Palladium-Catalyzed Synthesis of Spiro[2.4]heptanes: Ligand-Dependent Position-Control in the Nucleophilic Attack to a π-Allylpalladium Intermediate

Ryo Shintani,* Soyoung Park, and Tamio Hayashi*

Department of Chemistry, Graduate School of Science, Kyoto University,
Sakyo, Kyoto 606-8502, Japan

Supporting Information

I. General

All air- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under nitrogen or in a glove box under argon.

CH_2Cl_2 and 1,2-dichloroethane were distilled over CaH_2 under nitrogen.

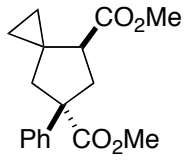
Methyl acrylate (Wako Chemicals), ethyl acrylate (Kanto Chemicals), *tert*-butyl acrylate (Wako Chemicals), acrylonitrile (Aldrich), 2-cyclopenten-1-one (Zeon), 2(5*H*)-furanone (Aldrich), triphenylphosphine (Wako Chemicals), dppf (Fluka), trimethyl phosphite (TCI), triisopropyl phosphite (TCI), 2-(di-*tert*-butylphosphino)biphenyl (Wako Chemicals), and tri-*o*-tolylphosphine (Kanto Chemicals) were used as received. **1a**–**1e**,[1] $PdCp(\eta^3\text{-}C_3H_5)$,[2] and binap[3] were synthesized following the literature procedures.

All other chemicals and solvents were purchased from Aldrich, Wako Chemicals, TCI, or Kanto Chemicals and used as received.

II. Catalytic Reactions

General Procedure for Table 2.

A solution of $PdCp(\eta^3\text{-}C_3H_5)$ (3.2 mg, 15 μmol), $P(O\textit{i}\text{-}Pr)_3$ (7.4 μL, 30 μmol), compound **1** (0.54 mmol), and electron-deficient olefin **2** (0.30 mmol) in CH_2Cl_2 (1.5 mL) was stirred for 24 h at 40 °C. The reaction mixture was directly passed through a pad of silica gel with EtOAc and the solvent was removed under vacuum. The residue was purified by silica gel preparative TLC to afford cycloadducts.



4aa

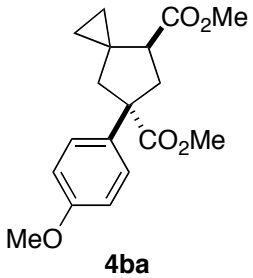
Entry 1. 86% yield (dr = 79/21) along with 5% yield of **3aa**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4aa**: ^{1}H NMR ($CDCl_3$): δ 7.34-7.29 (m, 4H), 7.26-7.23 (m, 1H), 3.650 (s, 3H), 3.649 (s, 3H), 3.25 (ddd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 8.2 Hz and $^4J_{HH}$ = 2.4 Hz,

[1] Shintani, R.; Murakami, M.; Hayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, asap.
[2] Parker, G.; Werner, H. *Helv. Chim. Acta* **1973**, *56*, 2819.
[3] Cai, D.; Payack, J. F.; Bender, D. R.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 7180.

1H), 2.74 (t, $^3J_{HH}$ = 8.3 Hz, 1H), 2.51 (d, $^2J_{HH}$ = 12.1 Hz, 1H), 2.35 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.4 Hz, 1H), 2.25 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.3 Hz, 1H), 0.66-0.60 (m, 2H), 0.59-0.52 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 176.0, 175.6, 142.2, 128.5, 127.2, 126.7, 58.7, 52.5, 51.7, 49.0, 45.0, 40.0, 24.7, 17.2, 7.7. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 71.10; H, 6.99.

Minor diastereomer of **4aa**: ^{1}H NMR ($CDCl_3$): δ 7.39 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.33 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.25 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 3.64 (s, 6H), 3.07 (dd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 7.7 Hz, 1H), 2.78 (dd, $^3J_{HH}$ = 8.1 and 7.8 Hz, 1H), 2.70 (d, $^2J_{HH}$ = 13.1 Hz, 1H), 2.59 (ddd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 8.4 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 2.12 (dd, $^2J_{HH}$ = 13.1 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 0.56-0.49 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 175.6, 174.4, 142.7, 128.6, 127.1, 126.6, 57.8, 52.5, 51.7, 48.6, 45.7, 39.5, 24.0, 14.2, 10.2. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.82; H, 7.15.

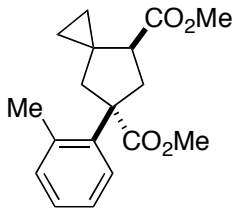


4ba

Entry 2. 91% yield (dr = 74/26) along with 7% yield of **3ba**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4ba**: ^{1}H NMR ($CDCl_3$): δ 7.25 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 6.84 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 3.79 (s, 3H), 3.65 (s, 3H), 3.64 (s, 3H), 3.22 (ddd, $^2J_{HH}$ = 12.8 Hz and $^3J_{HH}$ = 8.2 Hz and $^4J_{HH}$ = 2.3 Hz, 1H), 2.73 (t, $^3J_{HH}$ = 8.4 Hz, 1H), 2.46 (d, $^2J_{HH}$ = 12.1 Hz, 1H), 2.32 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.5 Hz, 1H), 2.23 (dd, $^2J_{HH}$ = 12.1 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 0.65-0.58 (m, 2H), 0.58-0.50 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 176.1, 175.5, 158.7, 134.5, 127.8, 113.8, 57.9, 55.3, 52.4, 51.6, 49.0, 45.2, 40.1, 24.6, 17.1, 7.7. Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 68.11; H, 7.01.

