γ -Methylidene- δ -valerolactones as a Coupling Partner for Cycloaddition: Palladium-Catalyzed [4 + 3] Cycloaddition with Nitrones

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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.

MeOH was distilled over Mg turnings under nitrogen. THF was purified by passing through a neutral alumina column under nitrogen. CH₂Cl₂ was distilled over CaH₂ under nitrogen.

Phenylmalonic acid (Avocado), (2-methylphenyl)acetic acid (Wako Chemicals), 1-naphthaleneacetic acid (TCI), methyl (4-methoxyphenyl)acetate (Alfa Aesar), methyl 3-thiopheneacetate (Wako Chemicals), 4-methylbenzaldehyde (Wako Chemicals), 4-chlorobenzaldehyde (Wako Chemicals), triphenylphosphine (Wako Chemicals), triisopropyl phosphite (TCI), thionyl chloride (Wako Chemicals), dimethyl carbonate (Wako Chemicals), TBAF (Aldrich; 1.0 M solution in THF), and NaH (Kanto Chemicals; 60 wt% in mineral oil) were used as received. 2-(*tert*-Butyldimethylsiloxy)methyl-2-propen-1-yl methanesulfonate,¹ PdCp(η^3 -C₃H₅),² **2a**,³ **2d**,⁴ **4**,⁵ (*S*)-**5**,⁶ (*S,R,R*)-**6**,⁷ and **7**⁸ 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. Synthesis of Substrates

The yields have not been optimized.

α -Methoxycarbonyl- α -phenyl- γ -methylidene- δ -valerolactone (1a**)**

¹ Kitamura, T.; Sato, Y.; Mori, M. *Adv. Synth. Catal.* **2002**, *344*, 678.

² Parker, G.; Werner, H. *Helv. Chim. Acta* **1973**, *56*, 2819.

³ Shintani, R.; Park, S.; Duan, W.-L.; Hayashi, T. *Angew. Chem., Int. Ed.* **2007**, *46*, in press.

⁴ R. Shintani, T. Hayashi, *J. Am. Chem. Soc.* **2006**, *128*, 6330.

⁵ Durán, J.; Gulías, M.; Castedo, L.; Mascareñas, J. L. *Org. Lett.* **2005**, *7*, 5693.

⁶ Arnold, L. A.; Imbos, R.; Mandolin, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.

⁷ Rimkus, A.; Sewald, N. *Org. Lett.* **2003**, *5*, 79.

⁸ Shintani, R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 10778.

Thionyl chloride (3.65 mL, 50.0 mmol) was added to a solution of phenylmalonic acid (3.60 g, 20.0 mmol) in methanol (60 mL) at 0 °C. The mixture was stirred for 26 h at room temperature and the solvent was removed under vacuum. The residual solid was washed with hexane and dried under vacuum to afford dimethyl phenylmalonate (CAS 37434-59-6) as a white solid (3.95 g, 19.0 mmol; 95% yield).

¹H NMR (CDCl₃): δ 7.41-7.32 (m, 5H), 4.65 (s, 1H), 3.76 (s, 6H). ¹³C NMR (CDCl₃): δ 168.7, 132.7, 129.4, 128.8, 128.5, 57.7, 53.0.

A solution of dimethyl phenylmalonate (2.08 g, 10.0 mmol) in THF (15 mL) was added to a suspension of NaH (420 mg, 10.5 mmol; 60 wt% in mineral oil) in THF (5 mL) at 0 °C. The mixture was stirred for 15 min at 0 °C and a solution of 2-(*tert*-butyldimethylsiloxy)methyl-2-propen-1-yl methanesulfonate (3.23 g, 11.5 mmol) in THF (12 mL) was added to it. The resulting mixture was stirred for 35 h at 35 °C and was quenched with water. After extraction with Et₂O, the organic layer was washed with NaCl (saturated aqueous), dried over MgSO₄, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/12 to afford dimethyl (2-(*tert*-butyldimethylsiloxy)methyl-2-propen-1-yl)(phenyl)malonate as a colorless oil (3.85 g, 9.82 mmol; 98% yield).

