S,O-Ligand-Promoted Palladium-Catalyzed C-H Functionalization Reactions of Nondirected Arenes

Naksomboon, K.; Valderas, C.; Gomez-Martinez, M.; Alvarez-Casao, Y.; Fernández Ibáñez, M.A.

DOI
10.1021/acscatal.7b02356

Publication date
2017

Document Version
Other version

Published in
ACS Catalysis

Citation for published version (APA):

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Supporting information

**S,O-Ligand-Promoted Palladium-Catalyzed C–H Functionalization Reactions of Nondirected Arenes**

Kananat Naksomboon, Carolina Valderas, Melania Gómez-Martínez, Yolanda Álvarez-Casao,
M. Ángeles Fernández-Ibáñez*

*Corresponding author. Email: m.a.fernandeziban@uva.nl

Van’t Hoff Institute for Molecular Sciences, University of Amsterdam,
Science Park 904, 1098 XH Amsterdam, The Netherlands.
Table of contents

1. General information S2
2. Synthesis of S,O-ligands S2
   2.1 General procedure for α-bromination of carboxylic acids S2
   2.2 General procedure for the addition of thiols to α-bromocarboxylic acids S3
   2.3 Procedure for the synthesis of 1-(phenylthio)cyclopropanecarboxylic acid (L5) S6
   2.4 Procedure for the synthesis of 2-(phenylthio)benzoic acid (L8) S7
   2.5 Procedure for the synthesis of tetrahydrothiophene-2-carboxylic acid (L17) S8
   2.6 Procedure for the synthesis of methyl 2-methyl-2-(phenylthio)propanoate (L22), 2-methyl-2-(phenylsulfinyl)propanoic acid (L19) and 2-methyl-2-(phenylsulfonyl)propanoic acid (L20) S9
3. Pd-catalyzed C-H functionalization reactions S11
   3.1 Pd-catalyzed C-H olefination of benzene S11
      -Ligand optimization
      -Kinetic profile of the Pd-catalyzed C-H olefination of benzene with 3-methyl-2-(phenylthio)butanoic acid (L2) and without ligand
      Reaction optimization study
      -Loading of the ligand
      -Loading of the catalyst
      -Screening of the amount of benzene
      -Screening of the oxidant
   3.2 General procedure for the Pd-catalyzed C-H olefination of simple arenes S15
   3.3 General procedure for the Pd-catalyzed C-H olefination of benzene with activated olefins S22
   3.4 General procedure for the Pd-catalyzed C-H olefination of estrone and naproxen derivatives S24
   3.5 General procedure for the Pd-catalyzed C-H acetoxylation of benzene S25
      -Kinetic profile of the Pd-catalyzed C-H acetoxylation of benzene with 3-methyl-2-(phenylthio)butanoic acid (L2), with pyridine and without ligand
   3.6 General procedure for the Pd-catalyzed C-H allylation of benzene S27
      -Kinetic profile of the Pd-catalyzed C-H allylation of benzene with 3-methyl-2-(phenylthio)butanoic acid (L2) and without ligand
4. Synthesis of the palladium complex and crystal structure information S29
5. NMR spectra S30
6. References S70
1. General information

Chromatography: Silicycle Silica Flash P60 size 40-63 µm (230-400 mesh), TLC: Merck silica gel 60 (0.25mm). Visualization of the chromatogram was performed by UV, phosphomolybdic acid, K$_2$Cr$_2$O$_7$ and oleum staining. Mass spectra were recorded on AccuTOF GC v 4g, JMS-T100GCV mass spectrometers. $^1$H, $^{13}$C and $^{19}$F were recorded on Bruker 500 AMX, 400 and Bruker DRX 300 using CDCl$_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CDCl$_3$: δ 7.26 for $^1$H, δ 77.16 for $^{13}$C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, bs = broad singlet, m = multiplet), coupling constants (Hz), and integration. Infrared spectra were recorded on a Bruker IFS 28 FT-spectrophotometer and wavelengths are reported in cm$^{-1}$. ATR technique was used in IR spectroscopy. Melting point was measured by POLYTERM A Heiztisch Mikroskop. GC measurements were performed on Thermo Scientific TRACE Ultra Gas Chromatograph using RTX1 achiral column and Shimadzu GC-2010 Plus Gas Chromatograph using SH-Rxi-SHT (30 meter 0.25 mmID 0.25 µm) column. THF was dried over sodium/benzophenone and used freshly distilled. Acetonitrile was dried over CaH$_2$ and distilled. The glassware was pre-heated for moisture-sensitive reactions. All reagents and solvents were used as received. Pd(OAc)$_2$ was purchased from Strem. (Phenythio)acetic acid (L6), α-(phenylthio)phenylacetic acid (L7), 2-thiophenecarboxylic acid (L18) and thioanisole (L21) were purchased from commercial suppliers.

2. Synthesis of S,O-ligands

2.1 General procedure for α-bromination of carboxylic acids

α-Bromocarboxylic acids were prepared following the procedure described in the literature.$^1$ The solution of the corresponding carboxylic acid (1 equiv), N-bromosuccinimide (1.5 equiv), conc. H$_2$SO$_4$ and trifluoroacetic acid were heated at 85 °C overnight. The reaction was concentrated under reduced pressure. The crude was then purified by distillation.

2-Bromobutanoic acid$^2$

\[
\begin{align*}
\text{O} & \quad \text{Br} \\
\text{CH}_2\text{COOH} & \quad \\
\end{align*}
\]

2-Bromobutanoic acid was prepared following the general procedure using butyric acid (2.5 g, 28.37 mmol, 1 equiv), N-bromosuccinimide (7.57 g, 42.56 mmol, 1.5 equiv), conc. H$_2$SO$_4$ (0.75 mL) and trifluoroacetic acid (15 mL). Purification by distillation under reduced pressure (3 mbar, 93 °C) provided the entitled compound as a yellow liquid (4.12 g, 87% yield). $^1$H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.$^2$ $^1$H NMR (300 MHz) δ = 9.80 (bs, 1H), 4.20 (t, J = 7.2 Hz, 1H), 2.19 – 1.98 (m, 2H), 1.07 (t, J = 7.3 Hz, 3H).

2-Bromo-3,3-dimethylbutanoic acid

\[
\begin{align*}
\text{O} & \quad \text{Br} \\
\text{CH}_2\text{COOH} & \quad \\
\end{align*}
\]

2-Bromo-3,3-dimethylbutanoic acid was prepared following the general procedure using 3,3-dimethylbutyric acid (2.5 g, 21.52 mmol, 1 equiv), N-bromosuccinimide (5.75 g, 32.28 mmol, 1.5 equiv), conc. H$_2$SO$_4$ (0.57 mL) and trifluoroacetic acid (11 mL). Purification by distillation under reduced pressure (2 mbar, 100 °C) provided the entitled compound as a yellow solid (3.42 g, 81% yield). $^1$H NMR (400 MHz) δ = 4.10 (s, 1H), 1.15 (s, 9H); $^{13}$C NMR (101 MHz) δ = 175.4, 57.9, 34.4, 26.9; IR ν = 2960, 2916, 2871, 1703, 1418, 1367, 1268, 1179, 1164, 922, 884, 699, 501, 412 cm$^{-1}$; HRMS (FD) calcd for C$_8$H$_{13}$BrO$_2$ [M]+: 193.9942; found: 193.9947; M.p. 55 – 58 °C.
2.2 General procedure for the addition of thiols to α-bromocarboxylic acids

S,O-ligands were prepared following the procedure described in the literature. To a solution of the corresponding α-bromocarboxylic acid (1 equiv) and NaOH (2 or 2.5 equiv) in EtOH or tBuOH (0.16 - 0.33 M), the corresponding thiol (1 equiv) was added at room temperature. The reaction was refluxed overnight and concentrated under reduced pressure. The resulting crude was dissolved in water (10 mL) and acidified (6 M aqueous HCl solution) until pH = 1. The aqueous layer was extracted with Et₂O (3 x 10 mL). The combined organic layers were washed with saturated aqueous NaHCO₃ (3 x 10 mL). Then, the combined NaHCO₃ aqueous layers were acidified by 6 M aqueous HCl solution until pH = 1. The aqueous layer was extracted with Et₂O (3 x 20 mL). The combined organic layers were dried over anh. MgSO₄, filtered and concentrated under reduced pressure to obtain the desired product.

2-(Phenylthio)butanoic acid (L1)

Ligand L1 was prepared following the general procedure using 2-bromobutanoic acid (0.84 g, 5 mmol, 1 equiv), NaOH (0.4 g, 10 mmol, 2 equiv) and thiophenol (0.51 mL, 5 mmol, 1 equiv) in EtOH (15 mL) providing the entitled compound as a yellow oil (0.8 g, 81% yield). ¹H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound. ¹H NMR (300 MHz) δ = 7.49 – 7.46 (m, 2H), 7.35 – 7.26 (m, 3H), 3.57 (dd, J = 7.9, 7.0 Hz, 1H), 1.98 – 1.77 (m, 2H), 1.08 (t, J = 7.4 Hz, 3H).

3-Methyl-2-(phenylthio)butanoic acid (L2)

Ligand L2 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.91 g, 5 mmol, 1 equiv), NaOH (0.4 g, 10 mmol, 2 equiv) and thiophenol (0.51 mL, 5 mmol, 1 equiv) in EtOH (15 mL) providing the entitled compound as a colourless oil (0.76 g, 73% yield). ¹H NMR (400 MHz) δ = 7.48 – 7.46 (m, 2H), 7.32 – 7.26 (m, 3H), 3.43 (d, J = 8.5 Hz, 1H), 2.20 – 2.11 (m, 1H), 1.18 (d, J = 6.7 Hz, 3H), 1.10 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz) δ = 178.7, 134.0, 132.3, 129.1, 127.8, 59.0, 30.3, 20.5, 20.1; IR ν = 2963, 2931, 2872, 1701, 1284, 1220, 1186, 743, 690 cm⁻¹; HRMS (EI) calcd for C₁₃H₁₄O₂S [M⁺]: 210.0715; found: 210.0719.

3,3-Dimethyl-2-(phenylthio)butanoic acid (L3)

Ligand L3 was prepared following the general procedure using 2-bromo-3,3-dimethylbutanoic acid (0.49 g, 2.5 mmol, 1 equiv), NaOH (0.2 g, 5 mmol, 2 equiv) and thiophenol (0.26 mL, 2.5 mmol, 1 equiv) in EtOH (7.5 mL) providing the entitled compound as a yellow solid (0.45 g, 80% yield). ¹H NMR (300 MHz) δ = 11.58 (bs, 1H), 7.55 – 7.52 (m, 2H), 7.36 – 7.25 (m, 3H), 3.56 (s, 1H), 1.24 (s, 9H); ¹³C NMR (75 MHz) δ = 179.0, 135.2, 131.8, 129.2, 127.6, 63.3, 34.5, 27.6; IR ν = 3077, 3059, 2964, 2905, 2870, 2667, 2562, 1694, 1271, 1182, 1026, 739, 689, 483 cm⁻¹; HRMS (EI) calcd for C₁₂H₁₆O₂S [M⁺]: 224.0871; found: 224.0887; M.p. 50 – 53 °C.
2-Methyl-2-(phenylthio)propanoic acid (L4)

Ligand L4 was prepared following the general procedure using 2-bromo-2-methylpropionic acid (0.84 g, 5 mmol, 1 equiv), NaOH (0.5 g, 12.5 mmol, 2.5 equiv) and thiophenol (0.51 mL, 5 mmol, 1 equiv) in tBuOH (15 mL) providing the entitled compound as a pale yellow solid (0.82 g, 84% yield). $^1$H NMR (300 MHz) $\delta$ = 7.53 – 7.50 (m, 2H), 7.40 – 7.31 (m, 3H), 1.50 (s, 6H); $^{13}$C NMR (75 MHz) $\delta$ = 180.3, 136.8, 131.1, 129.6, 128.8, 50.7, 25.5; IR ν = 3055, 2974, 2932, 2650, 2545, 1688, 1283, 1164, 751, 691 cm$^{-1}$; HRMS (EI) calcd for C$_{10}$H$_{13}$S$^+$: 196.0558; found: 196.0560; M.p. 45 – 48 °C.

