), 6.36 (d, *J* = 15.1 Hz, 1 H), 6.06 (d, *J* = 15.9 Hz, 1 H), 2.43 (qt, *J* = 5.6 Hz, 4 H), 2.19 (s, 3 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 197.8, 150.6, 147.5, 146.1, 144.2, 132.2, 130.5, 129.0, 124.5, 30.0, 29.9, 27.2.

HRMS: m/z [M + 1] calcd for C<sub>14</sub>H<sub>16</sub>NO<sub>5</sub>S: 310.0747; found: 310.0749.

## **9-(4-Nitro-benzenesulfonyl)-nona-3,8-diene-2-one (12a)** Yield: 68%; mp 81–82 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1675, 1628, 1535, 1422, 1351, 1265, 1149, 1086, 979, 896  $\rm cm^{-1}.$ 

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.32 (d, *J* = 8.9 Hz, 2 H), 8.02 (d, *J* = 8.9 Hz, 2 H), 7.03 (dt, *J* = 15.0, 7.0 Hz, 1 H), 6.68 (dt, *J* = 16.1, 6.7 Hz, 1 H), 6.32 (d, *J* = 15.0 Hz, 1 H), 6.0 (d, *J* = 16.1 Hz, 1 H), 2.24 (m, 7 H), 1.65 (qt, *J* = 7.5 Hz, 2 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 198.2, 150.4, 148.6, 146.1, 146.1, 131.8, 129.7, 128.9, 124.4, 31.4, 30.8, 26.9, 25.7.

HRMS: m/z [M + 1] calcd for C<sub>15</sub>H<sub>18</sub>NO<sub>5</sub>S: 324.0906; found: 324.0906.

#### Cyclization of Substrates 6a-12a; General Procedure

To a solution of substrate (100 mol%) in the indicated solvent (0.2 M) under an atmosphere of Ar was added tributylphosphine (10–20 mol%). The reaction was allowed to stir at the indicated temperature until consumption of the starting material was observed, at which the solvent was removed under reduced pressure and the resulting oil was purified using flash chromatography (SiO<sub>2</sub>: hexane–EtOAc) to provide cyclized products **6b–12b**.

### 5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enecarbothioic Acid S-Ethyl Ester (6b)

Yield: 89%; mp 102-103 °C.

FTIR (film): 3054, 2987, 2685, 2410, 2305, 1650, 1609, 1536, 1422, 1351, 1265, 1151, 1087, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz,  $CDCl_3$ ):  $\delta = 8.39$  (d, J = 8.9 Hz, 2 H), 8.12 (m, J = 8.5 Hz, 2 H), 6.89 (d, J = 1.7 Hz, 1 H), 3.79 (dd, J = 14.4, 1.9 Hz, 1 H), 3.24 (m, 1 H), 3.03 (dd, J = 14.0, 10.9 Hz, 1 H), 2.82 (m, 2 H), 2.55 (m, 2 H), 2.23 (m, 2 H), 1.18 (t, J = 7.5 Hz, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 188.7, 150.8, 145.3, 145.1, 145.1, 143.1, 129.5, 124.4, 58.1, 39.6, 32.1, 28.8, 23.0, 14.6.

HRMS: m/z [M + 1] calcd for C<sub>14</sub>H<sub>16</sub>NO<sub>5</sub>S: 356.0626; found: 356.0631.

### 6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enecarbothioic Acid S-Ethyl Ester (7b)

Yield: 86%; mp 104–105 °C.

FTIR (film): 3054, 2987, 2685, 2410, 2305, 1650, 1609, 1536, 1422, 1351, 1265, 1151, 1087, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.40 (d, *J* = 8.5 Hz, 2 H), 8.12 (d, *J* = 8.5 Hz, 2 H), 7.06 (t, *J* = 3.4 Hz, 1 H), 3.34 (d, *J* = 3.7 Hz, 1 H), 3.07 (m, 2 H), 2.76 (m, 2 H), 2.21 (m, 3 H), 1.63 (m, 3 H), 1.14 (t, *J* = 7.5 Hz, 3 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 192.1, 150.7, 144.7, 142.2, 138.4, 129.6, 124.3, 57.3, 28.8, 25.5, 24.9, 23.0, 16.7, 14.6.

HRMS: m/z [M + 1] calcd for C<sub>15</sub>H<sub>18</sub>NO<sub>5</sub>S: 384.0943; found: 384.0939.

### 3-(4-Nitro-benzenesulfonylmethyl)-1-toluene-4-sulfonyl)-1,2,3,6-tetrahydro-pyridine-4-carbothioic Acid S-Ethyl Ester (8b)

Yield: 76%; mp 134–136 °C.

FTIR (film): 3055, 2987, 2685, 2305, 1670, 1631, 1536, 1422, 1350, 1265, 1163, 1152, 1086, 972, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.37 (d, *J* = 8.9 Hz, 2 H), 8.03 (d, *J* = 8.9 Hz, 2 H), 7.62 (d, *J* = 8.2 Hz, 2 H), 7.29 (d, *J* = 7.9 Hz, 2 H), 6.92 (dt, *J* = 15.0, 4.9 Hz, 1 H), 6.52 (d, *J* = 15.0 Hz, 1 H), 6.42 (dt, *J* = 15.4, 5.9 Hz, 1 H), 5.97 (d, *J* = 15.4 Hz, 1 H), 3.94 (d, *J* = 4.8 Hz, 2 H), 3.88 (d, *J* = 6.2 Hz, 2 H), 2.89 (q, *J* = 7.4 Hz, 2 H), 2.40 (s, 3 H), 1.23 (t, *J* = 7.3 Hz, 3 H).