¹H NMR (CDCl₃): δ 7.50 (d, ³J_{HH} = 7.0 Hz, 2H), 7.32 (t, ³J_{HH} = 7.2 Hz, 2H), 7.28 (t, ³J_{HH} = 7.0 Hz, 1H), 5.13 (s, 1H), 4.71 (s, 1H), 3.76 (s, 2H), 3.73 (s, 6H), 3.10 (s, 2H), 0.87 (s, 9H), -0.01 (s, 6H). ¹³C NMR (CDCl₃): δ 170.9, 143.8, 136.7, 128.3, 128.2, 127.8, 113.2, 66.3, 62.6, 52.8, 38.8, 26.0, 18.5, -5.3.

TBAF (10.8 mL, 10.8 mmol; 1.0 M solution in THF) was added to a solution of dimethyl (2-(*tert*-butyldimethylsiloxy)methyl-2-propen-1-yl)(phenyl)malonate (3.85 g, 9.82 mmol) in THF (25 mL) at -65 °C. The mixture was stirred for 4.5 h while gradually raising the temperature to 0 °C and the reaction was quenched with water. After extraction with Et₂O, the organic layer was washed with NaCl (saturated aqueous), dried over MgSO₄, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/5→1/3 to afford **1a** as a white solid (1.62 g, 6.56 mmol; 67% yield).

¹H NMR (CDCl₃): δ 7.41-7.31 (m, 5H), 5.09 (quint, *J*_{HH} = 1.8 Hz, 1H), 5.00 (quint, *J*_{HH} = 1.7 Hz, 1H), 4.73 (d, ²*J*_{HH} = 14.7 Hz, 1H), 4.54 (dd, ²*J*_{HH} = 14.7 Hz and ⁴*J*_{HH} = 1.5 Hz, 1H), 3.77 (s, 3H), 3.51 (dd, ²*J*_{HH} = 16.4 Hz and ⁴*J*_{HH} = 1.6 Hz, 1H), 3.31 (d, ²*J*_{HH} = 16.5 Hz, 1H). ¹³C NMR (CDCl₃): δ 170.0, 169.1, 136.1, 134.7, 129.0, 128.5, 127.4, 112.3, 71.5, 59.6, 53.5, 35.9. Anal. Calcd for C₁₄H₁₄O₄: C, 68.28; H, 5.73. Found: C, 68.24; H, 5.66.

α-Methoxycarbonyl-α-(4-methoxyphenyl)-γ-methylidene-δ-valerolactone (**1b**)

A solution of methyl (4-methoxyphenyl)acetate (1.27 mL, 8.00 mmol) in dimethyl carbonate (10 mL) was added to NaH (640 mg, 16.0 mmol; 60 wt% in mineral oil) at 0 °C.

The mixture was stirred for 25 h at room temperature and was quenched with water. After extraction with Et₂O, the organic layer was washed with NaCl (saturated aqueous), dried over MgSO₄, filtered, and concentrated under vacuum. The residual solid was washed with hexane and dried under vacuum to afford dimethyl (4-methoxyphenyl)malonate (CAS 71146-13-9) as a white solid (1.49 g, 6.26 mmol; 78% yield).

¹H NMR (CDCl₃): δ 7.32 (d, ³J_{HH} = 8.8 Hz, 2H), 6.89 (d, ³J_{HH} = 8.8 Hz, 2H), 4.60 (s, 1H), 3.80 (s, 3H), 3.75 (s, 6H). ¹³C NMR (CDCl₃): δ 169.0, 159.7, 130.5, 124.8, 114.2, 56.9, 55.4, 52.9.

Dimethyl (4-methoxyphenyl)malonate was converted to **1b** following the procedure for **1a**. White solid. 50% yield.

¹H NMR (CDCl₃): δ 7.26 (d, ³J_{HH} = 8.8 Hz, 2H), 6.91 (d, ³J_{HH} = 8.7 Hz, 2H), 5.10 (t, *J*_{HH} = 1.6 Hz, 1H), 5.01 (t, *J*_{HH} = 1.7 Hz, 1H), 4.72 (d, ²J_{HH} = 14.6 Hz, 1H), 4.54 (dd, ²J_{HH} = 14.7 Hz and ⁴J_{HH} = 1.6 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.50 (dd, ²J_{HH} = 16.5 Hz and ⁴J_{HH} = 1.6 Hz, 1H), 3.28 (d, ²J_{HH} = 16.5 Hz, 1H). ¹³C NMR (CDCl₃): δ 170.3, 169.3, 159.6, 136.3, 128.6, 126.4, 114.4, 112.2, 71.4, 58.8, 55.4, 53.5, 35.7. Anal. Calcd for C₁₅H₁₆O₅: C, 65.21; H, 5.84. Found: C, 65.08; H, 5.85.