Minor diastereomer of **4ba**: ^{1}H NMR ($CDCl_3$): δ 7.31 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 6.86 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 3.80 (s, 3H), 3.641 (s, 3H), 3.636 (s, 3H), 3.03 (dd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 7.8 Hz, 1H), 2.77 (t, $^3J_{HH}$ = 8.0 Hz, 1H), 2.67 (d, $^2J_{HH}$ = 13.1 Hz, 1H), 2.56 (ddd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 8.2 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 2.09 (dd, $^2J_{HH}$ = 13.1 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 0.54-0.48 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 175.8, 174.5, 158.6, 134.6, 127.7, 113.9, 57.1, 55.4, 52.4, 51.6, 48.5, 45.7, 39.6, 23.9, 14.3, 10.2. Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.93; H, 6.84.



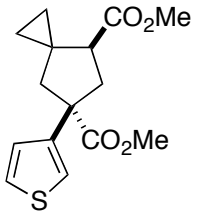
4ca

Entry 3. 91% yield (dr = 77/23) along with 6% yield of **3ca**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4ca**: ^{1}H NMR ($CDCl_3$): δ 7.38-7.35 (m, 1H), 7.20-7.15 (m, 2H),

7.12-7.10 (m, 1H), 3.641 (s, 3H), 3.636 (s, 3H), 3.30 (ddd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 8.3 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 2.84 (t, $^3J_{HH}$ = 8.2 Hz, 1H), 2.72 (d, $^2J_{HH}$ = 12.2 Hz, 1H), 2.32 (s, 3H), 2.30 (dd, $^2J_{HH}$ = 13.0 Hz and $^3J_{HH}$ = 8.0 Hz, 1H), 2.18 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 0.64-0.53 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 176.4, 175.6, 140.6, 136.7, 131.8, 127.3, 127.0, 126.1, 58.4, 52.4, 51.6, 49.0, 46.1, 39.2, 23.9, 21.2, 16.7, 7.5. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.61; H, 7.28.

Minor diastereomer of **4ca**: ^{1}H NMR ($CDCl_3$): δ 7.39 (dd, $^3J_{HH}$ = 7.0 Hz and $^4J_{HH}$ = 2.1 Hz, 1H), 7.22-7.14 (m, 3H), 3.66 (s, 3H), 3.65 (s, 3H), 3.05 (dd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 9.7 Hz, 1H), 2.86 (dd, $^3J_{HH}$ = 9.6 and 7.6 Hz, 1H), 2.70 (d, $^2J_{HH}$ = 13.2 Hz, 1H), 2.53 (ddd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 7.7 Hz and $^4J_{HH}$ = 1.7 Hz, 1H), 2.21 (s, 3H), 2.08 (dd, $^2J_{HH}$ = 13.2 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 0.59-0.57 (m, 2H), 0.50-0.48 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 176.6, 174.0, 140.9, 136.2, 132.0, 127.1, 126.5, 125.9, 57.1, 52.6, 51.7, 48.7, 46.5, 39.9, 23.9, 20.5, 14.0, 10.6. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.38; H, 7.34.

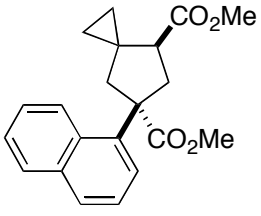


4da

Entry 4. 87% yield (dr = 72/28) along with 7% yield of **3da**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4da**: ^{1}H NMR ($CDCl_3$): δ 7.25 (dd, $^3J_{HH}$ = 5.0 Hz and $^4J_{HH}$ = 2.9 Hz, 1H), 7.11 (dd, $^4J_{HH}$ = 2.9 and 1.3 Hz, 1H), 7.05 (dd, $^3J_{HH}$ = 5.0 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.16 (ddd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.2 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 2.72 (t, $^3J_{HH}$ = 8.3 Hz, 1H), 2.46 (d, $^2J_{HH}$ = 12.2 Hz, 1H), 2.39 (dd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 8.4 Hz, 1H), 2.22 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 0.64-0.58 (m, 2H), 0.57-0.51 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 175.5, 175.4, 142.9, 126.7, 125.7, 120.8, 56.0, 52.5, 51.7, 49.0, 45.9, 40.0, 24.7, 16.9, 7.7. Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16. Found: C, 61.38; H, 6.01.

Minor diastereomer of **4da**: ^{1}H NMR ($CDCl_3$): δ 7.27 (dd, $^3J_{HH}$ = 5.0 Hz and $^4J_{HH}$ = 2.9 Hz, 1H), 7.16 (dd, $^4J_{HH}$ = 2.9 and 1.3 Hz, 1H), 7.08 (dd, $^3J_{HH}$ = 5.0 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 3.67 (s, 3H), 3.64 (s, 3H), 2.97 (dd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 8.2 Hz, 1H), 2.75 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 2.69 (d, $^2J_{HH}$ = 13.1 Hz, 1H), 2.57 (ddd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 8.1 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 2.05 (dd, $^2J_{HH}$ = 13.1 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 0.56-0.49 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 175.1, 174.5, 143.6, 127.0, 125.9, 121.1, 55.2, 52.5, 51.7, 48.7, 46.0, 40.1, 24.0, 15.0, 9.7. Anal. Calcd for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.16. Found: C, 61.14; H, 6.22.

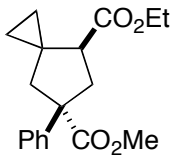


4ea

Entry 5. 97% yield (dr = 70/30) along with 3% yield of **3ea**. The relative configuration was determined by X-ray crystallographic analysis of the major diastereomer.

Major diastereomer of **4ea**: ^{1}H NMR ($CDCl_3$): δ 8.12-8.09 (m, 1H), 7.86-7.84 (m, 1H), 7.78 (d, $^3J_{HH}$ = 8.2 Hz, 1H), 7.58 (dd, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.0 Hz, 1H), 7.48-7.43 (m, 3H), 3.63 (s, 3H), 3.58 (s, 3H), 3.49 (ddd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 8.2 Hz and $^4J_{HH}$ = 2.1 Hz, 1H), 2.98 (t, $^3J_{HH}$ = 8.1 Hz, 1H), 2.88 (d, $^2J_{HH}$ = 12.2 Hz, 1H), 2.43 (dd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 8.1 Hz, 1H), 2.34 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.0 Hz, 1H), 0.70-0.63 (m, 3H), 0.59-0.55 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 177.2, 175.4, 138.7, 134.4, 132.1, 129.2, 128.4, 126.1, 125.44, 125.38, 124.8, 124.0, 58.2, 52.6, 51.6, 49.2, 46.4, 40.3, 23.9, 16.4, 7.8. Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.67; H, 6.61.