 $^{13}$ C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 188.8, 150.6, 145.4, 144.5, 143.2, 136.1, 135.5, 131.8, 131.2, 130.1, 129.1, 127.1, 124.6, 49.1, 47.7, 23.3, 21.5, 14.5.

HRMS: m/z [M + 1] calcd for C<sub>22</sub>H<sub>25</sub>N<sub>2</sub>O<sub>7</sub>S<sub>3</sub>: 525.0836; found: 525.0824.

#### [5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enyl]-phenylmethanone (9b)

Yield: 97%; mp 105–106 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 8.39$  (d, J = 9.0 Hz, 2 H), 8.15 (d, J = 8.9 Hz, 2 H), 7.62 (d, J = 7.5 Hz, 2 H), 7.51 (t, J = 7.4 Hz, 1 H), 7.39 (t, J = 7.4 Hz, 2 H), 6.64 (q, J = 2.3 Hz, 1 H), 3.91 (dd, J = 13.9, 2.4 Hz, 1 H), 3.46 (m, 1 H), 3.14 (m, 1 H), 2.72, (m, 1 H), 2.58 (m, 1 H), 2.39 (m, 1 H), 2.24 (m, 1 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 193.3, 150.8, 149.6, 145.2, 143.1, 138.2, 132.4, 129.5, 128.7, 128.3, 57.9, 40.2, 32.8, 28.8.

HRMS: m/z [M + 1] calcd for C<sub>19</sub>H<sub>18</sub>NO<sub>5</sub>S: 372.0907; found: 372.0906.

### [6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enyl]-phenylmethanone (10b)

Yield: 74%; mp 127-128 °C.

FTIR (film): 3054, 2987, 2685, 2305, 1686, 1606, 1535, 1421, 1350, 1266, 1149, 1086, 1013, 896  $\rm cm^{-1}.$ 

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.39 (d, *J* = 8.9 Hz, 2 H), 8.14 (d, *J* = 8.9 Hz, 2 H), 7.47 (m, 3 H), 7.36 (m, 2 H), 6.70 (t, *J* = 3.6 Hz, 1 H), 3.46 (d, *J* = 13.3 Hz, 1 H), 3.23 (m, 2 H), 2.33 (m, 2 H), 2.22 (m, 1 H), 1.76 (m, 3 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 196.9, 150.6, 147.8, 144.7, 138.2, 137.9, 131.7, 129.6, 128.9, 128.1, 124.3, 57.5, 28.7, 25.8, 25.4, 17.2.

HRMS: m/z [M + 1] calcd for C<sub>20</sub>H<sub>20</sub>NO<sub>5</sub>S: 386.1060; found: 386.1062.

# 1-[5-(4-Nitro-benzenesulfonylmethyl)-cyclopent-1-enyl]-ethanone (11b)

Yield: 84%; mp 100-101 °C.

FTIR (film): 3054, 2987, 2935, 2870, 2305, 1661, 1606, 1533, 1422, 1351, 1302, 1265, 1152, 1086, 896 cm<sup>-1</sup>.

<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.39 (d, *J* = 7.8 Hz, 2 H), 8.13 (d, *J* = 8.5 Hz, 2 H), 6.83 (t, *J* = 1.0 Hz, 1 H), 3.79 (d, *J* = 14.0 Hz, 1 H), 3.24 (m, 1 H), 2.99 (t, *J* = 12.3 Hz, 1 H), 2.60 (m, 2 H), 2.23 (m, 5 H).

 $^{13}\text{C}$  NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 196.0, 150.7, 147.6, 145.1, 144.5, 129.5, 124.4, 57.9, 39.0, 32.3, 28.6, 26.8.

HRMS: m/z [M + 1] calcd for C<sub>14</sub>H<sub>16</sub>NO<sub>5</sub>S: 310.0752; found: 310.0749.

# 1-[6-(4-Nitro-benzenesulfonylmethyl)-cyclohex-1-enyl]-ethanone (12b)

Yield: 80%; mp 126–127 °C.

FTIR (film): 3054, 2987, 2935, 2870, 2305, 1661, 1606, 1533, 1422, 1351, 1302, 1265, 1152, 1086, 896 cm<sup>-1</sup>.

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<sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.40 (d, *J* = 8.7 Hz, 2 H), 8.14 (d, *J* = 8.7 Hz, 2 H), 7.00 (t, *J* = 3.9 Hz, 1 H), 3.27 (d, *J* = 14.0 Hz, 1 H), 3.07 (m, 1 H), 2.90 (d, *J* = 10.4 Hz, 1 H), 2.29 (m, 2 H), 2.15 (s, 3 H), 1.70 (m, 2 H), 1.56 (m, 2 H).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 198.1, 150.7, 145.1, 144.8, 139.2, 129.8, 124.2, 57.2, 27.6, 25.8, 25.2, 24.6, 16.5.

HRMS: m/z [M + 1] calcd for C<sub>15</sub>H<sub>18</sub>NO<sub>5</sub>S: 324.0895; found: 324.0906.

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