α-Methoxycarbonyl-α-(2-methylphenyl)-γ-methylidene-δ-valerolactone (**1c**)

Thionyl chloride (875 μL, 12.0 mmol) was added to a solution of (2-methylphenyl)acetic acid (1.20 g, 7.99 mmol) in methanol (20 mL) at 0 °C. The mixture was stirred for 30 h at room temperature and the solvent was removed under vacuum. The residue was dissolved in dimethyl carbonate (10 mL) and this solution was added to NaH (640 mg, 16.0 mmol; 60 wt% in mineral oil) at 0 °C. The mixture was stirred for 16 h at 50 °C and was quenched with water. After extraction with Et₂O, the organic layer was washed with NaCl (saturated aqueous), dried over MgSO₄, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with EtOAc/hexane = 1/3 to afford dimethyl (2-methylphenyl)malonate (CAS 49769-79-1) as a pale yellow oil (1.19 g, 5.37 mmol; 67% yield).

¹H NMR (CDCl₃): δ 7.41-7.37 (m, 1H), 7.25-7.19 (m, 3H), 4.91 (s, 1H), 3.76 (s, 6H), 2.35 (s, 3H). ¹³C NMR (CDCl₃): δ 168.9, 136.6, 131.5, 130.7, 129.0, 128.4, 126.6, 54.2, 52.9, 19.9.

Dimethyl (2-methylphenyl)malonate was converted to **1c** following the procedure for **1a**. White solid. 44% yield.

¹H NMR (CDCl₃): δ 7.24-7.20 (m, 2H), 7.18 (td, ³J_{HH} = 7.8 Hz and ⁴J_{HH} = 1.8 Hz, 1H), 7.09 (dd, ³J_{HH} = 7.7 Hz and ⁴J_{HH} = 0.8 Hz, 1H), 4.99 (t, *J*_{HH} = 1.6 Hz, 1H), 4.93 (t, *J*_{HH} = 1.5 Hz, 1H), 4.85 (d, ²J_{HH} = 14.5 Hz, 1H), 4.74 (dd, ²J_{HH} = 14.6 Hz and ⁴J_{HH} = 1.5 Hz, 1H), 3.79 (s, 3H), 3.44 (d, ²J_{HH} = 15.9 Hz, 1H), 3.31 (d, ²J_{HH} = 15.7 Hz, 1H), 2.28 (s, 3H). ¹³C NMR (CDCl₃): δ 170.6, 169.2, 136.9, 136.2, 134.4, 132.7, 128.4, 127.5, 126.4, 112.0, 71.8, 61.2, 53.5, 37.2, 21.0. Anal. Calcd for C₁₅H₁₆O₄: C, 69.22; H, 6.20. Found: C, 69.23; H, 6.22.

α-Methoxycarbonyl-α-(3-thienyl)-γ-methylidene-δ-valerolactone (**1d**)

This was synthesized from methyl 3-thiopheneacetate, following the procedure for compound **1b**. White solid. 34% yield.

^1H NMR (CDCl_3): δ 7.35 (dd, $^3J_{\text{HH}} = 5.0$ Hz and $^4J_{\text{HH}} = 2.9$ Hz, 1H), 7.28 (dd, $^4J_{\text{HH}} = 2.9$ and 1.5 Hz, 1H), 7.13 (dd, $^3J_{\text{HH}} = 5.1$ Hz and $^4J_{\text{HH}} = 1.4$ Hz, 1H), 5.12 (quint, $J_{\text{HH}} = 1.7$ Hz, 1H), 5.07 (quint, $J_{\text{HH}} = 1.7$ Hz, 1H), 4.76 (d, $^2J_{\text{HH}} = 14.4$ Hz, 1H), 4.65 (d, $^2J_{\text{HH}} = 14.5$ Hz, 1H), 3.79 (s, 3H), 3.55 (d, $^2J_{\text{HH}} = 16.1$ Hz, 1H), 3.17 (d, $^2J_{\text{HH}} = 16.1$ Hz, 1H). ^{13}C NMR (CDCl_3): δ 169.6, 168.5, 135.9, 135.5, 127.3, 126.3, 123.5, 112.8, 71.6, 56.6, 53.6, 36.7. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_4\text{S}$: C, 57.13; H, 4.79. Found: C, 56.90; H, 4.75.