2-(Mesitylthio)-3-methylbutanoic acid (L9)

Ligand L9 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (100 mg, 0.55 mmol, 1 equiv), NaOH (44 mg, 1.1 mmol, 2 equiv) and 2,4,6-trimethylbenzenethiol (0.1 mL, 0.55 mmol, 1 equiv) in EtOH (1.7 mL) providing the entitled compound as a white solid (0.73 mg, 53% yield). $^1$H NMR (300 MHz) $\delta$ = 6.91 (s, 2H), 3.12 (d, $J$ = 8.9 Hz, 1H), 2.48 (s, 6H), 2.25 (s, 3H), 2.19 – 2.11 (m, 1H), 1.22 (d, $J$ = 6.7 Hz, 3H), 1.09 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (101 MHz) $\delta$ = 178.4, 159.9, 135.8, 123.6, 114.5, 60.0, 54.0, 31.7, 20.5, 19.7; IR ν = 2967, 2924, 2874, 1696, 1297, 1281, 872, 690, 555, 496 cm$^{-1}$; HRMS (EI) calcd for C$_{14}$H$_{20}$O$_2$S$^+$: 252.1184; found: 252.1184; M.p. 118 – 123 °C.

3-Methyl-2-(tritylthio)butanoic acid (L10)

Ligand L10 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.26 g, 1.45 mmol, 1 equiv), NaOH (0.15 g, 3.63 mmol, 2.5 equiv) and triphenylmethanethiol (0.4 g, 1.45 mmol, 1 equiv) in EtOH (7.25 mL) providing the entitled compound as a white solid (0.21 g, 39% yield). $^1$H NMR (300 MHz) $\delta$ = 7.54 – 7.50 (m, 6H), 7.32 – 7.19 (m, 9H), 2.80 (d, $J$ = 6.3 Hz, 1H), 2.03 – 1.92 (m, 1H), 1.04 (d, $J$ = 6.7 Hz, 3H), 0.97 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (75 MHz) $\delta$ = 178.9, 144.4, 129.7, 128.0, 126.9, 68.1, 54.0, 31.7, 20.5, 19.7; IR ν = 2964, 1697, 1470, 1419, 1255, 1184, 745, 676, 528 cm$^{-1}$; HRMS (FD): calcd for C$_{28}$H$_{32}$O$_2$S$^+$: 376.1497; found 376.1495. M.p. 164 – 167 °C.

2-[(4-Methoxyphenyl)thio]-3-methylbutanoic acid (L11)

Ligand L11 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.45 g, 2.5 mmol, 1 equiv), NaOH (0.2 g, 5 mmol, 2 equiv) and 4-methoxymethylphenol (0.31 mL, 2.5 mmol, 1 equiv) in EtOH (7.5 mL) providing the entitled compound as a colourless oil (0.56 g, 96% yield). $^1$H NMR (400 MHz) $\delta$ = 7.44 (d, $J$ = 8.9 Hz, 2H), 6.84 (d, $J$ = 8.9 Hz, 2H); 3.79 (s, 3H), 3.24 (d, $J$ = 8.9 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.18 (d, $J$ = 6.7 Hz, 3H); $^{13}$C NMR (101 MHz) $\delta$ = 178.4, 159.9, 135.8, 123.6, 114.5, 60.0, 55.1, 29.7, 20.5, 20.0; IR ν = 2962, 2936, 2872, 2836, 1699, 1591, 1493, 1285, 1244, 1172, 1030, 827 cm$^{-1}$; HRMS (EI) calcd for C$_{15}$H$_{18}$O$_2$S$^+$: 240.0820; found: 240.0825.
3-Methyl-2-[(2,4,6-trimethoxyphenyl)thio]butanoic acid (L12)

Ligand L12 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.14 g, 0.8 mmol, 1 equiv), NaOH (0.08 g, 2.5 mmol, 2.5 equiv) and 2,4,6-trimethoxybenzenethiol (0.16 g, 0.8 mmol, 1 equiv) in EtOH (5 mL) providing the entitled compound as a pale brown solid (0.16 g, 66% yield). ¹H NMR (400 MHz) δ = 6.12 (s, 2H), 3.84 (s, 6H), 3.82 (s, 3H), 3.27 (d, J = 7.6 Hz, 1H), 2.23 – 2.17 (m, 1H), 1.17 (d, J = 6.7 Hz, 3H), 1.10 (d, J = 6.7 Hz, 3H); ¹³C NMR (101 MHz) δ = 177.3, 162.6, 162.1, 99.8, 91.0, 59.4, 56.1, 55.4, 30.6, 20.7, 19.8; IR ν = 3001, 2981, 2958, 2838, 1691, 1578, 1467, 1405, 1366, 1121, 951, 802 cm⁻¹; HRMS (FD): calcd for C₁₄H₁₀O₂S [M]⁺: 300.1031; found: 300.1031; M.p.131 – 136 °C.

3-Methyl-2-[(perfluorophenyl)thio]butanoic acid (L13)

Ligand L13 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.18 g, 1 mmol, 1 equiv), NaOH (0.1 g, 2.5 mmol, 2.5 equiv) and 2,3,4,5,6-pentafluorothiophenol (0.13 mL, 1 equiv) in ³BuOH (3.5 mL) providing the entitled compound as a pale yellow oil (0.28 g, 94% yield). ¹H NMR (300 MHz) δ = 8.82 (bs, 1H), 3.32 (d, J = 8.9 Hz, 1H), 2.17 – 2.05 (m, 1H), 1.22 (d, J = 6.6 Hz, 3H), 1.09 (d, J = 6.6 Hz, 3H); ¹³C NMR (75 MHz) δ = 177.2, 148.5 (d, J_CF = 247.3 Hz), 142.4 (d, J_CF = 257.3 Hz), 137.4 (d, J_CF = 256.0 Hz), 107.4 – 106.8 (m), 58.4, 30.3, 20.6, 19.9; ¹⁹F NMR (282 MHz) δ = -130.99 (d, J = 18.3 Hz), -150.30 (t, J = 20.8 Hz), -160.57 – -160.74 (m); IR ν = 2969, 1706, 1512, 1486, 1289, 1092, 980, 862 cm⁻¹; HRMS (El) calcd for C₁₁H₉F₄O₃S [M]⁺: 300.0243; found: 300.0256.

2-[(4-Trifluoromethylphenyl)thio]-3-methylbutanoic acid (L14)

Ligand L14 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.45 g, 2.5 mmol, 1 equiv), NaOH (0.2 g, 5 mmol, 2 equiv) and 4-(trifluoromethyl)thiophenol (0.32 mL, 2.5 mmol, 1 equiv) in EtOH (7.5 mL) providing the entitled compound as a pale yellow oil (0.41 g, 59% yield). ¹H NMR (300 MHz) δ = 7.57 – 7.50 (m, 4H), 3.55 (d, J = 8.4 Hz, 1H), 2.26 – 2.14 (m, 1H), 1.18 (d, J = 6.7 Hz, 3H), 1.12 (d, J = 6.7 Hz, 3H); ¹³C NMR (75 MHz) δ = 178.5, 139.8, 130.5, 129.2 (q, J_CF = 32.8 Hz), 126.0 (q, J_CF = 3.7 Hz), 122.3, 57.8, 30.6, 20.5, 20.0; ¹⁹F NMR (282 MHz) δ = -62.64; IR ν = 2966, 2933, 2875, 1705, 1607, 1323, 1164, 1123, 1094, 1063, 1014, 828 cm⁻¹; HRMS (El) calcd for C₁₂H₁₃F₂O₃S [M]⁺: 278.0588; found: 278.0595.

2-(Benzylthio)-3-methylbutanoic acid (L15)

Ligand L15 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.45 g, 2.5 mmol, 1 equiv), NaOH (0.2 g, 5 mmol, 2 equiv) and benzyl mercaptan (0.29 mL, 2.5 mmol, 1 equiv) in EtOH (7.5 mL) providing the entitled compound as a pale brown oil (0.5 g, 90% yield). ¹H NMR (400 MHz) δ = 7.36 – 7.30 (m, 4H), 7.27 – 7.24 (m, 1H), 3.84 (s, 2H), 2.91 (d, J = 8.6 Hz, 1H), 2.12 – 2.03 (m, 1H), 1.01 (d, J = 2.9 Hz, 3H), 0.99 (d, J = 2.9 Hz, 3H); ¹³C NMR (101 MHz) δ = 179.2, 137.2, 129.1, 128.4, 127.2, 53.5, 36.0, 29.2, 20.7, 19.7; IR ν = 3028, 2962, 2928, 2872, 1698, 1289, 1190, 929, 766, 670 cm⁻¹; HRMS (El) calcd for C₁₂H₁₆O₂S [M]⁺: 224.0871; found: 224.0878.
2-(Isopropylthio)-3-methylbutanoic acid (L16)

Ligand L16 was prepared following the general procedure using 2-bromo-3-methylbutanoic acid (0.91 g, 5 mmol, 1 equiv), NaOH (0.5 g, 12.5 mmol, 2.5 equiv) and 2-propanethiol (0.46 mL, 5 mmol, 1 equiv) in tBuOH (15 mL) providing the entitled compound as a colourless oil (0.79 g, 89% yield). 1H NMR (400 MHz) δ = 10.86 (s, 1H), 3.06 – 3.00 (m, 2H), 2.05 – 2.01 (m, 1H), 1.28 (d, J = 6.5 Hz, 3H), 1.26 (d, J = 6.5 Hz, 3H), 1.08 (d, J = 6.5 Hz, 3H), 1.04 (d, J = 6.5 Hz, 3H); 13C NMR (75 MHz) δ = 179.7, 53.9, 36.2, 30.3, 23.6, 23.4, 20.9, 20.1; IR ν = 2962, 2928, 2869, 1698, 1461, 1367, 928, 699 cm⁻¹; HRMS (FD): calcd for C₈H₁₆O₂S1 [M]+: 176.0871; found 176.0869.

2.3 Procedure for the synthesis of 1-(phenylthio)cyclopropanecarboxylic acid (L5)

Scheme 1. Synthetic route of 1-(phenylthio)cyclopropanecarboxylic acid (L5)

Procedure for the synthesis of 1,1,3-(trisphenylthio)propane

1,1,3-(Trisphenylthio)propane was synthesized following the procedure described in the literature. Acrolein (1.34 mL, 20 mmol, 1 equiv) and thiophenol (6.4 mL, 62 mmol, 3.1 equiv) were stirred in dry acetonitrile (10 mL) under nitrogen atmosphere at -50 °C. SnCl₄ (0.47 mL, 4 mmol, 20 mol%) was added to the reaction at -50 °C and stirred overnight at room temperature. The reaction was quenched with aqueous NaOH solution (0.5 M, 25 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with aqueous NaOH solution (0.5 M, 3 x 20 mL), dried over anh. MgSO₄, filtered and concentrated under reduced pressure to afford 1,1,3-(trisphenylthio)propane (7.09 g, 96% yield).

1,1,3-(Tristhiophenyl)propane

1H NMR spectra data of the isolated material matched with the spectra data reported in the literature. 1H NMR (400 MHz) δ = 7.47 – 7.44 (m, 3H), 7.32 – 7.20 (m, 12H), 4.64 (t, J = 6.8 Hz, 1H), 3.22 (t, J = 6.9 Hz, 2H), 2.20 – 2.13 (m, 2H).