Minor diastereomer of **4ea**: ^{1}H NMR ($CDCl_3$): δ 7.92-7.89 (m, 1H), 7.88-7.85 (m, 1H), 7.79 (d, $^3J_{HH}$ = 8.3 Hz, 1H), 7.59 (dd, $^3J_{HH}$ = 7.2 Hz and $^4J_{HH}$ = 1.0 Hz, 1H), 7.48-7.44 (m, 3H), 3.66 (s, 3H), 3.57 (s, 3H), 3.18 (dd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 9.5 Hz, 1H), 2.92 (d, $^2J_{HH}$ = 13.3 Hz, 1H), 2.88 (dd, $^3J_{HH}$ = 9.5 and 7.6 Hz, 1H), 2.81 (ddd, $^2J_{HH}$ = 13.1 Hz and $^3J_{HH}$ = 7.6 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 2.30 (dd, $^2J_{HH}$ = 13.1 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 0.61-0.58 (m, 1H), 0.54-0.48 (m, 2H), 0.43-0.41 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 177.2, 174.1, 138.2, 134.7, 131.3, 129.4, 128.4, 126.2, 125.5, 125.1, 124.5, 124.2, 57.1, 52.7, 51.7, 48.7, 46.8, 40.3, 23.8, 14.5, 10.1. Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.26; H, 6.65.

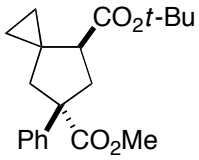


4ab

Entry 6. 92% yield (dr = 79/21) along with 7% yield of **3ab**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4ab**: ^{1}H NMR ($CDCl_3$): δ 7.35-7.29 (m, 4H), 7.24 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 4.16 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 3.65 (s, 3H), 3.24 (ddd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.1 Hz and $^4J_{HH}$ = 2.3 Hz, 1H), 2.72 (t, $^3J_{HH}$ = 8.2 Hz, 1H), 2.51 (d, $^2J_{HH}$ = 12.2 Hz, 1H), 2.35 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.5 Hz, 1H), 2.26 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.3 Hz, 1H), 1.23 (t, $^3J_{HH}$ = 7.1 Hz, 3H), 0.68-0.62 (m, 2H), 0.59-0.51 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 176.0, 175.1, 142.3, 128.5, 127.2, 126.7, 60.5, 58.6, 52.5, 49.0, 45.1, 40.0, 24.6, 17.1, 14.5, 7.6. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.67; H, 7.40.

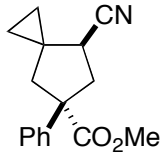
Minor diastereomer of **4ab**: ^{1}H NMR ($CDCl_3$): δ 7.39 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.33 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.25 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 4.11 (q, $^3J_{HH}$ = 7.2 Hz, 2H), 3.64 (s, 3H), 3.07 (ddd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 7.7 Hz and J_{HH} = 0.5 Hz, 1H), 2.76 (dd, $^3J_{HH}$ = 8.1 and 7.9 Hz, 1H), 2.70 (d, $^2J_{HH}$ = 13.1 Hz, 1H), 2.59 (ddd, $^2J_{HH}$ = 13.5 Hz and $^3J_{HH}$ = 8.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 2.12 (dd, $^2J_{HH}$ = 13.1 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 1.24 (t, $^3J_{HH}$ = 7.1 Hz, 3H), 0.59-0.55 (m, 1H), 0.54-0.50 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 175.7, 173.9, 142.8, 128.6, 127.1, 126.6, 60.5, 57.8, 52.5, 48.5, 45.8, 39.5, 24.0, 14.5, 14.1, 10.1. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.53; H, 7.40.



4ac

Entry 7. 77% yield (dr = 90/10) along with 8% yield of **3ac**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4ac**: ^{1}H NMR ($CDCl_3$): δ 7.33 (d, $^3J_{HH}$ = 7.1 Hz, 2H), 7.30 (t, $^3J_{HH}$ = 7.1 Hz, 2H), 7.23 (tt, $^3J_{HH}$ = 7.0 Hz and $^4J_{HH}$ = 1.6 Hz, 1H), 3.64 (s, 3H), 3.21 (ddd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.1 Hz and $^4J_{HH}$ = 2.3 Hz, 1H), 2.60 (t, $^3J_{HH}$ = 8.3 Hz, 1H), 2.49 (d, $^2J_{HH}$ = 12.1 Hz, 1H), 2.30 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.5 Hz, 1H), 2.24 (dd, $^2J_{HH}$ = 12.2 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 1.42 (s, 9H), 0.75-0.71 (m, 1H), 0.63-0.60 (m, 1H), 0.58-0.50 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 176.1, 174.4, 142.5, 128.5, 127.1, 126.7, 80.5, 58.6, 52.4, 49.8, 45.1, 40.1, 28.3, 24.6, 16.8, 7.5. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.53; H, 7.88.



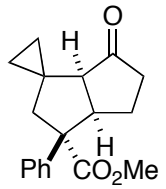
4ad

Entry 8. 88% yield (dr = 76/24) along with 7% yield of **3ad**. The relative configuration was assigned by analogy with **4ea** (entry 5).