α -Methoxycarbonyl- α -(1-naphthyl)- γ -methylidene- δ -valerolactone (1e**)**

This was synthesized from 1-naphthaleneacetic acid, following the procedure for compound **1c**. White solid. 31% yield.

^1H NMR (CDCl_3): δ 7.90-7.87 (m, 1H), 7.84 (d, $^3J_{\text{HH}} = 8.2$ Hz, 1H), 7.68-7.66 (m, 1H), 7.52-7.48 (m, 2H), 7.41 (t, $^3J_{\text{HH}} = 7.7$ Hz, 1H), 7.29 (dd, $^3J_{\text{HH}} = 7.3$ Hz and $^4J_{\text{HH}} = 0.8$ Hz, 1H), 4.91 (d, $^2J_{\text{HH}} = 14.2$ Hz, 1H), 4.86 (dd, $^2J_{\text{HH}} = 14.2$ Hz and $^4J_{\text{HH}} = 1.2$ Hz, 1H), 4.85 (s, 1H), 4.78 (s, 1H), 3.76 (s, 3H), 3.66 (d, $^2J_{\text{HH}} = 15.5$ Hz, 1H), 3.57 (d, $^2J_{\text{HH}} = 15.5$ Hz, 1H). ^{13}C NMR (CDCl_3): δ 171.2, 169.3, 135.6, 134.8, 132.5, 130.4, 129.8, 126.6, 126.0, 125.8, 125.0, 124.0, 112.6, 71.8, 61.6, 53.7, 37.8. Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_4$: C, 72.96; H, 5.44. Found: C, 72.88; H, 5.61.

***N*-(4-Ethoxycarbonylphenyl)- α -(4-methylphenyl)nitron (**2b**)**

This was synthesized from 4-methylbenzaldehyde, following the procedure for compound **2d**.⁴ White solid, 62% yield.

^1H NMR (C_6D_6): δ 8.44 (d, $^3J_{\text{HH}} = 8.1$ Hz, 2H), 8.00 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.48 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.34 (s, 1H), 7.05 (d, $^3J_{\text{HH}} = 7.9$ Hz, 2H), 4.10 (q, $^3J_{\text{HH}} = 7.2$ Hz, 2H), 2.06 (s, 3H), 1.01 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR ($\text{DMSO}-d_6$): δ 164.8, 151.4, 141.2, 134.4, 130.7, 130.0, 129.12, 129.09, 128.2, 121.8, 61.1, 21.3, 14.1.

***N*-(4-Ethoxycarbonylphenyl)- α -(4-chlorophenyl)nitron (**2c**)**

This was synthesized from 4-chlorobenzaldehyde, following the procedure for compound **2d**.⁴ White solid, 91% yield.

¹H NMR (DMSO-*d*₆, 80 °C): δ 8.13 (s, 1H), 8.07 (d, ³*J*_{HH} = 8.4 Hz, 2H), 7.66 (d, ³*J*_{HH} = 8.4 Hz, 2H), 7.61 (d, ³*J*_{HH} = 8.5 Hz, 2H), 7.12 (d, ³*J*_{HH} = 8.3 Hz, 2H), 3.93 (q, ³*J*_{HH} = 7.1 Hz, 2H), 0.92 (t, ³*J*_{HH} = 7.1 Hz, 3H). ¹³C NMR (DMSO-*d*₆, 80 °C): δ 164.4, 151.0, 134.6, 133.0, 130.9, 130.2, 129.6, 129.4, 128.2, 121.5, 60.7, 13.7.

III. Catalytic Reactions

General Procedure for Table 1 and Equation 2.

A solution of PdCp(η³-C₃H₅) (1.1 mg, 5.2 μmol), ligand (10 μmol), nitron or azomethine imine (0.10 mmol), and compound **1** (0.18 mmol) in CH₂Cl₂ (0.5 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 the cycloadduct.

Entry 3. Colorless oil. 99% yield, dr = 90/10. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6. Pure major diastereomer was obtained by further purification for analytical purpose.

