SUPPLEMENTARY INFORMATION FOR:

Comparison of Free-Radical Inhibiting Antioxidant Properties of Carvedilol and its Phenolic Metabolites

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Figure S1. Calibration curve of absorbance of DPPH at 515 nm vs. concentration.

Figure S2. Kinetic plot for photolysis of Se-phenyl $p$-tolueneselenosulfonate (12) performed in the presence of cyclopropylacetylene and the absence of an antioxidant in CDCl$_3$. 
Preparation of 1-{[(1E)-2-cyclopropyl-2-(phenylseleno)ethenyl]sulfonyl}-4-methylbenzene (14) and 1-methyl-4-{[5-(phenylseleno)-1,2-pentadien-1-yl]sulfonyl}benzene (16).

The products were obtained by a variation of our previous procedure. Selenosulfonate 12 (468 mg, 1.50 mmol) and cyclopropylacetylene (99 mg, 1.5 mmol) in chloroform (10 mL) were irradiated with UV light (254 nm) for 4 h. The crude mixture was then subjected to flash chromatography using hexanes-ethyl acetate (4:1) as eluent to obtain 14 (363 mg, 64%) as a white solid; mp 113-114 °C; IR (film) 1598, 1564, 1311, 1276, 1141, 1080, 755 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.71 (crude d, J = 8.3 Hz, 2 H), 7.50 – 7.34 (m, 5 H), 7.31 (crude d, J = 8.0 Hz, 2 H), 5.91 (d, J = 0.8 Hz, 1 H), 2.97 – 2.88 (m, 1 H), 2.46 (s, 3 H), 1.02 – 0.96 (m, 4 H); ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 143.7, 139.7, 136.3, 130.1, 129.7, 129.6, 126.9, 125.9, 125.8, 21.6, 14.7, 9.3; HRMS (EI-TOF) m/z [M⁺] calcd for C₁₈H₁₈O₂SSe: 376.0201; found: 376.0213.

Further elution afforded 16 (40 mg, 7%) as a clear oil; IR (film) 1957, 1597, 1582, 1321, 1147, 1085, 737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (crude d, J = 8.3 Hz, 2 H), 7.52 – 7.48 (m, 2 H), 7.33 (crude d, J = 8.0 Hz, 2 H), 7.30 – 7.28 (m, 3 H), 6.24 (dt, J = 5.8, 2.9 Hz, 1 H), 5.92 (td, J = 6.1, 5.9 Hz, 1 H), 2.90 (crude t, J = 7.5 Hz, 2 H), 2.55 – 2.48 (m, 2 H), 2.46 (s, 3 H); ¹³C NMR (101 MHz, CDCl₃) δ 205.3, 144.5, 138.3, 133.1, 129.8, 129.3, 129.2, 127.7, 127.3, 102.2, 100.1, 28.5, 25.7, 21.6; HRMS (EI-TOF) m/z [M⁺] calcd for C₁₈H₁₈O₂SSe: 376.0201; found: 376.0212.
Preparation of vinyl sulfone 20.

\[
\text{Ar}^+\text{S}^\text{ONa} + \text{CH}_2\text{I}_2 \xrightarrow{\text{CH}_3\text{SO}} \text{Ar}^+\text{S}^\text{OI} \xrightarrow{140^\circ \text{C}} \text{Ar}^+\text{S}^\text{OPPh}_3 \xrightarrow{\text{THF reflux}} \text{H} = \text{SO}_2\text{Ar}
\]

Diiodomethane (2.20 mL, 27.3 mmol) was added to a solution of sodium \(p\)-toluenesulinate (5.00 g, 28.0 mmol) in DMSO (15 mL) and heated at 80 \(^\circ\)C for 4 h. The orange solution was diluted with water (100 mL) and the product precipitated. The crude product was recrystallized from hot ethanol, washed with cold hexanes, and dried in vacuo to obtain iodomethyl \(p\)-tolyl sulfone (6.81 g, 84%) as white crystals; mp 129-130 \(^\circ\)C (lit. \(^\circ\)C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.83 (crude d, \(J = 8.3\) Hz, 2 H), 7.37 (crude d, \(J = 8.3\) Hz, 2 H), 4.44 (s, 2 H), 2.46 (s, 3 H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 145.8, 133.1, 130.1, 129.1, 21.8, 17.1; HRMS (EI-TOF) \(m/z\) [M]+ calcd for C\(_8\)H\(_9\)O\(_2\)SI: 295.9368; found: 295.9374.