Major diastereomer of **4ad**: ^{1}H NMR ($CDCl_3$): δ 7.36-7.26 (m, 5H), 3.66 (s, 3H), 3.44 (ddd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 8.3 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 2.93 (t, $^3J_{HH}$ = 8.7 Hz, 1H), 2.49 (d, $^2J_{HH}$ = 12.7 Hz, 1H), 2.41 (dd, $^2J_{HH}$ = 12.7 Hz and $^4J_{HH}$ = 2.2 Hz, 1H), 2.28 (dd, $^2J_{HH}$ = 12.9 Hz and $^3J_{HH}$ = 9.1 Hz, 1H), 1.02-0.99 (m, 1H), 0.79-0.71 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 175.0, 141.0, 128.7, 127.6, 126.5, 121.2, 58.4, 52.8, 44.4, 41.4, 35.0, 23.7, 16.5, 9.9.

Minor diastereomer of **4ad**: ^{1}H NMR ($CDCl_3$): δ 7.37-7.26 (m, 5H), 3.69 (s, 3H), 3.20 (ddd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 6.1 Hz and $^4J_{HH}$ = 1.4 Hz, 1H), 3.02 (dd, $^3J_{HH}$ = 9.3 and 6.2 Hz, 1H), 2.58 (dd, $^2J_{HH}$ = 13.3 Hz and $^3J_{HH}$ = 9.2 Hz, 1H), 2.57 (dd, $^2J_{HH}$ = 12.9 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 2.30 (d, $^2J_{HH}$ = 12.9 Hz, 1H), 1.06-1.02 (m, 1H), 0.72-0.62 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 174.7, 141.2, 128.8, 127.6, 126.4, 120.2, 58.1, 52.8, 44.4, 40.7, 34.3, 23.2, 13.3, 11.2.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.11; H, 6.86.



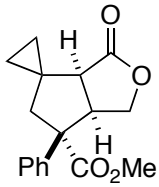
4ae

Entry 9. 89% yield (dr = 65/35) along with 2% yield of **3ae**. The relative configuration was determined by X-ray crystallographic analysis of the minor diastereomer.

Major diastereomer of **4ae**: ^{1}H NMR ($CDCl_3$): δ 7.35-7.25 (m, 5H), 3.99 (q, $^3J_{HH}$ = 8.9 Hz, 1H), 3.63 (s, 3H), 2.52 (d, $^2J_{HH}$ = 12.5 Hz, 1H), 2.34 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 2.26-2.13 (m, 3H), 1.82-1.75 (m, 1H), 1.21-1.13 (m, 2H), 0.58 (ddd, $^2J_{HH}$ = 9.9 Hz and $^3J_{HH}$ = 6.4 and 3.9 Hz, 1H), 0.52-0.44 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 219.9, 176.0, 139.3, 128.6, 127.5 127.4, 62.1, 55.5, 52.5, 48.5, 41.5, 38.9, 23.7, 23.5, 17.4, 5.3. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.80; H, 7.15.

Minor diastereomer of **4ae**: ^{1}H NMR ($CDCl_3$): δ 7.43 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.35 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 7.28 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 3.65 (s, 3H), 3.56 (q, $^3J_{HH}$ = 8.5 Hz, 1H), 2.82 (d, $^2J_{HH}$ = 13.7 Hz, 1H), 2.45-2.40 (m, 1H), 2.36 (d, $^3J_{HH}$ = 7.7 Hz, 1H), 2.33-2.22 (m, 2H), 1.92 (dd, $^2J_{HH}$ = 13.7 Hz and $^4J_{HH}$ = 1.0 Hz, 1H), 1.81-1.73 (m, 1H), 0.97-0.93

(m, 1H), 0.36-0.29 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 218.9, 174.4, 142.4, 128.7, 127.3, 126.2, 62.0, 55.8, 52.2, 50.1, 44.3, 38.8, 25.0, 22.1, 17.2, 6.8. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 75.88; H, 7.10.



4af

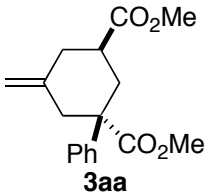
Entry 10. 94% yield (dr = 57/43) along with trace amount of **3af**. The relative configuration was assigned by analogy with **4ae** (entry 9).

Major diastereomer of **4af**: ^{1}H NMR ($CDCl_3$): δ 7.33 (t, $^3J_{HH}$ = 7.8 Hz, 2H), 7.29 (tt, $^3J_{HH}$ = 7.7 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 7.23 (d, $^3J_{HH}$ = 8.3 Hz, 2H), 4.35 (dddd, $^3J_{HH}$ = 10.0, 8.8, and 7.3 Hz and $^4J_{HH}$ = 1.1 Hz, 1H), 4.17 (t, J_{HH} = 10.0 Hz, 1H), 3.65 (s, 3H), 3.52 (dd, $^2J_{HH}$ = 10.0 Hz and $^3J_{HH}$ = 7.1 Hz, 1H), 2.59 (d, $^3J_{HH}$ = 8.8 Hz, 1H), 2.54 (d, $^2J_{HH}$ = 12.7 Hz, 1H), 2.21 (dd, $^2J_{HH}$ = 12.8 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 1.31-1.24 (m, 1H), 0.66-0.59 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 178.5, 175.0, 138.2, 129.1, 128.0 127.1, 69.0, 62.0, 52.7, 48.8, 46.3, 40.7, 24.8, 17.5, 4.8. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.40; H, 6.59.