Major diastereomer: ¹H NMR (CDCl₃): δ 7.95 (d, ³*J*_{HH} = 8.6 Hz, 2H), 7.47-7.45 (m, 2H), 7.40 (d, ³*J*_{HH} = 7.4 Hz, 2H), 7.34 (t, ³*J*_{HH} = 7.7 Hz, 2H), 7.27 (t, ³*J*_{HH} = 6.8 Hz, 1H), 7.21-7.17 (m, 5H), 5.71 (s, 1H), 4.67 (s, 1H), 4.66 (d, ²*J*_{HH} = 14.0 Hz, 1H), 4.47 (d, ²*J*_{HH} = 14.4 Hz, 1H), 4.33 (q, ³*J*_{HH} = 7.1 Hz, 2H), 4.17 (s, 1H), 3.84 (d, ²*J*_{HH} = 13.7 Hz, 1H), 3.18 (s, 3H), 2.93 (d, ²*J*_{HH} = 13.7 Hz, 1H), 1.36 (t, ³*J*_{HH} = 7.1 Hz, 3H). ¹³C NMR (CDCl₃): δ 174.2, 166.5, 152.8, 144.0, 142.5, 135.9, 131.1, 130.4, 128.3, 128.2, 127.8, 127.1, 127.0, 123.3, 114.6, 114.4, 76.7, 71.1, 60.7, 59.2, 51.8, 42.2, 14.5. Anal. Calcd for C₂₉H₂₉NO₅: C, 73.87; H, 6.20. Found: C, 73.99; H, 6.20.

3ba

Entry 4. Colorless oil. 95% yield, dr = 93/7. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6. Pure major diastereomer was obtained by further purification for analytical purpose.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.93 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.45-7.43 (m, 2H), 7.31 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 7.19-7.15 (m, 5H), 6.86 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 5.66 (s, 1H), 4.68 (s, 1H), 4.65 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 4.46 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 4.33 (q, $^3J_{\text{HH}} = 7.2$ Hz, 2H), 4.23 (s, 1H), 3.81 (s, 3H), 3.80 (d, $^2J_{\text{HH}} = 13.6$ Hz, 1H), 3.17 (s, 3H), 2.90 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 174.4, 166.4, 158.3, 152.9, 142.6, 136.1, 135.9, 131.1, 130.4, 128.2, 128.1, 127.8, 123.2, 114.7, 114.3, 113.6, 76.8, 71.2, 60.7, 58.5, 55.3, 51.8, 42.1, 14.5. Anal. Calcd for $\text{C}_{30}\text{H}_{31}\text{NO}_6$: C, 71.84; H, 6.23. Found: C, 71.62; H, 6.34.

3ca

Entry 5. Colorless oil. 62% yield, dr = 87/13. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.93 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 7.72 (d, $^3J_{\text{HH}} = 7.7$ Hz, 1H), 7.52-7.48 (m, 2H), 7.20-7.14 (m, 8H), 5.64 (s, 1H), 4.69 (d, $^2J_{\text{HH}} = 14.1$ Hz, 1H), 4.63 (s, 1H), 4.49 (d, $^2J_{\text{HH}} = 13.9$ Hz, 1H), 4.32 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 4.13 (s, 1H), 3.85 (d, $^2J_{\text{HH}} = 13.6$ Hz, 1H), 3.15 (s, 3H), 2.97 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 2.24 (s, 3H), 1.35 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 174.4, 166.5, 152.7, 142.9, 142.1, 135.4, 135.2, 132.2, 131.13, 131.09, 128.4, 128.2, 127.6, 127.1, 125.9, 123.2, 114.4, 114.1, 76.7, 72.4, 60.7, 58.6, 52.0, 38.0, 20.8, 14.5. Anal. Calcd for $\text{C}_{30}\text{H}_{31}\text{NO}_5$: C, 74.21; H, 6.43. Found: C, 74.28; H, 6.80.