The above sulfone (3.00 g, 10.1 mmol) and triphenylphosphine (2.66 g, 10.1 mmol) were heated at 140\(^\circ\)C for 2 days. The resulting solid was dissolved in dichloromethane (25 mL) and precipitated by adding toluene (50 mL). The solid was washed with toluene and dried in vacuo to yield the corresponding phosphonium salt as a white solid (3.49 g, 62%); mp 240-244 \(^\circ\)C (lit. \(^\circ\)C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.96 – 7.86 (m, 8 H), 7.79 – 7.73 (m, 3 H), 7.67 – 7.60 (m, 6 H), 7.29 (d, \(J = 8.1\) Hz, 2 H), 6.10 (d, \(J = 12.3\) Hz, 2 H), 2.35 (s, 3 H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 146.3, 136.4, 135.5 (d, \(J = 3.2\) Hz), 134.6 (d, \(J = 11.1\) Hz), 130.2 (d, \(J = 13.5\) Hz), 130.2,
128.6, 116.6 (d, \( J = 89.1 \) Hz), 51.0 (d, \( J = 45.7 \) Hz), 21.8; HRMS (EI-TOF) \( m/z \) [M]+ calcd for C_{26}H_{24}O_2PS: 431.1229; found: 431.1237.

The above phosphonium salt (1.50 g, 2.70 mmol) and 60% sodium hydride in mineral oil (108 mg, 2.70 mmol) were added to THF (12 mL) and stirred for 16 h. The solvent was removed under reduced pressure and the residue was redissolved in dichloromethane and filtered through basic aluminum oxide. The solvent was removed under reduced pressure and the solid was recrystallized from toluene to obtain the corresponding Wittig reagent (882 mg, 76%) as a white solid; mp 181-184 °C (lit.\(^4\) mp 186-187 °C); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.69 – 7.62 (m, 6 H), 7.57 – 7.51 (m, 3 H), 7.46 – 7.39 (m, 6 H), 7.33 (crude d, \( J = 8.2 \) Hz, 2 H), 6.99 (crude d, \( J = 7.9 \) Hz, 2 H), 2.96 (d, \( J = 13.9 \) Hz, 1 H), 2.31 (s, 3 H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 147.2, 139.9, 133.4 (d, \( J = 10.4 \) Hz), 132.2 (d, \( J = 3.0 \) Hz), 128.8 (d, \( J = 12.5 \) Hz), 128.7, 127.3 (d, \( J = 93.2 \) Hz), 125.1, 34.4 (d, \( J = 123.4 \) Hz, C-6), 21.4 (C-1); HRMS (EI-TOF) \( m/z \) [M]+ calcd for C_{26}H_{23}O_2PS: 430.1156; found: 430.1158.

A solution of the above ylide (500 mg, 1.16 mmol) and cyclopropanecarboxaldehyde (105 mg, 1.50 mmol) in THF (5 mL) was refluxed for 12 h. The mixture was concentrated \textit{in vacuo} and subjected to flash chromatography using hexanes-ethyl acetate (4:1) to afford 20 as an inseparable mixture of E/Z isomers (84 mg, 32%) as a white solid; mp 78-84 °C; IR (film) 1621, 1590, 1315, 1301, 1281, 1145 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( E \) isomer: \( \delta \) 7.77 (crude d, \( J = 8.3 \) Hz, 2 H), 7.34 (crude d, \( J = 8.3 \) Hz, 2 H), 6.41 (dd, \( J = 14.8, 9.3 \) Hz, 1 H), 6.35 (d, \( J = 14.8 \) Hz, 1 H), 2.45 (s, 3 H), 1.62 – 1.53 (m, 1 H), 1.03 – 0.98 (m, 2 H), 0.73 – 0.69 (m, 2 H); Z isomer: 7.84 (crude d, \( J = 8.3 \) Hz, 2 H), 7.36 (crude d, \( J = 8.3 \) Hz, 2 H), 6.17 (d, \( J = 11.0 \) Hz, 1 H), 5.48 (t, \( J = 11.1 \) Hz, 2.85 – 2.76 (m, 1 H), 2.46 (s, 3 H), 1.10 – 1.04 (m, 2 H), 0.61 – 0.57 (m, 2 H); \(^13\)C NMR (101 MHz, CDCl\(_3\)) both isomers \( \delta \) 151.5, 151.3, 143.9, 139.3, 138.3, 129.79, 129.77, 127.6, 127.5,
127.2, 127.1, 21.58, 21.56, 13.9, 10.8, 9.4, 9.0; HRMS (EI-TOF) m/z [M]^+ calcd for C_{12}H_{14}O_2S: 222.0715; found: 222.0713.

References

$^1$H and $^{13}$C NMR Spectra of 1,2-Addition Product 14 (400 MHz, CDCl₃)
$^1$H and $^{13}$C NMR Spectra of Allene 16 (400 MHz, CDCl$_3$)
$^1$H and $^{13}$C NMR Spectra of (E/Z)-Vinyl Sulfone 20 (400 MHz, CDCl₃)

20 $E:Z = 5:1$

H

SO₂Ar

H

H

SO₂Ar

20 $E:Z = 5:1$