Procedure for the synthesis of 1,1-bis(phenylthio)cyclopropane

1,1-Bis(phenylthio)cyclopropane was synthesized following the procedure described in the literature. TMEDA (1.70 mL, 11.2 mmol, 2 equiv) was added to a solution of 1,1,3-(trisphenylthio)propane (2.06 g, 5.6 mmol, 1 equiv) in dry THF (30 mL) under nitrogen atmosphere. The reaction was cooled to 0 °C. MeLi (1.6 M, 5.6 mL, 8.96 mmol, 1.6 equiv) was added to the mixture and the reaction was stirred for 3 h at 0 °C. The mixture was quenched with saturated aqueous ammonium chloride (30 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over anh. MgSO₄, filtered and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel using Et₂O:petroleum ether (1:49 v/v) as an eluent to afford 1,1-bis(phenylthio)cyclopropane (0.71 g, 49% yield).
1,1-Bis(phenylthio)cyclopropane\(^{10}\)

\[
\begin{array}{c}
\text{Ph} \quad \text{S} \\
\text{O} \\
\text{S} \quad \text{Ph}
\end{array}
\]

\(^1\)H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.\(^{10}\) \(^1\)H NMR (400 MHz) \(\delta = 7.51 - 7.48\) (m, 4H), 7.38 - 7.34 (m, 4H), 7.30 - 7.26 (m, 2H), 1.52 (s, 4H).

Procedure for the synthesis of 1-(phenylthio)cyclopropanecarboxylic acid (L5)\(^{11}\)

Ligand L5 was synthesized following the procedure described in the literature.\(^{11}\) The solution of lithium naphthalenide (0.5 M, 8.4 mL, 4.2 mmol, 1.8 equiv) (dry THF (10 mL) was added to freshly prepared Li (52 mg, 7.5 mmol, 1.5 equiv) and naphthalene (0.64 g, 5 mmol, 1 equiv) under nitrogen atmosphere. The reaction was sonicated at maximum energy for 5 min at room temperature to afford a green solution. The reaction was stirred for another 1 h at room temperature to give a dark green solution in dry THF (10 mL) under nitrogen atmosphere was cooled to -70 °C. The solution of 1,1-bis(phenylthio)cyclopropane (0.6 g, 2.32 mmol, 1 equiv) in dry THF (3 mL) was added to the reaction and stirred for 15 min. Dry CO\(_2\) (s) (excess) was added and the mixture was stirred at -70 °C for 5 min and then at room temperature for 3 h. The reaction was quenched by adding saturated aqueous ammonium chloride (25 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over anh. MgSO\(_4\), filtered and concentrated under reduced pressure. The crude was then purified by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) as an eluent to afford 1-(phenylthio)cyclopropanecarboxylic acid (L5) as a pale yellow solid (0.15 g, 33% yield).

\(^1\)H NMR (300 MHz) \(\delta = 7.39 - 7.28\) (m, 4H), 7.28 - 7.20 (m, 1H), 1.92 - 1.88 (m, 2H), 1.51 - 1.45 (m, 2H); \(^{13}\)C NMR (75 MHz) \(\delta = 179.0, 135.8, 129.1, 128.4, 126.4, 26.9, 21.9\); IR \(\nu = 3059, 3017, 2924, 2853, 1689, 1439, 1302, 930, 737, 690\) cm\(^{-1}\); HRMS (FD): calcd for C\(_{10}\)H\(_{10}\)O\(_2\)S\([\text{M}]^+\): 194.0402; found 194.0407; M.p. 77 – 83 °C.

2.4 Procedure for the synthesis of 2-(phenylthio)benzoic acid (L8)\(^{13}\)

Ligand L8 was synthesized following the procedure described in the literature.\(^{13}\) A mixture of thiophenol (0.34 mL, 3.25 mmol, 1.3 equiv), 2-bromobenzoic acid (0.5 g, 2.5 mmol, 1 equiv), potassium carbonate (0.35 g, 5 mmol, 1 equiv), copper powder (14.3 mg, 0.23 mmol, 9 mol%) and copper oxide (16.1 mg, 0.11 mmol, 4.5 mol%) in EtOH (1 mL) was refluxed for 4 h. Then, the reaction was cooled to room temperature and the solvent was concentrated under reduced pressure. The residue was poured into water (15 mL) and acidified with diluted hydrochloric acid until pH = 5 giving a precipitate, which was dissolved in aqueous Na\(_2\)CO\(_3\) solution (5%). The solution was filtered thought Celite, acidified again with diluted HCl and filtered giving 2-(phenylthio)benzoic acid (L8) as a white solid (0.15 g, 26% yield).

\(^1\)H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.\(^{13}\) \(^1\)H NMR (400 MHz) \(\delta = 8.16\) (dd, \(J = 7.8, 1.6\) Hz, 1H), 7.63 – 7.60 (m, 2H), 7.49 – 7.46 (m, 3H), 7.33 – 7.29 (m, 1H), 7.18 (td, \(J = 7.6, 1.2\) Hz, 1H), 6.84 (dd, \(J = 8.2, 1.1\) Hz, 1H).
2.5 Procedure for the synthesis of tetrahydrothiophene-2-carboxylic acid (L17)  

\[ \text{NC} - \text{Cl} \xrightarrow{1) K_2CO_3, MeCN, 40 \degree C} \text{NC} - \text{S} - \text{Cl} \xrightarrow{2) H_2S, 45 \degree C, overnight} \text{NC} - \text{S} - \text{CN} \xrightarrow{\text{TEBA, 50\% NaOH, RT, 1 h}} \text{NC} - \text{S} - \text{CN} \xrightarrow{\text{HCl 6 M, reflux, 3 h}} \text{NC} - \text{O} \]

Scheme 2. Synthetic route of tetrahydrothiophene-2-carboxylic acid (L17)

Procedure for the synthesis of 2-[(3-chloropropyl)thio]acetonitrile  
2-[(3-Chloropropyl)thio]acetonitrile was synthesized following the procedure described in the literature.  

Potassium carbonate (0.87 g, 6.33 mmol, 1 equiv) was added in one portion to a solution of chloroacetonitrile (0.8 mL, 12.66 mmol, 2 equiv) in acetonitrile (7 mL). The reaction was heated at 40 °C and a solution of 3-chloropropanethiol (0.7 mL, 6.33 mmol, 1 equiv) in acetonitrile (2 mL) was added dropwise to the reaction. Then, the reaction mixture was heated at 45 °C overnight. The inorganic salts were filtered off and the solvent was removed under reduced pressure. The reaction was extracted with Kugelrohr distillation (760 mmHg, 220 °C) giving 2-[(3-chloropropyl)thio]acetonitrile as a colourless oil (0.49 g, 52% yield).

2-[(3-Chloropropyl)thio]acetonitrile  

\(^1\)H NMR spectra data of the isolated material matched with the spectra data reported in the literature.  
\(^1\)H NMR (400 MHz)  
\(\delta = 3.62 \ (t, J = 6.2 \ Hz, 2H), 3.29 \ (s, 2H), 2.83 \ (t, J = 7.0 \ Hz, 2H), 2.09 - 2.02 \ (m, 2H)\)

Procedure for the synthesis of tetrahydrothiophene-2-carbonitrile  
Tetrahydrothiophene-2-carbonitrile was synthesized following the procedure described in the literature. Aqueous NaOH solution (50% v/v, 2.2 mL) was added dropwise to the mixture of 2-[(3-chloropropyl)thio]acetonitrile (0.49 g, 3.27 mmol, 1 equiv) and benzyltriethylammonium chloride (TEBA) (22.5 mg, 98.6 μmol, 3 mol%). The mixture was stirred for 1 h. The reaction was extracted with CH₂Cl₂ (3 x 5 mL). The combined organic layers were washed with aqueous HCl solution (10%, 15 mL) and water (15 mL). The organic layers were dried over anh. MgSO₄, filtered and evaporated under reduced pressure. Purification of the mixture was carried out by Kugelrohr distillation (760 mmHg, 220 °C) giving tetrahydrothiophene-2-carbonitrile as a colourless oil (0.28 g, 76% yield).

Tetrahydrothiophene-2-carbonitrile  

\(^1\)H NMR spectra data of the isolated material matched with the spectra data reported in the literature.  
\(^1\)H NMR (400 MHz)  
\(\delta = 3.95 - 3.93 \ (m, 1H), 3.06 - 3.03 \ (m, 1H), 2.91 - 2.88 \ (m, 1H), 2.29 - 2.26 \ (m, 1H), 2.17 - 2.07 \ (m, 3H)\)

Procedure for the synthesis of tetrahydrothiophene-2-carboxylic acid (L17)  
Aqueous HCl solution (6 M, 1.5 mL) was added to tetrahydrothiophene-2-carbonitrile (0.28 g, 2.48 mmol, 1 equiv) and the reaction was refluxed for 3 h. Then, the reaction mixture was extracted with EtOAc (3 x 5 mL). The combined organic layers were dried over anh. MgSO₄, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) as an eluent to obtain tetrahydrothiophene-2-carboxylic acid (L17) as a white solid (0.2 g, 61% yield).
Tetrahydrothiophene-2-carboxylic acid (L17)

\[ \text{H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.} \]

\[ ^1\text{H NMR (400 MHz) } \delta = 11.92 (bs, 1H), 3.94 (dd, J = 7.2, 4.4 Hz, 1H), 3.01 – 2.96 (m, 1H), 2.91 – 2.85 (m, 1H), 2.30 – 2.27 (m, 1H), 2.18 – 1.98 (m, 3H). \]

2.6 Procedure for the synthesis of methyl 2-methyl-2-(phenylthio)propanoate (L22), 2-methyl-2-(phenylsulfinyl)propanoic acid (L19) and 2-methyl-2-(phenylsulfonyl)propanoic acid (L20)

**Scheme 3. Synthetic route of methyl 2-methyl-2-(phenylthio)propanoate (L22), 2-methyl-2-(phenylsulfinyl)propanoic acid (L19) and 2-methyl-2-(phenylsulfonyl)propanoic acid (L20)**

**Procedure for the esterification of 2-methyl-2-(phenylthio)propanoic acid (L4)**

A solution of 2-methyl-2-(phenylthio)propanoic acid (L4) (0.69 g, 3.52 mmol, 1 equiv) and p-TsOH·H₂O (0.67 g, 3.52 mmol, 1 equiv) in MeOH (10 mL) was refluxed overnight. The reaction was evaporated to dryness. The crude obtained was dissolved in NaOH solution, basified until pH = 14 and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried over anh. MgSO₄, filtered and concentrated under reduced pressure to afford methyl 2-methyl-2-(phenylthio)propanoate (L22) as a white solid (0.64 g, 86% yield).

**Methyl 2-methyl-2-(phenylthio)propanoate (L22)**

\[ ^1\text{H NMR (300 MHz) } \delta = 7.51 – 7.40 (m, 2H), 7.38 – 7.22 (m, 3H), 3.66 (s, 3H), 1.49 (s, 6H); ^{13}\text{C NMR (101 MHz) } \delta = 174.5, 136.8, 131.5, 129.5, 128.8, 52.3, 51.2, 25.9; \text{IR } \nu = 3003, 2953, 1715, 1437, 1269, 1152, 1124, 750, 689, 482 \text{ cm}^{-1}; \text{HRMS (EI) calcld for } C_{11}H_{14}O_2S [M]^+: 210.0715; \text{found: } 210.0721; \text{M.p. } 34 – 37 \degree \text{C.} \]

**Procedure for the oxidation of methyl 2-methyl-2-(phenylthio)propanoate (L22)**

\[ m\text{-CPBA (77%, 1 equiv or 3 equiv) was added to a solution of methyl 2-methyl-2-(phenylthio)propanoate (L22) (1 equiv) in CH}_2\text{Cl}_2 \text{ at } 0 \degree \text{C. The reaction was stirred at room temperature overnight. The reaction mixture was quenched with saturated aqueous Na}_2\text{SO}_4 \text{ (10 mL) and extracted with CH}_2\text{Cl}_2 \text{ (3 x 15 mL). The combined organic layers were washed with saturated aqueous NaHCO}_3 \text{ (30 mL), dried over anh. MgSO}_4 \text{, filtered and concentrated under reduced pressure. The crude mixture was purified as specified in each case to obtain the desired product.} \]
Methyl 2-methyl-2-(phenylsulfonyl)propanoate

Methyl 2-methyl-2-(phenylsulfonyl)propanoate was synthesized following the general procedure using m-CPBA (0.36 g, 1.62 mmol, 1 equiv) and methyl 2-methyl-2-(phenylthio)propanoate (L22) (0.34 g, 1.62 mmol, 1 equiv) in CH₂Cl₂ (7 mL).