3da

Entry 6. Colorless oil. 92% yield, dr = 91/9. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6. Pure major diastereomer was obtained by further purification for analytical purpose.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.94 (d, $^3J_{\text{HH}} = 8.7$ Hz, 2H), 7.44-7.41 (m, 2H), 7.31 (dd, $^4J_{\text{HH}} = 2.9$ and 1.4 Hz, 1H), 7.28 (dd, $^3J_{\text{HH}} = 5.0$ Hz and $^4J_{\text{HH}} = 2.9$ Hz, 1H), 7.20-7.17 (m, 3H), 7.15 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 6.99 (dd, $^3J_{\text{HH}} = 5.0$ Hz and $^4J_{\text{HH}} = 1.4$ Hz, 1H), 5.63 (s, 1H), 4.71 (s, 1H), 4.66 (d, $^2J_{\text{HH}} = 14.2$ Hz, 1H), 4.48 (d, $^2J_{\text{HH}} = 13.9$ Hz, 1H), 4.330 (s, 1H), 4.327 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 3.75 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.24 (s, 3H), 2.92 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 173.7, 166.4, 153.0, 143.9, 142.9, 135.8, 131.2, 130.2, 128.3, 127.9, 126.8, 125.0, 123.4, 121.7, 114.5, 114.4, 76.7, 72.2, 60.7, 57.4, 52.0, 41.4, 14.5. Anal. Calcd for $\text{C}_{27}\text{H}_{27}\text{NO}_5\text{S}$: C, 67.90; H, 5.70. Found: C, 67.61; H, 5.75.

3ea

Entry 7. Pale yellow oil. 96% yield, dr = 94/6. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.98-7.94 (m, 1H), 7.96 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.89-7.87 (m, 1H), 7.86 (d, $^3J_{\text{HH}} = 7.4$ Hz, 1H), 7.79 (d, $^3J_{\text{HH}} = 8.3$ Hz, 1H), 7.61-7.58 (m, 2H), 7.47-7.41 (m, 3H), 7.25-7.22 (m, 5H), 5.80 (s, 1H), 4.70 (d, $^2J_{\text{HH}} = 14.2$ Hz, 1H), 4.48 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 4.44 (s, 1H), 4.33 (q, $^3J_{\text{HH}} = 7.2$ Hz, 2H), 4.00 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 3.72 (s, 1H), 3.42 (d, $^2J_{\text{HH}} = 13.6$ Hz, 1H), 3.10 (s, 3H), 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 175.0, 166.4, 152.8, 143.0, 139.2, 135.1, 134.5, 131.3, 131.2, 129.9, 128.6, 128.5, 127.8, 126.4, 126.0, 125.1, 125.0, 123.3, 123.2, 114.1, 113.8, 76.5, 72.4, 60.7, 59.1, 52.1, 38.3, 14.5. Anal. Calcd for $\text{C}_{33}\text{H}_{31}\text{NO}_5$: C, 75.99; H, 5.99. Found: C, 75.92; H, 6.06.

3eb

Entry 8. Colorless oil. 77% yield, dr = 92/8. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.98-7.95 (m, 1H), 7.96 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.89-7.86 (m, 1H), 7.84 (d, $^3J_{\text{HH}} = 7.6$ Hz, 1H), 7.78 (d, $^3J_{\text{HH}} = 8.2$ Hz, 1H), 7.49-7.44 (m, 4H), 7.41 (t, $^3J_{\text{HH}} = 7.9$ Hz, 1H), 7.24 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 7.02 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 5.78 (s, 1H), 4.69 (d, $^2J_{\text{HH}} = 14.2$ Hz, 1H), 4.47 (d, $^2J_{\text{HH}} = 14.3$ Hz, 1H), 4.42 (s, 1H), 4.33 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 3.99 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 3.71 (s, 1H), 3.41 (d, $^2J_{\text{HH}} = 13.5$ Hz, 1H), 3.12 (s, 3H), 2.25 (s, 3H), 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 175.0, 166.5, 152.8, 143.1, 139.2, 138.2, 134.5, 132.1, 131.3, 131.2, 131.1, 129.9, 128.6, 128.5, 126.4, 126.0, 125.08, 125.05, 123.3, 123.1, 114.1, 113.7, 76.5, 72.0, 60.7, 59.1, 52.2, 38.2, 21.2, 14.5. Anal. Calcd for $\text{C}_{34}\text{H}_{33}\text{NO}_5$: C, 76.24; H, 6.21. Found: C, 76.00; H, 6.19.