Minor diastereomer of **4af**: ^{1}H NMR ($CDCl_3$): δ 7.42 (d, $^3J_{HH}$ = 7.9 Hz, 2H), 7.38 (t, $^3J_{HH}$ = 7.9 Hz, 2H), 7.32 (tt, $^3J_{HH}$ = 7.4 Hz and $^4J_{HH}$ = 1.4 Hz, 1H), 4.66 (dd, $^2J_{HH}$ = 9.9 Hz and $^3J_{HH}$ = 9.5 Hz, 1H), 4.07 (dd, $^2J_{HH}$ = 10.0 Hz and $^3J_{HH}$ = 8.1 Hz, 1H), 3.91 (dddd, $^3J_{HH}$ = 9.4, 8.4, and 8.2 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 3.65 (s, 3H), 2.77 (d, $^2J_{HH}$ = 13.9 Hz, 1H), 2.58 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 2.02 (dd, $^2J_{HH}$ = 13.8 Hz and $^4J_{HH}$ = 1.2 Hz, 1H), 1.13 (ddd, $^2J_{HH}$ = 11.5 Hz and $^3J_{HH}$ = 6.5 and 5.3 Hz, 1H), 0.49 (ddd, $^2J_{HH}$ = 11.7 Hz and $^3J_{HH}$ = 6.5 and 5.1 Hz, 1H), 0.46-0.42 (m, 1H), 0.35 (ddd, $^2J_{HH}$ = 10.0 Hz and $^3J_{HH}$ = 6.0 and 4.4 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 177.8, 173.7, 140.8, 129.0, 127.9, 126.1, 70.7, 61.8, 52.6, 48.7, 48.6, 43.4, 23.3, 18.5, 6.4. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.24; H, 6.46.

Typical Procedure for Equation 1.

A solution of PdCp(η^3-C_3H_5) (3.2 mg, 15 μmol), P(*o*-Tol)$_3$ (9.1 mg, 30 μmol), **1a** (133 mg, 0.54 mmol), and **2a** (27 μL, 0.30 mmol) in 1,2-dichloroethane (0.75 mL) was stirred for 48 h at 60 °C. The reaction mixture was directly passed through a pad of silica gel with EtOAc and the solvent was removed under vacuum. The residue was purified by silica gel preparative TLC with hexane/EtOAc/CH_2Cl_2 = 10/2/1 to afford cycloadducts.



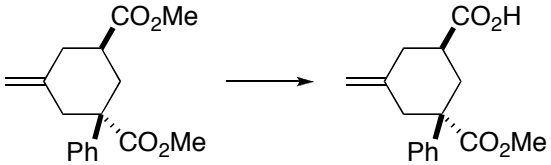
3aa

83% yield (dr = 71/29) along with 4% yield of **4aa**. The relative configuration was determined by X-ray crystallographic analysis of the major diastereomer after converting it to the corresponding monocarboxylic acid (**S1**).

Major diastereomer of **3aa**: ^{1}H NMR ($CDCl_3$): δ 7.38 (d, $^3J_{HH}$ = 7.2 Hz, 2H), 7.34 (t, $^3J_{HH}$ = 7.2 Hz, 2H), 7.26 (tt, $^3J_{HH}$ = 7.1 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 4.89 (q, J_{HH} = 1.7 Hz, 1H), 4.88 (q, J_{HH} = 1.6 Hz, 1H), 3.70 (s, 3H), 3.63 (s, 3H), 3.21 (dt, $^2J_{HH}$ = 12.9 Hz and $^4J_{HH}$ = 2.0 Hz,

1H), 2.91-2.87 (m, 1H), 2.76 (tt, $^3J_{HH}$ = 12.7 and 4.0 Hz, 1H), 2.58 (ddt, $^2J_{HH}$ = 13.2 Hz and $^3J_{HH}$ = 4.3 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 2.36 (dq, $^2J_{HH}$ = 12.8 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 2.17 (tq, J_{HH} = 12.9 Hz and $^4J_{HH}$ = 1.3 Hz, 1H), 1.75 (dd, $^2J_{HH}$ = 13.4 Hz and $^3J_{HH}$ = 12.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 175.3, 174.2, 143.3, 143.0, 128.8, 127.4, 125.5, 112.2, 52.8, 52.3, 51.9, 42.2, 41.9, 37.3, 36.7. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 71.06; H, 7.00.

Minor diastereomer of **3aa**: ^{1}H NMR ($CDCl_3$): δ 7.45 (d, $^3J_{HH}$ = 7.3 Hz, 2H), 7.33 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 7.23 (tt, $^3J_{HH}$ = 7.3 Hz and $^4J_{HH}$ = 1.1 Hz, 1H), 4.91 (q, J_{HH} = 1.8 Hz, 1H), 4.87 (q, J_{HH} = 1.8 Hz, 1H), 3.68 (s, 3H), 3.61 (s, 3H), 3.33 (dt, $^2J_{HH}$ = 14.4 Hz and $^4J_{HH}$ = 1.9 Hz, 1H), 2.92 (dq, $^2J_{HH}$ = 14.2 Hz and $^4J_{HH}$ = 2.4 Hz, 1H), 2.52 (dq, $^2J_{HH}$ = 14.4 Hz and $^4J_{HH}$ = 1.7 Hz, 1H), 2.50-2.46 (m, 1H), 2.31 (tdd, $^3J_{HH}$ = 12.5, 3.7, and 3.1 Hz, 1H), 2.20 (tq, J_{HH} = 12.9 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 2.10 (dd, $^2J_{HH}$ = 14.1 Hz and $^3J_{HH}$ = 12.6 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 175.6, 175.3, 142.2, 139.3, 128.7, 127.7, 127.1, 113.4, 52.6, 51.9, 50.4, 40.1, 38.9, 36.6, 36.0. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 71.01; H, 7.12.

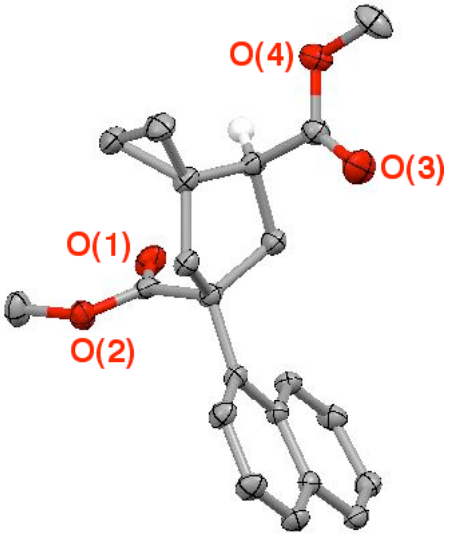


3aa **S1**

A solution of KOH (265 mg, 4.01 mmol; 85%) in MeOH/H_2O (2.0 mL/1.0 mL) was added to a solution of **3aa** (170 mg, 0.590 mmol; major diastereomer) in MeOH (7.0 mL) and the mixture was refluxed for 12 h. After cooled to room temperature, the solvent was concentrated under vacuum, and this was diluted with H_2O (10 mL). The mixture was washed with Et_2O (20 mL) and the aqueous layer was acidified with 6 N HCl*aq*. This was then extracted with Et_2O (20 mL x 7 times), and the organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was purified by silica gel preparative TLC with hexane/EtOAc = 1/1 to afford **S1** as a pale yellow solid (114 mg, 0.416 mmol; 70% yield).