Purification by column chromatography on silica gel using EtOAc:petroleum ether (3:7 v/v) as an eluent provided the entitled compound as a white solid (0.15 g, 87% yield). ¹H NMR (300 MHz) δ = 7.49 – 7.42 (m, 5H), 3.65 (s, 3H), 1.58 (s, 3H), 1.29 (s, 3H); ¹³C NMR (75 MHz) δ = 171.4, 140.2, 131.9, 128.8, 69.3, 53.2, 20.4, 18.6; IR ν = 2953, 2926, 2852, 1724, 1460, 1444, 1282, 1272, 1154, 1081, 751, 692 cm⁻¹.

Methyl 2-methyl-2-(phenylsulfinyl)propanoate

Methyl 2-methyl-2-(phenylsulfinyl)propanoate was synthesized following the general procedure using m-CPBA (0.64 g, 2.85 mmol, 3 equiv) and methyl 2-methyl-2-(phenylthio)propanoate (L22) (0.20 g, 0.95 mmol, 1 equiv) in CH₂Cl₂ (5 mL) providing the entitled compound as a white solid (0.2 g, 87% yield). ¹H NMR (400 MHz) δ = 7.84 (dd, J = 8.4, 1.2 Hz, 2H), 7.69 – 7.65 (m, 1H), 7.55 (dd, J = 10.7, 4.8 Hz, 2H), 3.68 (s, 3H), 1.61 (s, 6H); ¹³C NMR (101 MHz) δ = 169.4, 135.8, 134.3, 130.5, 128.8, 69.3, 53.2, 20.4; IR ν = 3001, 2957, 1736, 1448, 1301, 1276, 1152, 1123, 1075, 835, 765, 723, 695, 608, 563 cm⁻¹.

Procedure for the hydrolysis of methyl 2-methylpropanoate derivatives

The corresponding methyl 2-methylpropanoate (1 equiv) and NaOH (20 equiv) were stirred at room temperature overnight in a mixture of THF, MeOH and H₂O (1:1:1). Then, the reaction was evaporated to dryness. The obtained crude was dissolved in H₂O (10 mL) and washed with CH₂Cl₂ (3 x 10 mL). The aqueous layer was acidified with aqueous HCl solution (1 M) to pH = 1 and extracted with CH₂Cl₂ (3 x 15 mL). The combined organic layers were dried over anh. MgSO₄, filtered and concentrated under reduced pressure to afford the desired product.

2-Methyl-2-(phenylsulfinyl)propanoic acid (L19)

2-Methyl-2-(phenylsulfinyl)propanoic acid (L19) was synthesized following the general procedure using methyl 2-methyl-2-(phenylsulfinyl)propanoate (0.14 g, 0.62 mmol, 1 equiv) and NaOH (0.5 g, 12.4 mmol, 20 equiv) in a mixture of THF, MeOH and H₂O (1, 1 and 1 mL, respectively) providing the entitled compound as a white solid (0.11 g, 84% yield). ¹H NMR (300 MHz) δ = 8.41 (bs, 1H), 7.63 – 7.47 (m, 5H), 1.43 (s, 3H), 1.42 (s, 3H); ¹³C NMR (75 MHz) δ = 173.2, 138.0, 132.5, 129.1, 126.2, 65.0, 19.4, 18.6; IR ν = 2982, 2936, 1712, 1440, 1225, 1145, 1120, 1011, 995, 749, 686, 591, 510, 485 cm⁻¹; HRMS (FD) calcd for C₁₀H₁₂O₄S [M⁺]: 212.0507; found: 212.0498; M.p. 131 – 134 °C.

2-Methyl-2-(phenylsulfonyl)propanoic acid (L20)

2-Methyl-2-(phenylsulfonyl)propanoic acid (L20) was synthesized following the general procedure using methyl 2-methyl-2-(phenylsulfonyl)propanoate (0.16 g, 0.66 mmol, 1 equiv) and NaOH (0.53 g, 13.2 mmol, 20 equiv) in a mixture of THF, MeOH and H₂O (1, 1 and 1 mL, respectively) providing the entitled compound as a white solid (0.13 g, 86% yield). ¹H NMR (300 MHz) δ = 9.92 (bs, 1H), 7.89 (d, J = 7.6 Hz, 2H), 7.40 – 7.30 (m, 5H), 2.18 (s, 3H), 1.28 (s, 3H); ¹³C NMR (101 MHz) δ = 171.4, 140.2, 131.9, 128.8, 125.7, 66.5, 52.7, 20.7, 16.1; IR ν = 2953, 2926, 2852, 1724, 1460, 1444, 1272, 1154, 1081, 751, 692 cm⁻¹.
7.69 (t, J = 7.4 Hz, 1H), 7.56 (t, J = 7.6 Hz, 2H), 1.62 (s, 6H); $^{13}$C NMR (75 MHz) δ = 175.2, 135.2, 134.5, 130.6, 129.0, 69.1, 20.3; IR ν = 3066, 3002, 2918, 1700, 1284, 1128, 1073, 898, 723, 695, 606, 569, 532 cm$^{-1}$; HRMS (FD) calcd for C$_{15}$H$_{20}$O$_{4}$S [M+H]$^{+}$: 229.0535; found: 229.0526; M.p. 134 – 140 °C.

3. Pd-catalyzed C-H functionalization reactions

3.1 Pd-catalyzed C-H olefination of benzene

**Ligand optimization**

\[
\begin{align*}
\text{C}_6\text{H}_6 + \text{CO}_2\text{Et} & \xrightarrow{\text{Pd(OAc)}_2 (5 \text{ mol\%}) \quad \text{Ligand (5 \text{ mol\%})}} \quad \text{PhCO}_2\text{Et} \\
(11.2 \text{ equiv}) & \quad (1 \text{ equiv}) & \quad \text{AcOH, 100 °C, 2 h}
\end{align*}
\]

The corresponding ligand (12.5 µmol, 5 mol%) (some ligands were prepared in stock solution in CH$_2$Cl$_2$. In that case, the solution was added to the pressure tube and dried with nitrogen stream until dryness), Pd(OAc)$_2$ (2.8 mg, 12.5 µmol, 5 mol%), tert-butyl peroxybenzoate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), benzene (0.25 mL, 2.8 mmol, 11.2 equiv) and AcOH (1.25 mL, 0.2 M) were added into a pressure tube. The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 2 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard.

**Ethyl cinnamate (1)**

$^1$H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.$^{15}$ $^1$H NMR (300 MHz) δ = 7.69 (d, J = 16.0 Hz, 1H), 7.54 – 7.51 (m, 2H), 7.40 – 7.36 (m, 3H), 6.44 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H).

**Kinetic profile of the Pd-catalyzed C-H olefination of benzene with 3-methyl-2-(phenylthio)butanoic acid (L2) and without ligand**

3-Methyl-2-(phenylthio)butanoic acid (L2) (5.2 mg, 25 µmol, 5 mol%), Pd(OAc)$_2$ (5.6 mg, 25 µmol, 5 mol%), tert-butyl peroxybenzoate (94 µL, 0.5 mmol, 1 equiv), ethyl acrylate (53 µL, 0.5 mmol, 1 equiv), benzene (0.5 mL, 5.6 mmol, 11.2 equiv) and AcOH (2.5 mL, 0.2 M) were added into a pressure tube. The pressure tube was sealed with a crimp cap with septa and the reaction was placed in 100 °C pre-heated oil bath. The reaction was followed during time by sampling 0.1 mL. PhCl (20 µL) was added in each sample as internal standard for quantitative GC analysis. The reaction mixture was diluted with EtOAc (1 mL). The organic layer was quenched with aqueous Na$_2$SO$_3$ solution (10%, 1 mL) and washed with saturated aqueous NaHCO$_3$ solution (2 x 2 mL). The organic layer was filtered through a plug of Celite and analyzed by GC.
A parallel reaction without ligand was also performed to compare the kinetic profile. Pd(OAc)$_2$ (5.6 mg, 25 µmol, 5 mol%), tert-butyl peroxybenzoate (94 µL, 0.5 mmol, 1 equiv), ethyl acrylate (53 µL, 0.5 mmol, 1 equiv), benzene (0.5 mL, 5.6 mmol, 11.2 equiv) and AcOH (2.5 mL, 0.2 M) were added into a pressure tube. The pressure tube was sealed with a crimper cap with septa and the reaction was placed in 100 °C pre-heated oil bath. The reaction was followed during time by sampling 0.1 mL. PhCl (20 µL) was added in each sample as internal standard for quantitative GC analysis. The reaction mixture was diluted with EtOAc (1 mL). The organic layer was quenched with aqueous Na$_2$SO$_3$ solution (10%, 1 mL) and washed with saturated aqueous NaHCO$_3$ solution (2 x 2 mL). The organic layer was filtered through a plug of Celite and analyzed by GC.

Table S1. Kinetic studies of the Pd-catalyzed C-H olefination of benzene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction time</th>
<th>GC yield (L2)</th>
<th>GC yield (no ligand)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 min</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>10 min</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>3</td>
<td>15 min</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>4</td>
<td>30 min</td>
<td>26%</td>
<td>4%</td>
</tr>
<tr>
<td>5</td>
<td>45 min</td>
<td>38%</td>
<td>6%</td>
</tr>
<tr>
<td>6</td>
<td>1 h</td>
<td>50%</td>
<td>9%</td>
</tr>
<tr>
<td>7</td>
<td>1.5 h</td>
<td>65%</td>
<td>15%</td>
</tr>
<tr>
<td>8</td>
<td>2 h</td>
<td>69%</td>
<td>30%</td>
</tr>
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</table>
Reaction optimization study

**Loading of the ligand**

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH$_2$Cl$_2$) was added into a pressure tube and dried with nitrogen steam until dryness followed by Pd(OAc)$_2$ (2.8 mg, 12.5 µmol, 5 mol%), tert-butyl peroxybenzoate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), benzene (0.25 mL, 2.8 mmol, 11.2 equiv) and AcOH (1.25 mL, 0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 6 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard.

**Table S2. Screening of ligand loading**

<table>
<thead>
<tr>
<th>Entry</th>
<th>X mol% Ligand</th>
<th>Stock solution ligand (µL)</th>
<th>NMR yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.5</td>
<td>74</td>
<td>36%</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>148</td>
<td>63%</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>295</td>
<td>50%</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>443</td>
<td>11%</td>
</tr>
</tbody>
</table>

**Loading of the catalyst**

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH$_2$Cl$_2$) was added into a pressure tube and dried with nitrogen steam until dryness followed by the corresponding amount of Pd(OAc)$_2$, tert-butyl peroxybenzoate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), benzene (0.25 mL, 2.8 mmol, 11.2 equiv) and AcOH (1.25 mL, 0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 6 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard.
Table S3. Screening of catalyst loading

<table>
<thead>
<tr>
<th>Entry</th>
<th>X mol% Catalyst (µmol)</th>
<th>Pd(OAc)$_2$ (mg)</th>
<th>Stock solution ligand (µL)</th>
<th>NMR yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 mol% (12.5 µmol)</td>
<td>2.8</td>
<td>148</td>
<td>63%</td>
</tr>
<tr>
<td>2</td>
<td>4 mol% (10 µmol)</td>
<td>2.2</td>
<td>118</td>
<td>55%</td>
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<tr>
<td>3</td>
<td>3 mol% (7.5 µmol)</td>
<td>1.7</td>
<td>88</td>
<td>46%</td>
</tr>
<tr>
<td>4</td>
<td>2 mol% (5 µmol)</td>
<td>1.1</td>
<td>60</td>
<td>43%</td>
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</table>

Screening of the amount of benzene

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH$_2$Cl$_2$) (148 µL, 12.5 µmol, 5 mol%) was added into a pressure tube and dried with nitrogen steam until dryness followed by Pd(OAc)$_2$ (2.8 mg, 12.5 µmol, 5 mol%), tert-butyld peroxymonooate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), benzene (11.2 - 2 equiv) and AcOH (1.25 mL, 0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 6 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard.