3ec

Entry 9. Colorless oil, solidified on standing. 98% yield, dr = 93/7. The relative configuration was determined by X-ray crystallographic analysis of the major diastereomer obtained through asymmetric catalysis (Table 2, entry 6). Pure major diastereomer was obtained by further purification for analytical purpose.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.97 (d, $^3J_{\text{HH}} = 8.4$ Hz, 2H), 7.96-7.93 (m, 1H), 7.90-7.88 (m, 1H), 7.86 (d, $^3J_{\text{HH}} = 7.5$ Hz, 1H), 7.80 (d, $^3J_{\text{HH}} = 8.2$ Hz, 1H), 7.53 (d, $^3J_{\text{HH}} = 8.3$ Hz, 2H), 7.48-7.45 (m, 2H), 7.43 (t, $^3J_{\text{HH}} = 7.7$ Hz, 1H), 7.22 (d, $^3J_{\text{HH}} = 8.8$ Hz, 2H), 7.20 (d, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 5.77 (s, 1H), 4.68 (d, $^2J_{\text{HH}} = 14.3$ Hz, 1H), 4.48 (d, $^2J_{\text{HH}} = 14.3$ Hz, 1H), 4.45 (s, 1H), 4.34 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 3.93 (d, $^2J_{\text{HH}} = 13.5$ Hz, 1H), 3.73 (s, 1H), 3.42 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 3.14 (s, 3H), 1.37 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 174.9, 166.3, 152.6, 142.7, 139.0, 134.6, 134.5, 133.6, 132.5, 131.24, 131.17, 130.0, 128.7, 128.0, 126.5, 126.0, 125.2, 125.0, 123.6, 123.1, 114.2, 114.1, 76.6, 72.1, 60.7, 59.0, 52.3, 38.3, 14.5. Anal. Calcd for $\text{C}_{33}\text{H}_{30}\text{ClNO}_5$: C, 71.28; H, 5.44. Found: C, 71.23; H, 5.43.

3ed

Entry 10. Pale yellow oil, solidified on standing. 98% yield, dr = 94/6. The relative configuration of the major diastereomer was assigned by analogy with Table 2, entry 6. Pure major diastereomer was obtained by further purification for analytical purpose.

Major diastereomer: ^1H NMR (CDCl_3): δ 7.97 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 7.95-7.88 (m, 2H), 7.87 (d, $^3J_{\text{HH}} = 7.5$ Hz, 1H), 7.81 (d, $^3J_{\text{HH}} = 8.2$ Hz, 1H), 7.72 (d, $^3J_{\text{HH}} = 8.1$ Hz, 2H), 7.49 (d, $^3J_{\text{HH}} = 8.6$ Hz, 2H), 7.47-7.42 (m, 3H), 7.23 (d, $^3J_{\text{HH}} = 8.9$ Hz, 2H), 5.86 (s, 1H), 4.70 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 4.49 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 4.48 (s, 1H), 4.33 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 3.95 (d, $^2J_{\text{HH}} = 13.5$ Hz, 1H), 3.75 (s, 1H), 3.44 (d, $^2J_{\text{HH}} = 13.7$ Hz, 1H), 3.10 (s, 3H), 1.36 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 174.8, 166.3, 152.4, 142.5, 138.94, 138.86, 134.5, 131.5, 131.3, 131.1, 130.5 (q, $^2J_{\text{CF}} = 32.6$ Hz), 130.0, 128.8, 126.5, 126.0, 125.2, 125.0, 124.7 (q, $^3J_{\text{CF}} = 3.6$ Hz), 124.0 (q, $^1J_{\text{CF}} = 272$ Hz), 123.7, 123.0, 114.3, 114.1, 76.7, 72.3, 60.8, 58.9, 52.3, 38.4, 14.5. Anal. Calcd for $\text{C}_{34}\text{H}_{30}\text{F}_3\text{NO}_5$: C, 69.26; H, 5.13. Found: C, 69.45; H, 5.26.

8

Equation 2. Colorless oil, solidified on standing. 79% yield of the major diastereomer (crude dr = 87/13). The relative configuration was determined by X-ray crystallographic analysis of the major diastereomer.