^{1}H NMR ($CDCl_3$): δ 7.39-7.32 (m, 4H), 7.27 (tt, $^3J_{HH}$ = 7.1 Hz and $^4J_{HH}$ = 1.5 Hz, 1H), 4.92-4.89 (m, 2H), 3.63 (s, 3H), 3.23 (dt, $^2J_{HH}$ = 12.9 Hz and $^4J_{HH}$ = 1.8 Hz, 1H), 2.95-2.90 (m, 1H), 2.81 (tt, $^3J_{HH}$ = 12.7 and 3.9 Hz, 1H), 2.66-2.61 (m, 1H), 2.37 (d, $^2J_{HH}$ = 12.9 Hz, 1H), 2.18 (t, J_{HH} = 13.1 Hz, 1H), 1.76 (t, J_{HH} = 13.0 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 180.3, 174.2, 142.93, 142.87, 128.9, 127.5, 125.6, 112.5, 52.8, 52.4, 42.2, 41.7, 37.1, 36.5. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.82; H, 6.69.

III. X-ray Crystal Structure of Major Diastereomer of Compound 4ea



Data Collection

A colorless Et_2O solution of compound **4ea** was prepared. Crystals suitable for X-ray analysis were obtained by slow evaporation of the solvent.

A colorless prism crystal of $C_{21}H_{22}O_4$ having approximate dimensions of 0.50 x 0.40 x 0.40 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation.

Indexing was performed from 3 oscillations that were exposed for 60 seconds. The crystal-to-detector distance was 127.40 mm.

Cell constants and an orientation matrix for data collection corresponded to a C-centered monoclinic cell with dimensions:

a = 24.204(11) Å
b = 11.794(5) Å β = 131.987(16)°
c = 16.099(7) Å
V = 3416.0(26) Å^3

For Z = 6 and F.W. = 338.40, the calculated density is 0.987 g/cm^3. Based on the systematic absences of:

hkl: h + k ± 2n
h0l: l ± 2n

packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

C2/c (#15)

The data were collected at a temperature of –150 ± 1 °C to a maximum 2θ value of 55.0°. A total of 44 oscillation images were collected. A sweep of data was done using ω scans from 130.0 to 190.0° in 5.0° step, at χ = 45.0° and ϕ = 0.0°. The exposure rate was 60.0 [sec./°]. A second sweep was performed using ω scans from 0.0 to 160.0° in 5.0° step, at χ = 45.0° and ϕ = 180.0°. The exposure rate was 60.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 16311 reflections that were collected, 3916 were unique (R_{int} = 0.038).

The linear absorption coefficient, μ, for Mo-Kα radiation is 0.676 cm^{-1}. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[4] and expanded using Fourier techniques.[5] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotopically. The final cycle of full-matrix least-squares refinement[6] on F was based on 11643 observed reflections ($I > 2.00\sigma(I)$) and 314 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0469$$

$$R_W = [\; \Sigma \; w \; (|Fo| - |Fc|)^2 \; / \; \Sigma \; w \; Fo^2]^{1/2} = 0.0552$$

The standard deviation of an observation of unit weight[7] was 0.86. A Sheldrick weighting scheme was used. Plots of $\Sigma \; w \; (|Fo|-|Fc|)^2$ versus |Fo|, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.98 and –0.73 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.[8] Anomalous dispersion effects were included in Fcalc;[9] the values for Δf' and Δf" were those of Creagh and McAuley.[10] The values for the mass attenuation coefficients are those of Creagh and Hubbell.[11] All calculations were performed using the CrystalStructure[12,13] crystallographic software package.

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[4] SIR92: Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, *27*, 435.

[5] DIRDIF99: Beurskens, P. T.; Admiraal, G.; Beurskens, G.; Bosman, W. P.; de Gelder, R.; Israel, R.; Smits, J. M. M. The DIRDIF-99 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands (1999).

[6] Least Squares function minimized:

$\Sigma w(|F_o|-|F_c|)^2$ where w = Least Squares weights.

[7] Standard deviation of an observation of unit weight:

$[\Sigma w(|F_o|-|F_c|)^2/(N_o-N_v)]^{1/2}$

where: N_o = number of observations, N_v = number of variables

[8] Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

[9] Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.

[10] Creagh, D. C.; McAuley, W. J. "International Tables for Crystallography", Vol C, (Wilson, A. J. C. ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219–222 (1992).

[11] Creagh, D. C.; Hubbell, J. H. "International Tables for Crystallography", Vol C, (Wilson, A. J. C. ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200–206 (1992).

[12] CrystalStructure 3.8.0: Crystal Structure Analysis Package, Rigaku and Rigaku/MSC (2000-2006). 9009 New Trails Dr. The Woodlands TX 77381 USA.

[13] CRYSTALS Issue 11: Carruthers, J. R.; Rollett, J. S.; Betteridge, P. W.; Kinna, D.; Pearce, L.; Larsen, A.; Gabe, E. Chemical Crystallography Laboratory, Oxford, UK. (1999).