Table S4. Screening of the amount of benzene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amount of benzene</th>
<th>NMR yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.25 mL, 2.8 mmol, 11.2 equiv</td>
<td>63%</td>
</tr>
<tr>
<td>2</td>
<td>0.18 mL, 2 mmol, 8 equiv</td>
<td>46%</td>
</tr>
<tr>
<td>3</td>
<td>0.13 mL, 1.5 mmol, 6 equiv</td>
<td>32%</td>
</tr>
<tr>
<td>4</td>
<td>89 µL, 1 mmol, 4 equiv</td>
<td>23%</td>
</tr>
<tr>
<td>5</td>
<td>45 µL, 0.5 mmol, 2 equiv</td>
<td>10%</td>
</tr>
</tbody>
</table>

Screening of the oxidant

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH$_2$Cl$_2$) (148 µL, 12.5 µmol, 5 mol%) was added into a pressure tube and dried with nitrogen steam until dryness followed
by Pd(OAc)$_2$ (2.8 mg, 12.5 µmol, 5 mol%), the corresponding oxidant (0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), benzene (0.25 mL, 2.8 mmol, 11.2 equiv) and AcOH (1.25 mL, 0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 6 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard.

Table S5. Screening of the oxidant

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant</th>
<th>Amount of oxidant</th>
<th>NMR yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>tBuOOH</td>
<td>25 µL</td>
<td>49%</td>
</tr>
<tr>
<td>2</td>
<td>AcOOH</td>
<td>17 µL</td>
<td>5%</td>
</tr>
<tr>
<td>3</td>
<td>PhCO$_2$Bu</td>
<td>47 µL</td>
<td>63%</td>
</tr>
<tr>
<td>4</td>
<td>Oxygen</td>
<td>1 atm</td>
<td>12%</td>
</tr>
<tr>
<td>5</td>
<td>BQ</td>
<td>27 mg</td>
<td>19%</td>
</tr>
<tr>
<td>6</td>
<td>AgOAc</td>
<td>41.7 mg</td>
<td>39%</td>
</tr>
<tr>
<td>7</td>
<td>Ag$_2$CO$_3$</td>
<td>68.9 mg</td>
<td>25%</td>
</tr>
<tr>
<td>8</td>
<td>Na$_2$S$_2$O$_8$</td>
<td>59.5 mg</td>
<td>17%</td>
</tr>
<tr>
<td>9</td>
<td>K$_2$S$_2$O$_8$</td>
<td>67.6 mg</td>
<td>24%</td>
</tr>
<tr>
<td>10</td>
<td>Oxone</td>
<td>76.8 mg</td>
<td>39%</td>
</tr>
</tbody>
</table>

3.2 General procedure for the Pd-catalyzed C-H olefination of simple arenes

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH$_2$Cl$_2$) (148 µL, 12.5 µmol, 5 mol%) was added to a pressure tube and dried with nitrogen steam until dryness followed by Pd(OAc)$_2$ (2.8 mg, 12.5 µmol, 5 mol%), tert-butyl peroxybenzoate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (27 µL, 0.25 mmol, 1 equiv), the corresponding arene (10 - 32 equiv) and AcOH (1.25 mL, 0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 6 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na$_2$SO$_3$ solution (10%). The organic layer was washed with saturated aqueous NaHCO$_3$ solution, dried over anh. MgSO$_4$, filtered and concentrated under reduced pressure. The NMR yield was determined by adding CH$_2$Br$_2$ (17.5 µL, 0.25 mmol, 1 equiv) as internal standard. The crude mixture was purified as specified in each case to obtain the desired product.
Table S6. Substrate scope

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Yield [%]</th>
<th>Isomer Ratio</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>88% [76%]</td>
<td>(a:b = 1:1.9)</td>
<td>55% (a:b = 1:3)</td>
</tr>
<tr>
<td>3</td>
<td>88% [83%]</td>
<td>(a:b:c = 4.9:1:1.3)</td>
<td>52% (a:b:c = 3:0:1)</td>
</tr>
<tr>
<td>4</td>
<td>88% [84%]</td>
<td>[76%] on 3.5 mmol scale</td>
<td>10%</td>
</tr>
<tr>
<td>5</td>
<td>87% [76%]</td>
<td>(a:b = 2:1)</td>
<td>57% (a:b = 1:1.1)</td>
</tr>
<tr>
<td>6</td>
<td>80% [72%]</td>
<td>(α:μ = 1.5:1)</td>
<td>46% (α:μ = 1:1.7)</td>
</tr>
<tr>
<td>7</td>
<td>82% [81%]</td>
<td>(a:b = 1:4.9)</td>
<td>40% (a:b = 1:5.7)</td>
</tr>
<tr>
<td>8</td>
<td>[81%]</td>
<td>(a:b = 6:1)</td>
<td>[28%] (a:b = 4:1)</td>
</tr>
<tr>
<td>9</td>
<td>70% [70%]</td>
<td></td>
<td>52%</td>
</tr>
<tr>
<td>10</td>
<td>45% [42%]</td>
<td>(α:m:p = 1.2:3.3:1)</td>
<td>22% (α:m:p = 1:4:1.2)</td>
</tr>
<tr>
<td>11</td>
<td>78% [74%]</td>
<td>(a:b:c = 14:4:1:4:6)</td>
<td>36% (a:b:c = 5:7:1:1:9)</td>
</tr>
<tr>
<td>12</td>
<td>60% [60%]</td>
<td>(a:b = 1:1.2)</td>
<td>22% (a:b = 1:1.7)</td>
</tr>
<tr>
<td>13</td>
<td>66% [64%]</td>
<td></td>
<td>30%</td>
</tr>
<tr>
<td>14</td>
<td>82% [77%]</td>
<td>[66%] on 1.75 mmol scale</td>
<td>23%</td>
</tr>
<tr>
<td>15</td>
<td>64% [60%]</td>
<td>(a:b = 4:3:1)</td>
<td>20% (a:b = 4:1)</td>
</tr>
<tr>
<td>16</td>
<td>87% [82%]</td>
<td>(α:p = 1:9:1)</td>
<td>46% (α:p = 1:1.3)</td>
</tr>
</tbody>
</table>

Yields were determined by $^1\text{H}$ NMR analysis of the crude mixture using CH$_2$Br$_2$ as internal standard. Isolated yields were given in square bracket.

**(E)-Ethyl 3-(2,3-dimethylphenyl)acrylate (2a) and (E)-ethyl 3-(3,4-dimethylphenyl)acrylate (2b)**

General procedure was followed using o-xylene (0.3 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compounds as a clear oil (37.8 mg as a mixture of isomers a:b = 1:1.9, 76% yield). $^1\text{H}$ NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.$^{16}$ $^1\text{H}$ NMR (300 MHz) δ = 8.10 (d, J = 15.8 Hz, 1H$_a$), 7.67 (d, J = 16.0 Hz, 1H$_b$), 7.41 (d, J = 7.6 Hz, 1H$_c$), 7.40 – 7.11 (m, 5H$_{α+μ}$), 6.42 (d, J = 16.0 Hz, 1H$_d$), 6.34 (d, J = 15.8 Hz, 1H$_e$), 4.33 – 4.25 (m, 4H$_{α+μ}$), 2.35 (s, 3H$_a$), 2.33 (s, 3H$_b$), 2.30 (s, 6H$_μ$), 1.40 – 1.34 (m, 6H$_{α+μ}$).
A parallel reaction without ligand was also performed providing the entitled compounds in 55% NMR yield (isomers a:b = 1:3).

(E)-Ethyl 3-{(2,4-dimethylphenyl)acrylate (3a),17 (E)-ethyl 3-{(3,5-dimethylphenyl)acrylate (3b)18 and (E)-ethyl 3-{(2,6-dimethylphenyl)acrylate (3c)19

General procedure was followed using m-xylene (0.31 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compounds as a clear oil (42.3 mg as a mixture of isomers a:b:c = 4.9:1:1.3, 83% yield). 1H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.17-19 1H NMR (300 MHz) δ = 7.97 (dd, J = 15.8, 2.8 Hz, 1Hb), 7.86 (dd, J = 17.3, 1.9 Hz, 1Ha), 7.66 (dd, J = 14.3, 3.0 Hz, 1Hb), 7.50 – 7.47 (m, 1Hb), 7.29 – 7.27 (m, 2Hb), 7.17 – 6.95 (m, 6H+G, 6.43 (dd, J = 16.0, 3.0 Hz, 1Hb), 6.35 (dd, J = 15.8, 2.9 Hz, 1Hb), 6.09 (dd, J = 17.3, 1.9 Hz, 1Ha), 4.32 – 4.26 (m, 6H+G), 2.43 – 2.28 (m, 18H+G), 1.39 – 1.34 (m, 9H+2G).

A parallel reaction without ligand was also performed providing the entitled compounds in 52% NMR yield (isomers a:b:c = 3:0:1).

Ethyl (E)-3-mesitylacrylate (4)20

General procedure was followed using mesitylene (0.35 mL, 2.5 mmol, 10 equiv) as arene substrate. The product was obtained as a clear oil (46 mg, 84% yield). 1H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.20 1H NMR (400 MHz) δ = 7.85 (d, J = 16.3 Hz, 1H), 6.90 (s, 2H), 6.06 (d, J = 16.4 Hz, 1H), 4.28 (q, J = 7.1 Hz, 2H), 2.34 (s, 6H), 2.29 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H).

A parallel reaction using 2-methyl-2-(phenylthio)propanoic acid (L4) (0.0846 M in CHCl3) (148 µL, 12.5 µmol, 5 mol%) was also performed providing the entitled compound in 93% NMR yield.

A parallel reaction without ligand was also performed providing the entitled compound in 10% NMR yield.

Large-scale synthesis

General procedure was followed using 3-methyl-2-(phenyl-thio)butanoic acid (L2) (36.8 mg, 0.175 mmol, 5 mol%), Pd(OAc)2 (39.3 mg, 0.175 mmol, 5 mol%), tert-butyl peroxybenzoate (0.66 mL, 3.5 mmol, 1 equiv), ethyl acrylate (0.37 mL, 3.5 mmol, 1 equiv), mesitylene (4.87 mL, 35 mmol, 10 equiv) and AcOH (9 mL, 0.1 M). The product was obtained as a clear oil (0.58 g, 76% yield).

(E)-Ethyl 3-{(naphthalen-1-yl)acrylate (5a) and (E)-ethyl 3-{(naphthalen-2-yl)acrylate (5b)21

General procedure was followed using naphthalene (0.32 g, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using petroleum ether as an eluent provided the entitled compounds as a clear oil (43.2 mg as a mixture of isomers a:b = 2:1, 76% yield). 1H NMR spectra data of the isolated material matched with the
spectra data reported in the literature for these compounds.\textsuperscript{21} \textsuperscript{1}H NMR (400 MHz) $\delta = 8.56$ (d, $J = 15.9$ Hz, 1H$_a$), 8.23 (d, $J = 7.8$ Hz, 1H$_b$), 7.95 – 7.84 (m, 7H$_{ar}$), 7.78 (d, $J = 7.2$ Hz, 1H$_a$), 7.69 (dd, $J = 8.7$, 1.7 Hz, 1H$_b$), 7.63 – 7.48 (m, 5H$_{ar}$), 6.58 (d, $J = 16.0$, 1H$_b$), 6.56 (d, $J = 15.9$, 1H$_a$), 4.39 – 4.29 (m, 4H$_{ar}$), 1.44 – 1.37 (m, 6H$_{ar}$).

A parallel reaction using 2-methyl-2-(phenylthio)propanoic acid (L4) (0.0846 M in CH$_2$Cl$_2$) (148 $\mu$L, 12.5 $\mu$mol, 5 mol%) was also performed providing the entitled compound in 89% NMR yield (isomer $a:b = 2.2:1$).

A parallel reaction without ligand was also performed providing the entitled compound in 57% NMR yield (isomers $a:b = 1:1.1$).