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 659648). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

Experimental Details

A. Crystal Data

Empirical Formula	$C_{21}H_{22}O_4$
Formula Weight	338.40
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.40 X 0.40 mm
Crystal System	monoclinic
Lattice Type	C-centered
Indexing Images	3 oscillations @ 60.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 24.204(11) Å b = 11.794(5) Å c = 16.099(7) Å β = 131.987(16) ° V = 3416.0(26) $Å^3$
Space Group	C2/c (#15)
Z value	6
D_{calc}	0.987 g/cm^3
F_{000}	1080.00
μ(MoKα)	0.676 cm^{-1}

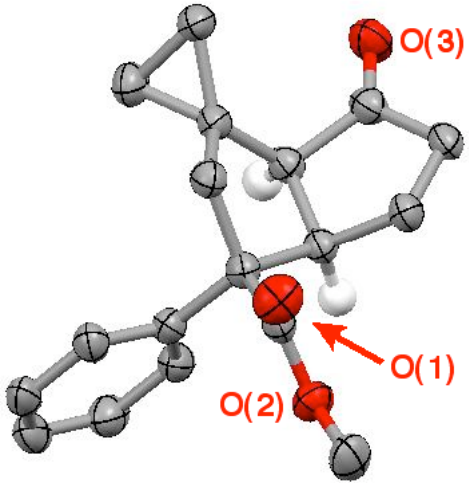
B. Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID
Radiation	MoKα (λ = 0.71075 Å) graphite monochromated
Detector Aperture	280 mm x 256 mm
Data Images	44 exposures
ω oscillation Range (χ=45.0, ϕ=0.0)	130.0 - 190.0°
Exposure Rate	60.0 sec./°
ω oscillation Range (χ=45.0, ϕ=180.0)	0.0 - 160.0°
Exposure Rate	60.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 16311 Unique: 3916 (R_{int} = 0.038)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	Σ w (|Fo| –| Fc|)^2
Least Squares Weights	1/ [0.0010Fo^2 + 3.0000σ(Fo^2) + 0.5000]
$2\theta_{max}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>2.00σ(I))	11643
No. Variables	314
Reflection/Parameter Ratio	37.08
Residuals: R (I>2.00σ(I))	0.0469
Residuals: Rw (I>2.00σ(I))	0.0552
Goodness of Fit Indicator	0.858
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.98 e$^-$/Å^3
Minimum peak in Final Diff. Map	–0.73 e$^-$/Å^3

IV. X-ray Crystal Structure of Minor Diastereomer of Compound 4ae



Data Collection

A colorless Et_2O solution of compound **4ae** was prepared. Crystals suitable for X-ray analysis were obtained by slow evaporation of the solvent.

A colorless prism crystal of $C_{18}H_{20}O_3$ having approximate dimensions of 0.50 x 0.30 x 0.05 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation.

Indexing was performed from 3 oscillations that were exposed for 2000 seconds. The crystal-to-detector distance was 127.40 mm.

Cell constants and an orientation matrix for data collection corresponded to a primitive orthorhombic cell with dimensions:

a = 25.14(4) Å
b = 7.838(19) Å
c = 15.20(3) Å
V = 2995.9(105) $Å^3$

For Z = 8 and F.W. = 284.53, the calculated density is 1.261 g/cm^3. The systematic absences of:

0kl: k ± 2n
h0l: l ± 2n
hk0: h + k ± 2n

uniquely determine the space group to be:

Pbcn (#60)

The data were collected at a temperature of –150 ± 1 °C to a maximum 2θ value of 55.0°. A total of 44 oscillation images were collected. A sweep of data was done using ω scans from 130.0 to 190.0° in 5.0° step, at χ = 45.0° and ϕ = 0.0°. The exposure rate was 400.0 [sec./°]. A second sweep was performed using ω scans from 0.0 to 160.0° in 5.0° step, at χ = 45.0° and ϕ = 180.0°. The exposure rate was 400.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 25285 reflections that were collected, 3370 were unique (R_{int} = 0.106).

The linear absorption coefficient, μ, for Mo-Kα radiation is 0.845 cm^{-1}. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[14] and expanded using Fourier techniques.[5] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotopically. The final cycle of full-matrix least-squares refinement[15] on F^2 was based on 3370 observed reflections and 271 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \; ||Fo| - |Fc|| \; / \; \Sigma \; |Fo| = 0.0641$$

$$wR2 = [\; \Sigma \; w \; (Fo^2 - Fc^2)^2 \; / \; \Sigma \; w \; (Fo^2)^2]^{1/2} = 0.1848$$

The standard deviation of an observation of unit weight[16] was 1.07. Unit weights were used. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.20 and –0.29 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.[8] Anomalous dispersion effects were included in Fcalc;[9] the values for Δf' and Δf'' were those of Creagh and McAuley.[10] The values for the mass attenuation coefficients are those of Creagh and Hubbell.[11] All calculations were performed using the CrystalStructure[12] crystallographic software package except for refinement, which was performed using SHELXL-97.[17]

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 659649). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

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[14] SIR97: Altomare, A.; Burla, M.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A.; Polidori, G.; Spagna, R. *J. Appl. Cryst.* **1999**, *32*, 115.

[15] Least Squares function minimized: (SHELXL97)

$\Sigma w(F_o^2 - F_c^2)^2$ where w = Least Squares weights.

[16] Standard deviation of an observation of unit weight:

$[\Sigma w(F_o^2 - F_c^2)^2/(N_o - N_v)]^{1/2}$

where: N_o = number of observations, N_v = number of variables

[17] SHELX97: Sheldrick, G. M. (1997).