(E)-Ethyl 3-(2-methoxyphenyl)acrylate (6o),\textsuperscript{22} (E)-ethyl 3-(3-methoxyphenyl)acrylate (6m)\textsuperscript{23} and (E)-ethyl 3-(4-methoxyphenyl)acrylate (6p)\textsuperscript{22}

\begin{center}
\includegraphics[width=0.2\textwidth]{6.png}
\end{center}

General procedure was followed using anisole (0.27 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:9 v/v) as an eluent provided the entitled compound as a clear oil (37.8 mg as a mixture of isomers $o:p = 1.5:1$ and trace amount of $m$, 72% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{22,23} \textsuperscript{1}H NMR (400 MHz) $\delta = 7.99$ (d, $J = 16.2$ Hz, 1H$_a$), 7.65 (d, $J = 16.0$ Hz, 1H$_b$), 7.64 (d, $J = 16.0$ Hz, 1H$_c$), 7.51 – 7.45 (m, 3H$_{ar}$), 7.36 – 7.28 (m, 2H$_{ar}$), 7.12 (d, $J = 7.6$ Hz, 1H$_m$), 7.04 (s, 1H$_m$), 6.98 – 6.88 (m, 5H$_{ar}$), 6.53 (d, $J = 16.2$ Hz, 1H$_a$), 6.42 (d, $J = 16.0$ Hz, 1H$_b$), 6.31 (d, $J = 16.0$ Hz, 1H$_c$), 4.29 – 4.22 (m, 6H$_{ar}$), 3.88 (s, 3H$_a$), 3.83 (s, 6H$_{ar}$), 1.35 – 1.31 (m, 9H$_{ar}$).

A parallel reaction without ligand was also performed providing the entitled compounds in 46% NMR yield (isomers $o:p = 1:1.7$).

(E)-Ethyl 3-(2,3-dimethoxyphenyl)acrylate (7a) and (E)-ethyl 3-(3,4-dimethoxyphenyl)acrylate (7b)\textsuperscript{16}

\begin{center}
\includegraphics[width=0.2\textwidth]{7.png}
\end{center}

General procedure was followed using 1,2-dimethoxybenzene (0.32 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compounds as a clear oil (50.9 mg as a mixture of isomers $a:b = 1:4.9$, 81% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{16} Isomer 7a: \textsuperscript{1}H NMR (300 MHz) $\delta = 7.99$ (d, $J = 16.2$ Hz, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 7.07 (d, $J = 7.9$ Hz, 1H), 6.94 (d, $J = 8.1$ Hz, 1H), 6.48 (d, $J = 16.2$ Hz, 1H), 4.27 (q, $J = 7.1$ Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H), 1.34 (t, $J = 7.1$ Hz, 3H). Isomer 7b: \textsuperscript{1}H NMR (500 MHz) $\delta = 7.63$ (d, $J = 16.0$ Hz, 1H), 7.10 (dd, $J = 8.3$, 2.0 Hz, 1H), 7.05 (d, $J = 2.0$ Hz, 1H), 6.87 (d, $J = 8.3$ Hz, 1H), 6.31 (d, $J = 15.9$ Hz, 1H), 4.26 (q, $J = 7.1$ Hz, 2H), 3.91 (s, 6H), 1.34 (t, $J = 7.1$ Hz, 3H).

A parallel reaction without ligand was also performed providing the entitled compounds in 40% NMR yield (isomers $a:b = 1:5.7$).
(E)-Ethyl 3-(2,4-dimethoxyphenyl)acrylate (8a)\textsuperscript{24} and (E)-ethyl 3-(2,6-dimethoxyphenyl)acrylate (8b)\textsuperscript{25}

General procedure was followed using 1,3-dimethoxybenzene (0.33 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:pentane ether (1:9 v/v) as an eluent provided the entitled compounds as a clear oil (48 mg as a mixture of isomers a:b = 6:1, 81% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{24,25} \textsuperscript{1}H NMR (400 MHz) \(\delta = 8.13\) (d, \(J = 16.3\) Hz, 1H\(_a\)), 7.90 (d, \(J = 16.1\) Hz, 1H\(_b\)), 7.44 (d, \(J = 8.5\) Hz, 1H\(_a\)), 6.88 (d, \(J = 16.5\) Hz, 1H\(_b\)), 6.56 (d, \(J = 8.5\) Hz, 2H\(_o\)), 6.50 (dd, \(J = 8.5, 2.4\) Hz, 2H\(_{ab}\)), 6.45 (s, 1H\(_o\)), 6.43 (d, \(J = 16.2\) Hz, 1H\(_a\)), 4.27 – 4.22 (m, 4H\(_{ab}\)), 3.88 (s, 6H\(_o\)), 3.87 (s, 3H\(_a\)), 3.84 (s, 3H\(_b\)), 1.35 – 1.31 (m, 6H\(_{ab}\)).

A parallel reaction without ligand was also performed providing the entitled compounds in 28% isolated yield (isomers a:b = 49:1).

(E)-Ethyl 3-(2,4,6-trimethoxyphenyl)acrylate (9)\textsuperscript{26}

General procedure was followed using 1,3,5-trimethoxybenzene (0.42 g, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:pentane ether (1:9 v/v) as an eluent provided the entitled compound as a yellow solid (46.6 mg, 70% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.\textsuperscript{26} \textsuperscript{1}H NMR (300 MHz) \(\delta = 8.08\) (d, \(J = 16.1\) Hz, 1H\(_a\)), 6.75 (d, \(J = 16.1\) Hz, 1H\(_b\)), 6.11 (s, 2H\(_o\)), 4.24 (q, \(J = 7.1\) Hz, 2H\(_p\)), 3.86 (s, 6H\(_o\)), 3.84 (s, 3H\(_a\)), 1.32 (t, \(J = 7.1\) Hz, 3H\(_p\)).

A parallel reaction without ligand was also performed providing the entitled compound in 52% NMR yield.

Ethyl 2-[[E]-2-[[ethoxycarbonyl]ethenyl]benzoate (10o),\textsuperscript{27} ethyl 3-[[E]-2-[[ethoxycarbonyl]ethenyl]benzoate (10m)\textsuperscript{28} and ethyl 4-[[E]-2-[[ethoxycarbonyl]ethenyl]benzoate (10p)\textsuperscript{29}

General procedure was followed using ethyl benzoate (0.90 mL, 6.27 mmol, 25.1 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:pentane ether (1:20 v/v) as an eluent provided the entitled compounds as a clear oil (26.0 mg as a mixture of isomers \(o:m:p = 1.2:3.3:1\), 42% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{27-29} \textsuperscript{1}H NMR (400 MHz) \(\delta = 8.45\) (d, \(J = 16.0\) Hz, 1H\(_h\)), 8.22 (s, 1H\(_m\)), 8.08 – 8.05 (m, 3H\(_{mp}\)), 7.98 (dd, \(J = 7.9, 1.4\) Hz, 1H\(_h\)), 7.75 – 7.69 (m, 4H\(_{ommp}\)), 7.60 (td, \(J = 5.2, 2.7\) Hz, 2H\(_p\)), 7.54 (td, \(J = 7.5, 1.2\) Hz, 1H\(_b\)), 7.50 – 7.43 (m, 2H\(_{pm}\)), 6.53 (d, \(J = 16.1\) Hz, 2H\(_{mp}\)), 6.31 (d, \(J = 16.0\) Hz, 1H\(_o\)), 4.44 – 4.39 (m, 6H\(_{ommp}\)), 4.32 – 4.27 (m, 6H\(_{ommp}\)), 1.45 – 1.40 (m, 9H\(_{ommp}\)), 1.38 – 1.31 (m, 9H\(_{ommp}\)).

A parallel reaction without ligand was also performed providing the entitled compounds in 22% NMR yield (isomers \(o:m:p = 1:4.1:1.2\)).
(E)-Ethyl 3-(2,4-dichlorophenyl)acrylate (11a),^30 (E)-ethyl 3-(3,5-dichlorophenyl)acrylate (11b) and (E)-ethyl 3-(2,6-dichlorophenyl)acrylate (11c)^30

General procedure was followed using 1,3-dichlorobenzene (0.92 mL, 8 mmol, 32 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compounds as a clear oil (45.2 mg as a mixture of isomers a:b:c = 14.4:1:4.6, 74% yield). ¹H NMR spectra data of the isolated compounds 11a and 11c matched with the spectra data reported in the literature for these compounds.³⁰ ¹H NMR (300 MHz) δ = 8.02 (d, J = 16.1 Hz, 1Hα), 7.80 (d, J = 16.4 Hz, 1Hβ), 7.57 (d, J = 8.5 Hz, 1Hγ), 7.45 (d, J = 2.1 Hz, 1Hδ), 7.40 (d, J = 1.7 Hz, 1Hε), 7.37 (d, J = 8.0 Hz, 2Hγ), 7.28 (dd, J = 8.5, 1.7 Hz, 1Hδ), 6.61 (d, J = 15.9 Hz, 1Hε), 6.43 (d, J = 16.1 Hz, 1Hδ), 4.30 – 4.27 (m, 4Hα), 1.39 – 1.34 (m, 6Hα). Trace amount of isomer 11b was also observed. Representative signal of isomer 11b: ¹H NMR (300 MHz) δ = 7.55 (d, J = 16.1 Hz, 1H), 6.45 (d, J = 16.1 Hz, 1H).

A parallel reaction without ligand was also performed providing the entitled compounds in 36% NMR yield (isomers a:b:c = 5.7:1:1.9).

(E)-Ethyl 3-(2,3-dichlorophenyl)acrylate (12a) and (E)-ethyl 3-(3,4-dichlorophenyl)acrylate (12b)^16

General procedure was followed using 1,2-dichlorobenzene (0.9 mL, 8 mmol, 32 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compounds as a clear oil (37 mg as a mixture of isomers a:b = 1:1.2, 60% yield). ¹H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.¹⁶ ¹H NMR (300 MHz) δ = 8.10 (d, J = 16.0 Hz, 1Hα), 7.62 – 7.61 (m, 2Hβ), 7.56 – 7.46 (m, 3Hα), 7.36 (dd, J = 8.3, 2.0 Hz, 1Hγ), 7.24 (t, J = 7.9 Hz, 1Hδ), 6.43 (d, J = 16.0 Hz, 2Hα), 4.34 – 4.25 (m, 4Hα), 1.39 – 1.33 (m, 6Hα).

A parallel reaction without ligand was also performed providing the entitled compounds in 22% NMR yield (isomers a:b = 1:1.7).

(E)-Ethyl 3-(2,5-dichlorophenyl)acrylate (13)

General procedure was followed using 1,4-dichlorobenzene (1.18 g, 8 mmol, 32 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:19 v/v) as an eluent provided the entitled compound as a clear oil (39.5 mg, 64% yield). ¹H NMR (300 MHz) δ = 8.01 (d, J = 16.0 Hz, 1H), 7.61 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.6 Hz, 1H), 7.29 (dd, J = 9.2, 1.5 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H).¹³C NMR (125 MHz) δ = 166.0, 139.1, 134.3, 133.1, 133.0, 131.2, 130.8, 127.4, 122.2, 60.9, 14.3; IR v = 2995, 2912, 1722, 1643, 1460, 1316, 1185, 1094, 1026, 973, 861, 809 cm⁻¹; HRMS (FD) calcd for C₁₃H₁₂Cl₂O₂ [M⁺]: 224.0052; found: 224.0045; M.p. 34 – 38 °C.

A parallel reaction without ligand was also performed providing the entitled compound in 30% NMR yield.
**General procedure** was followed using 1,3,5-trifluorobenzene (0.26 mL, 2.5 mmol, 10 equiv) as arene substrate. The product was obtained as a clear oil (44.4 mg, 77% yield). $^1$H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.$^{16}$ $^1$H NMR (400 MHz) $\delta$ = 7.68 (d, $J$ = 16.5 Hz, 1H), 6.72 (t, $J$ = 8.6 Hz, 2H), 6.67 (d, $J$ = 16.5 Hz, 1H), 4.27 (q, $J$ = 7.1 Hz, 2H), 1.33 (t, $J$ = 7.1 Hz, 3H).

A parallel reaction using 2-methyl-2-(phenylthio)propanoic acid (L4) (0.0846 M in CH$_2$Cl$_2$) (148 $\mu$L, 12.5 $\mu$mol, 5 mol%) was also performed providing the entitled compound in 62% NMR yield.

A parallel reaction without ligand was also performed providing the entitled compound in 23% NMR yield.

**Large-scale synthesis**

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (18.4 mg, 87.5 $\mu$mol, 5 mol%), Pd(OAc)$_2$ (19.6 mg, 87.5 $\mu$mol, 5 mol%), tert-butyl peroxybenzoate (0.33 mL, 1.75 mmol, 1 equiv), ethyl acrylate (0.19 mL, 1.75 mmol, 1 equiv), 1,3,5-trifluorobenzene (1.81 mL, 17.5 mmol, 10 equiv) and AcOH (8.75 mL). The product was obtained as a clear oil (0.27 g, 66% yield).

**General procedure** was followed using p-chloroanisole (0.31 mL, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:9 v/v) as an eluent provided the entitled compounds as a clear oil (36.2 mg as a mixture of isomers a:b = 4:3:1, 60% yield). $^1$H NMR spectra data of the isolated compound 15a matched with the spectra data reported in the literature for this compound.$^{31}$ Isomer 15a: $^1$H NMR (300 MHz) $\delta$ = 7.92 (d, $J$ = 16.1 Hz, 1H), 7.49 (d, $J$ = 2.6 Hz, 1H), 7.31 (dd, $J$ = 8.8, 2.6 Hz, 1H), 6.86 (d, $J$ = 8.8 Hz, 1H), 6.52 (d, $J$ = 16.1 Hz, 1H), 4.28 (q, $J$ = 7.2 Hz, 2H), 3.90 (s, 3H), 1.36 (t, $J$ = 7.2 Hz, 3H). Trace amount of isomer 15b was also observed. Representative signal of isomer 15b: $^1$H NMR (300 MHz) $\delta$ = 8.06 (d, $J$ = 16.1 Hz, 1H), 6.43 (d, $J$ = 16.1 Hz, 1H).

A parallel reaction without ligand was also performed providing the entitled compounds in 20% NMR yield (isomers a:b = 4:1).

**General procedure** was followed using phenol (0.24 g, 2.5 mmol, 10 equiv) as arene substrate. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) as an eluent provided the entitled compounds as a pale yellow oil (39.5 mg as a mixture of isomers a:p = 1.9:1, 82% yield). $^1$H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.$^{32,33}$ $^1$H NMR (400 MHz) $\delta$ = 8.05 (d, $J$ = 16.2 Hz, 1H$_p$), 7.63 (d, $J$ = 16.0 Hz, 1H$_m$), 7.46 (dd, $J$ = 7.7, 1.6 Hz, 1H$_p$), 7.41 (d, $J$ = 8.6 Hz,
The resulting mixture was determined by adding 0.8 mg, 56 µL, 0.25 mmol, 1 equiv) as internal standard. The crude mixture was purified as specified in each case to obtain the desired product.

**Methyl cinnamate (17)**

General procedure was followed using methyl acrylate (22.5 µL, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred for 6 h. The product was obtained as a pale yellow oil (31.4 mg, 76% yield). **H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.**

**Ethyl 3,3-diphenylacrylate (18)**

General procedure was followed using ethyl cinnamate (42 µL, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred for 6 h. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:49 v/v) as an eluent provided the entitled compound as a clear oil (34.8 mg, 56% yield). **H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.**

**(E)-Dimethyl styrylphosphonate (19)**

General procedure was followed using 1-dimethoxyphosphonate (30 µL, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred for 6 h. The product was obtained as a pale yellow oil (37.1 mg, 68% yield). **H NMR spectra data of the isolated material matched with the spectra data...
reported in the literature for this compound.\textsuperscript{35} \textsuperscript{1}H NMR (400 MHz) δ = 7.58 – 7.48 (m, 3H), 7.41 – 7.28 (m, 3H), 6.23 (t, J = 17.7 Hz, 1H), 3.79 (s, 3H), 3.76 (s, 3H).

\textit{N,N-Dimethylcinnamamide (20mono)}\textsuperscript{36} and \textit{N,N-dimethyl-3,3-diphenylacrylamide (20di)}\textsuperscript{37}

\begin{center}
\begin{tikzpicture}
  \node (mono) at (0,0) {CONMe\textsubscript{2}};
  \node (di) at (1.5,0) {CONMe\textsubscript{2}};
  \node (trans) at (0,-1.5) {CONMe\textsubscript{2}};
  \node (cis) at (1.5,-1.5) {CONMe\textsubscript{2}};
  \node (amide) at (0,-3) {CONMe\textsubscript{2}};
\end{tikzpicture}
\end{center}

General procedure was followed using \textit{N,N-dimethylacetamide} (26 µL, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred for 6 h. Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:1 v/v) as an eluent provided the entitled compounds as a pale yellow oil (18.7 mg, mono 34% and di 6% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{36,37} \textsuperscript{1}H NMR (400 MHz) δ = 7.69 (d, J = 15.4 Hz, H\textsubscript{mono}), 7.56 – 7.54 (m, 2H\textsubscript{mono}), 7.41 – 7.28 (m, 13H\textsubscript{mono+di}), 6.91 (d, J = 15.4 Hz, H\textsubscript{mono}), 6.37 (s, 1H\textsubscript{di}), 3.19 (s, 3H\textsubscript{mono}), 3.09 (s, 3H\textsubscript{mono}), 2.85 (s, 3H\textsubscript{di}), 2.77 (s, 3H\textsubscript{di}).

\textit{(E)-3-Phenylacrylonitrile (21trans),}\textsuperscript{38} \textit{(Z)-3-phenylacrylonitrile (21cis),}\textsuperscript{38} \textit{3,3-diphenylacrylonitrile (21di)}\textsuperscript{39} and \textit{cinnamamide (21amide)}\textsuperscript{40}

\begin{center}
\begin{tikzpicture}
  \node (trans) at (0,0) {CONMe\textsubscript{2}};
  \node (cis) at (1.5,0) {CONMe\textsubscript{2}};
  \node (di) at (0,-1.5) {CONMe\textsubscript{2}};
  \node (amide) at (1.5,-1.5) {CONMe\textsubscript{2}};
\end{tikzpicture}
\end{center}

General procedure was followed using acrylonitrile (16.5 µL, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred overnight. The yield was determined by NMR providing the entitled compounds in 64% yield (trans 37%, cis 14% and amide 37% yield). Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) and then MeOH:CH\textsubscript{3}Cl\textsubscript{2} (3:7 v/v) as an eluent provided the entitled compounds. Trace amount of di-alkenylated product was observed in \textsuperscript{1}H NMR after purify by column chromatography. \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for these compounds.\textsuperscript{38-40} \textsuperscript{1}H NMR (400 MHz) δ = 7.82 – 7.80 (m, 2H\textsubscript{cis}), 7.47 – 7.39 (m, 17H\textsubscript{cis+trans+di}), 7.31 – 7.29 (m, 2H\textsubscript{di}), 7.13 (d, J = 12.2 Hz, 1H\textsubscript{cis}), 5.89 (d, J = 16.6 Hz, 1H\textsubscript{trans}), 5.74 (s, 1H\textsubscript{di}), 5.45 (d, J = 12.2 Hz, 1H\textsubscript{cis}). \textit{21Amide:} \textsuperscript{1}H NMR (400 MHz) δ = 7.65 (d, J = 15.7 Hz, 1H), 7.52 (dd, J = 6.7, 2.9 Hz, 2H), 7.38 (dd, J = 5.0, 2.0 Hz, 3H), 6.46 (d, J = 15.7 Hz, 1H), 5.65 (bs, 2H).

\textit{(E)-[2-(Phenylsulfonyl)vinyl]benzene (22)}\textsuperscript{41}

\begin{center}
\begin{tikzpicture}
  \node (sulfone) at (0,0) {SO\textsubscript{2}Ph};
\end{tikzpicture}
\end{center}

General procedure was followed using phenyl vinyl sulfone (42 mg, 0.25 mmol, 1 equiv) as olefin substrate. The reaction was stirred overnight. Purification by column chromatography on silica gel using EtOAc:petroleum ether (3:7 v/v) as an eluent provided the entitled compound as a pale yellow oil (22.3 mg, 36% yield). \textsuperscript{1}H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.\textsuperscript{41} \textsuperscript{1}H NMR (400 MHz) δ = 7.97 – 7.94 (m, 2H), 7.69 (d, J = 15.4 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.57 – 7.53 (m, 2H), 7.50 – 7.48 (m, 2H), 7.42 – 7.37 (m, 3H), 6.86 (d, J = 15.4 Hz, 1H).
3.4 General procedure for the Pd-catalyzed C-H olefination of estrone and naproxen derivatives

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH₂Cl₂, 10 mol%) was added to a pressure tube and dried with nitrogen steam until dryness followed by Pd(OAc)₂ (10 mol%), the corresponding arene (1 equiv), tert-butyl peroxybenzoate (1 equiv), ethyl acrylate (1.5 equiv) and AcOH (0.2 M). The pressure tube was sealed with a screw cap and the reaction was placed in 100 °C pre-heated oil bath for 16 h. The resulting mixture was diluted with EtOAc and quenched with aqueous Na₂SO₃ solution (10%). The organic layer was washed with saturated aqueous NaHCO₃ solution, dried over anh. MgSO₄, filtered and concentrated under reduced pressure. The crude mixture was purified as specified in each case to obtain the desired product.

(E)-2-(2-Ethoxycarbonylvinyl)estrone methyl ether (23a) and (E)-4-(2-ethoxycarbonylvinyl)estrone methyl ether (23b)

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH₂Cl₂) (295 µL, 25 µmol, 10 mol%), Pd(OAc)₂ (5.6 mg, 25 µmol, 10 mol%), estrone 3-methyl ether (71 mg, 0.25 mmol, 1 equiv), tert-butyl peroxybenzoate (47 µL, 0.25 mmol, 1 equiv), ethyl acrylate (40 µL, 0.375 mmol, 1.5 equiv) and AcOH (1.25 mL). Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) as an eluent provided the entitled compounds as a clear oil (84 mg as a mixture of isomers a:b = 3:1, 88% yield). ¹H NMR (400 MHz) δ = 7.94 (d, J = 16.1 Hz, 1Hα), 7.87 (d, J = 16.2 Hz, 1Hβ), 7.42 (s, 1Hβ), 7.28 (d, J = 8.7 Hz, 1Hβ), 6.80 (d, J = 8.7 Hz, 1Hβ), 6.64 (s, 1Hβ), 6.63 (d, J = 16.1 Hz, 1Hβ), 6.51 (d, J = 16.1 Hz, 1Hβ), 4.30 – 4.23 (m, 4Hv₁v₂), 3.86 (s, 6Hv₃v₄), 2.94 (dd, J = 8.8, 4.2 Hz, 4Hv₅v₆), 2.52 (dd, J = 18.8, 8.6 Hz, 2Hv₇v₈), 2.46 – 2.38 (m, 2Hv₉v₁₀), 2.27 – 1.97 (m, 10Hv₁₁₋₁₉), 1.69 – 1.39 (m, 12Hv₁₁₋₁₉), 1.37 – 1.32 (m, 6Hv₁₁₋₁₉), 0.92 (s, 6Hv₁₁₋₁₉). ¹³C NMR (75 MHz) δ = 220.9, 220.8, 168.1, 167.8, 157.0, 156.5, 140.7, 140.4, 138.5, 137.7, 132.6, 132.1, 127.5, 126.3, 123.0, 121.1, 117.9, 111.5, 108.7, 60.4, 60.3, 55.6, 50.4, 48.0, 48.0, 44.3, 43.8, 38.3, 37.5, 36.0, 35.9, 31.7, 31.6, 30.0, 28.1, 26.6, 26.5, 26.3, 26.0, 21.7, 14.5, 13.9; IR ν = 2930, 2858, 1737, 1704, 1622, 1460, 1269, 1256, 1157, 1036, 864, 728 cm⁻¹; HRMS (EI) calcd for C₂₆H₃₀O₄ [M⁺]: 382.2144; found: 382.2129.

A parallel reaction using 3,5-dichloropyridine (3.7 mg, 25 µmol, 10 mol%) was also performed providing the entitled compound in 30% conversion.

A parallel reaction without ligand was also performed providing the entitled compounds in 10% conversion.