Experimental Details

A. Crystal Data

Empirical Formula	$C_{18}H_{20}O_3$
Formula Weight	284.35
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.30 X 0.05 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Indexing Images	3 oscillations @ 1999.8 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 25.14(4) Å b = 7.838(19) Å c = 15.20(3) Å V = 2995.9(105) Å^3
Space Group	Pbcn (#60)
Z value	8
D_{calc}	1.261 g/cm^3
F_{000}	1216.00
μ(MoKα)	0.845 cm^{-1}

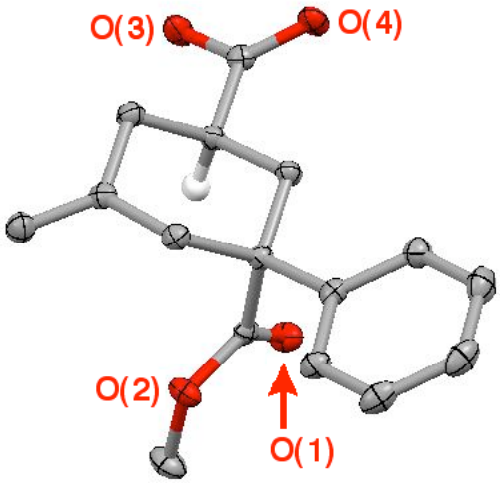
B. Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID
Radiation	MoKα (λ = 0.71075 Å) graphite monochromated
Detector Aperture	280 mm x 256 mm
Data Images	44 exposures
ω oscillation Range (χ=45.0, ϕ=0.0)	130.0 - 190.0°
Exposure Rate	400.0 sec./°
ω oscillation Range (χ=45.0, ϕ=180.0)	0.0 - 160.0°
Exposure Rate	400.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 25285 Unique: 3370 (R_{int} = 0.106)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ $[\sigma^2(Fo^2) + (0.1000 \bullet P)^2$ + 0.0000•P] where P = $(Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3370
No. Variables	271
Reflection/Parameter Ratio	12.44
Residuals: R1 (I>2.00σ(I))	0.0641
Residuals: R (All reflections)	0.0969
Residuals: wR2 (All reflections)	0.1848
Goodness of Fit Indicator	1.066
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.20 $e^-/Å^3$
Minimum peak in Final Diff. Map	–0.29 $e^-/Å^3$

V. X-ray Crystal Structure of Compound S1



Data Collection

A colorless Et_2O solution of compound **S1** was prepared. Crystals suitable for X-ray analysis were obtained by slow evaporation of the solvent.

A colorless prism crystal of $C_{16}H_{18}O_4$ having approximate dimensions of 0.50 x 0.40 x 0.30 mm was mounted on a glass fiber. All measurements were made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Mo-Kα radiation.

Indexing was performed from 3 oscillations that were exposed for 30 seconds. The crystal-to-detector distance was 127.40 mm.

Cell constants and an orientation matrix for data collection corresponded to a primitive triclinic cell with dimensions:

a = 7.328(5) Å	α = 72.48(3)°
b = 8.183(5) Å	β = 88.50(3)°
c = 12.226(10) Å	γ = 76.67(2)°
V = 679.6(8) Å^3	

For Z = 2 and F.W. = 274.32, the calculated density is 1.341 g/cm^3. Based on the statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

P–1 (#2)

The data were collected at a temperature of –150 ± 1 °C to a maximum 2θ value of 55.0°. A total of 44 oscillation images were collected. A sweep of data was done using ω scans from 130.0 to 190.0° in 5.0° step, at χ = 45.0° and ϕ = 0.0°. The exposure rate was 60.0 [sec./°]. A second sweep was performed using ω scans from 0.0 to 160.0° in 5.0° step, at χ = 45.0° and ϕ = 180.0°. The exposure rate was 60.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 6644 reflections that were collected, 3071 were unique (R_{int} = 0.026).

The linear absorption coefficient, μ, for Mo-Kα radiation is 0.956 cm^{-1}. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods[14] and expanded using Fourier techniques.[5] The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement[15] on F^2 was based on 3071 observed reflections and 182 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R1 = \Sigma \, ||Fo| - |Fc|| \, / \, \Sigma \, |Fo| = 0.0437$$

$$wR2 = [\, \Sigma \, w \, (Fo^2 - Fc^2)^2 \, / \, \Sigma \, w \, (Fo^2)^2 \,]^{1/2} = 0.1366$$

The standard deviation of an observation of unit weight[16] was 1.13. Unit weights were used. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.63 and –0.65 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.[8] Anomalous dispersion effects were included in Fcalc;[9] the values for Δf' and Δf" were those of Creagh and McAuley.[10] The values for the mass attenuation coefficients are those of Creagh and Hubbell.[11] All calculations were performed using the CrystalStructure[12] crystallographic software package except for refinement, which was performed using SHELXL-97.[17]

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 659650). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

Experimental Details

A. Crystal Data

Empirical Formula	$C_{16}H_{18}O_4$
Formula Weight	274.32
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.40 X 0.30 mm
Crystal System	triclinic
Lattice Type	Primitive
Indexing Images	3 oscillations @ 30.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	a = 7.328(5) Å b = 8.183(5) Å c = 12.226(10) Å α = 72.48(3)° β = 88.50(3)° γ = 76.67(2)° V = 679.6(8) Å^3
Space Group	P–1 (#2)
Z value	2
D_{calc}	1.341 g/cm^3
F_{000}	292.00
μ(MoKα)	0.956 cm^{-1}

B. Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID
Radiation	MoKα (λ = 0.71075 Å) graphite monochromated
Detector Aperture	280 mm x 256 mm
Data Images	44 exposures
ω oscillation Range (χ=45.0, ϕ=0.0)	130.0 - 190.0°
Exposure Rate	60.0 sec./°
ω oscillation Range (χ=45.0, ϕ=180.0)	0.0 - 160.0°
Exposure Rate	60.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	55.0°
No. of Reflections Measured	Total: 6644 Unique: 3071 (R_{int} = 0.026)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ $[\sigma^2(Fo^2) + (0.0670 \bullet P)^2$ + 0.2630•P] where P = $(Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3071
No. Variables	182
Reflection/Parameter Ratio	16.87
Residuals: R1 (I>2.00σ(I))	0.0437
Residuals: R (All reflections)	0.0528
Residuals: wR2 (All reflections)	0.1366
Goodness of Fit Indicator	1.129
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.63 $e^-/Å^3$
Minimum peak in Final Diff. Map	–0.65 $e^-/Å^3$