Large-scale synthesis

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (36.8 mg, 0.18 mmol, 10 mol%), Pd(OAc)₂ (39.3 mg, 0.18 mmol, 10 mol%), estrone 3-methyl ether (0.5 g, 1.75 mmol, 1 equiv), tert-butyl peroxybenzoate (0.33 mL, 1.75 mmol, 1 equiv), ethyl acrylate (0.28 mL, 2.63 mmol, 1.5 equiv) and AcOH (8.75 mL). Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:4 v/v) as an eluent provided the entitled compounds as a clear oil (0.5 g as a mixture of isomers a:b = 3:1, 75% yield).
(S,E)-5-(2-ethoxycarbonylvinyl)naproxen methyl ester (24a) and (S,E)-8-(2-ethoxycarbonylvinyl)naproxen methyl ester (24b)

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH₂Cl₂) (414 µL, 35 µmol, 10 mol%), Pd(OAc)₂ (7.8 mg, 35 µmol, 10 mol%), methyl ester of (S)-naproxen² (85.5 mg, 0.35 mmol, 1 equiv), tert-butyl peroxycbenzoate (66 µL, 0.35 mmol, 1 equiv), ethyl acrylate (56 µL, 0.52 mmol, 1.5 equiv) and AcOH (1.75 mL).

Purification by column chromatography on silica gel using EtOAc:petroleum ether (1:15 v/v) as an eluent provided the entitled compounds as a clear oil (76.1 mg as a mixture of isomers a:b:others = 76:10:14, 88% yield). Isomer 24a: ¹H NMR (400 MHz) δ = 8.32 (d, J = 16.2 Hz, 1H), 8.16 (d, J = 8.9 Hz, 1H), 3.83 (m, 1H), 3.67 (s, 3H), 1.58 (d, J = 7.2 Hz, 3H), 1.37 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz) δ = 175.0, 168.0, 156.8, 137.7, 136.0, 132.0, 131.5, 129.1, 127.4, 126.8, 123.9, 123.5, 116.7, 113.1, 60.5, 56.3, 52.2, 45.2, 18.6, 14.5; IR ν = 2978, 2939, 2843, 1732, 1704, 1620, 1592, 1267, 1250, 1154, 1041, 803 cm⁻¹; HRMS (FD) calcd for C₂₉H₂₂O₅ [M⁺]: 342.1467; found: 342.1471.

Isomer 24b: ¹H NMR (400 MHz) δ = 8.45 (d, J = 15.7 Hz, 1H), 7.78 – 7.68 (m, 3H), 7.38 (d, J = 2.2 Hz, 1H), 7.21 (dd, J = 8.9, 2.1 Hz, 1H), 6.57 (d, J = 15.7 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 3.98 (s, 3H), 3.95 – 3.86 (m, 1H), 3.70 (s, 3H), 1.60 (d, J = 7.2 Hz, 3H), 1.40 (t, J = 7.1 Hz, 3H); ¹³C NMR (101 MHz) δ = 175.0, 167.1, 158.6, 141.7, 135.4, 132.1, 131.2, 130.3, 129.5, 128.7, 125.6, 120.9, 119.4, 101.9, 60.8, 55.7, 52.3, 45.3, 18.7, 14.5; IR ν = 2979, 2932, 2851, 1735, 1713, 1627, 1604, 1260, 1175, 1032 cm⁻¹; HRMS (FD) calcd for C₂₉H₂₂O₅ [M⁺]: 342.1467; found: 342.1463.

A parallel reaction using 3,5-dichloropyrididine (5.2 mg, 35 µmol, 10 mol%) was also performed providing the entitled compound in 27% NMR yield.

A parallel reaction without ligand was also performed providing the entitled compounds in trace amount.

3.5 General procedure for the Pd-catalyzed C–H acetoxylation of benzene

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH₂Cl₂) (2 mol%) was added to a pressure tube and dried with nitrogen stream until dryness followed by Pd(OAc)₂ (2 mol%), Phl(OAc)₂ (1 equiv), benzene (10 equiv), AcOH and Ac₂O (1.2 M, in a ratio 9:1, respectively). The pressure tube was sealed with a screw cap or crimp cap septa (for kinetic profile) and the reaction was placed in 100 °C pre-heated oil bath over the time period indicated for each reaction. The reaction was cooled to room temperature. PhCl (20 µL) was added in each sample as internal standard for quantitative GC analysis. The reaction mixture was diluted with EtOAc (1 mL) and filtered through a plug of Celite. The filtrate was extracted with aqueous K₂CO₃ solution (3 M, 2 x 2 mL) to quench the acid. The organic layer was then carefully separated, diluted with additional EtOAc and analyzed by GC.

Phenyl acetate (25)

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (132 µL, 11.2 µmol, 2 mol%), Pd(OAc)₂ (2.5 mg, 11.2 µmol, 2 mol%), Phl(OAc)₂ (0.18 g, 0.56
mmol, 1 equiv), benzene (0.5 mL, 5.6 mmol, 10 equiv), AcOH (0.45 mL) and Ac₂O (0.05 mL). The reaction was stirred for 3 h. The phenyl acetate was obtained in 64% GC yield.

**Kinetic profile of the Pd-catalyzed C-H acetoxylation of benzene with 3-methyl-2-(phenylthio)butanoic acid (L₂), with pyridine and without ligand**

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L₂) (397 μL, 33.6 μmol, 2 mol%), Pd(OAc)₂ (7.5 mg, 33.6 μmol, 2 mol%), PhI(OAc)₂ (0.54 g, 1.68 mmol, 1 equiv), benzene (1.5 mL, 16.8 mmol, 10 equiv), AcOH (1.35 mL) and Ac₂O (0.15 mL). The reaction was followed during time by sampling 0.1 mL.

Parallel reaction with pyridine was also performed to compare the kinetic profile. General procedure was followed using pyridine (2.7 μL, 33.6 μmol, 2 mol%), Pd(OAc)₂ (7.5 mg, 33.6 μmol, 2 mol%), PhI(OAc)₂ (0.54 g, 1.68 mmol, 1 equiv), benzene (1.5 mL, 16.8 mmol, 10 equiv), AcOH (1.35 mL) and Ac₂O (0.15 mL). The reaction was followed during time by sampling 0.1 mL.

Parallel reaction without ligand was also performed to compare the kinetic profile. General procedure was followed using Pd(OAc)₂ (7.5 mg, 33.6 μmol, 2 mol%), PhI(OAc)₂ (0.54 g, 1.68 mmol, 1 equiv), benzene (1.5 mL, 16.8 mmol, 10 equiv), AcOH (1.35 mL) and Ac₂O (0.15 mL). The reaction was followed during time by sampling 0.1 mL.

**Table S7.** Kinetic studies of the Pd-catalyzed C-H acetoxylation of benzene

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reaction time</th>
<th>GC yield (L₂)</th>
<th>GC yield (pyridine)</th>
<th>GC yield (no ligand)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
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<td>0%</td>
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</tr>
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<td>4%</td>
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<tr>
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<td>2 h</td>
<td>52%</td>
<td>48%</td>
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</tr>
</tbody>
</table>
3.6 General procedure for the Pd-catalyzed C-H allylation of benzene

A stock solution of 3-methyl-2-(phenylthio)butanoic acid (L2) (0.0846 M in CH₂Cl₂) (10 mol%) was added to a pressure tube and dried with nitrogen steam until dryness followed Pd(OAc)₂ (10 mol%), AgOAc (1.5 equiv), allylbenzene (1 equiv), benzene (66 equiv) and DCE (0.5 M). The pressure tube was sealed with a screw cap or crimp cap septa (for kinetic profile) and the reaction was placed in 80 °C pre-heated oil bath over the time period indicated for each reaction. The reaction was cooled to room temperature, diluted with EtOAc (1 mL) and filtered through a plug of Celite. The filtrate was concentrated under reduced pressure. The NMR yield was determined by adding CH₂Br₂ (1 equiv) as internal standard.

(E)-prop-1-ene-1,3-diyl dibenzene (26)³³

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (295 µL, 25 µmol, 10 mol%), Pd(OAc)₂ (5.6 mg, 25 µmol, 10 mol%), AgOAc (63 mg, 0.375 mmol, 1.5 equiv), allylbenzene (33 µL, 0.25 mmol, 1 equiv), benzene (1.5 mL, 16.6 mmol, 66 equiv) and DCE (0.5 mL). The reaction was stirred overnight. The product was obtained as a pale yellow oil (26 mg, 54% yield). ¹H NMR spectra data of the isolated material matched with the spectra data reported in the literature for this compound.³³ ¹H NMR (400 MHz) δ = 7.47 – 7.23 (m, 10H), 6.53 – 6.37 (m, 2H), 3.60 (d, J = 6.6 Hz, 2H).

Kinetic profile of the Pd-catalyzed C-H allylation of benzene with 3-methyl-2-(phenylthio)butanoic acid (L2) and without ligand

General procedure was followed using 3-methyl-2-(phenylthio)butanoic acid (L2) (10.5 mg, 0.05 mmol, 10 mol%), Pd(OAc)₂ (11.2 mg, 0.05 mmol, 10 mol%), AgOAc (125 mg, 0.75 mmol, 1.5 equiv), allylbenzene (66 µL, 0.5 mmol, 1 equiv), benzene (3 mL, 33.3 mmol, 66 equiv) and DCE (1 mL). The reaction was followed during time by sampling 0.1 mL. PhCl (20 µL) was added in each sample as internal standard and diluted with EtOAc (1 mL). The organic layer was filtered through a plug of Celite and analyzed by GC.

A parallel reaction without ligand was also performed to compare the kinetic profile. General procedure was followed using Pd(OAc)₂ (11.2 mg, 0.05 mmol, 10 mol%), AgOAc (125 mg, 0.75 mmol,
1.5 equiv), allylbenzene (66 µL, 0.5 mmol, 1 equiv), benzene (3 mL, 33.3 mmol, 66 equiv) and DCE (1 mL). The reaction was followed during time by sampling 0.1 mL. PhCl (20 µL) was added in each sample as internal standard and diluted with EtOAc (1 mL). The organic layer was filtered through a plug of Celite and analyzed by GC.

**Table S8.** Kinetic studies of the Pd-catalyzed C-H allylation of benzene

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<th>Entry</th>
<th>Reaction time</th>
<th>GC yield (L2)</th>
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<tbody>
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<td>10 min</td>
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4. Synthesis of the palladium complex and crystal structure information

**Scheme 4.** Synthesis of palladium complex

A solution of 2-methyl-2-(phenylthio)propanoic acid (L4) (196 mg, 1.00 mmol, 2 equiv) and Pd(OAc)$_2$ (112 mg, 0.50 mmol, 1 equiv) in CH$_2$Cl$_2$ (15 mL) was stirred at room temperature overnight. The reaction was filtrated through a pad of Celite and evaporated to dryness to afford a mixture of Pd complexes. $^1$H NMR (500 MHz) $\delta =$ 8.01 – 7.87 (m, 4H$_{cis+trans}$), 7.65 – 7.16 (m, 16H$_{cis+trans}$), 1.92 (s, 6H$_{cis}$), 1.75 (s, 6H$_{trans}$), 1.22 (s, 6H$_{cis}$), 1.20 (s, 6H$_{trans}$); HRMS (FD) calcd for C$_{20}$H$_{22}$O$_4$PdS$_2$ [M]$^+$: 495.9994; found: 495.9972.

**Crystal structure information**

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<td>Chemical formula</td>
<td>C$<em>{20}$H$</em>{22}$O$_4$PdS$_2$</td>
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<td>Space group</td>
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<td>a</td>
<td>9.0235 (3)</td>
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<tr>
<td>b</td>
<td>10.1775 (4)</td>
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<tr>
<td>c</td>
<td>11.8976 (5)</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>81.443 (2)</td>
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<tr>
<td>$\beta$</td>
<td>73.982 (2)</td>
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<tr>
<td>$\gamma$</td>
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<td>V ($\text{Å}^3$)</td>
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<td>Z</td>
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<td>R-Factor (%)</td>
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5. NMR spectra
L10

\[ \text{Chemical structure diagram} \]

S36
5

6
6. References

(22) Lu, J.; Toy, P. H. *Synlett 2011*, 1723-1726.