^1H NMR (CDCl_3 , 45 $^\circ\text{C}$): δ 7.56-7.48 (m, 4H), 7.31-7.27 (m, 4H), 7.26-7.22 (m, 1H), 4.85 (s, 1H), 4.68 (s, 1H), 4.46 (d, $^2J_{\text{HH}} = 14.4$ Hz, 1H), 4.45 (s, 1H), 4.11 (d, $^2J_{\text{HH}} = 14.4$ Hz, 1H), 3.63-3.55 (m, 1H), 3.36 (ddd, $^2J_{\text{HH}} = 13.7$ Hz and $^3J_{\text{HH}} = 8.8$ and 5.0 Hz, 1H), 3.31 (d, $^2J_{\text{HH}} = 14.3$ Hz, 1H), 3.29 (s, 3H), 3.15 (d, $^2J_{\text{HH}} = 14.3$ Hz, 1H), 2.17-2.06 (m, 1H), 1.58-1.49 (m, 1H). ^{13}C NMR (CDCl_3 , 45 $^\circ\text{C}$): δ 175.1, 173.1, 142.6, 140.8, 139.1, 131.1, 130.9 (q, $^2J_{\text{CF}} = 32.6$ Hz), 128.3, 127.4, 127.3, 125.2 (q, $^3J_{\text{CF}} = 3.6$ Hz), 124.0 (q, $^1J_{\text{CF}} = 272$ Hz), 116.4, 76.3, 59.4, 51.8, 51.6, 51.5, 42.6, 30.0. Anal. Calcd for $\text{C}_{24}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_3$: C, 64.86; H, 5.22. Found: C, 64.58; H, 5.32.

General Procedure for Table 2.

A solution of $\text{PdCp}(\eta^3\text{-C}_3\text{H}_5)$ (1.6 mg, 7.5 μmol), ligand (*S,R,R*)-**6** (8.1 mg, 15 μmol), nitrene **2** (0.15 mmol), and compound **1** (0.27 mmol) in CH_2Cl_2 (0.75 mL) was stirred for 24 h at 40 $^\circ\text{C}$. 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 cycloadduct **3**.

3ad

Entry 2. Colorless oil. 98% yield, dr = 81/19. The ee of the major diastereomer was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 90/10, flow = 0.3 mL/min. Retention times: 16.6 min [minor enantiomer], 18.3 min [major enantiomer]. 83% ee. $[\alpha]_D^{20} +34.8$ (c 1.85, CHCl₃). The relative and absolute configurations were assigned by analogy with entry 6.

¹H NMR (CDCl₃): δ 7.95 (d, ³J_{HH} = 8.8 Hz, 2H), 7.56 (d, ³J_{HH} = 8.3 Hz, 2H), 7.45 (d, ³J_{HH} = 8.3 Hz, 2H), 7.39 (d, ³J_{HH} = 7.3 Hz, 2H), 7.34 (t, ³J_{HH} = 7.3 Hz, 2H), 7.28 (t, ³J_{HH} = 7.2 Hz, 1H), 7.16 (d, ³J_{HH} = 8.9 Hz, 2H), 5.75 (s, 1H), 4.69 (s, 1H), 4.65 (d, ²J_{HH} = 14.0 Hz, 1H), 4.48 (d, ²J_{HH} = 13.9 Hz, 1H), 4.33 (q, ³J_{HH} = 7.1 Hz, 2H), 4.19 (s, 1H), 3.78 (d, ²J_{HH} = 13.8 Hz, 1H), 3.19 (s, 3H), 2.95 (d, ²J_{HH} = 13.8 Hz, 1H), 1.36 (t, ³J_{HH} = 7.1 Hz, 3H). ¹³C NMR (CDCl₃): δ 173.9, 166.3, 152.4, 143.7, 141.9, 139.7, 131.2, 130.7, 130.2 (q, ²J_{CF} = 32.0 Hz), 128.4, 127.3, 126.8, 124.7 (q, ³J_{CF} = 3.6 Hz), 124.0 (q, ¹J_{CF} = 272 Hz), 123.8, 115.1, 114.4, 76.9, 71.0, 60.8, 59.0, 51.9, 42.3, 14.5. Anal. Calcd for C₃₀H₂₈F₃NO₅: C, 66.78; H, 5.23. Found: C, 66.48; H, 5.23.

3bd

Entry 3. Colorless oil. 99% yield, dr = 86/14. The ee of the major diastereomer was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 90/10, flow = 0.3 mL/min. Retention times: 31.9 min [minor enantiomer], 39.5 min [major enantiomer]. 84% ee. $[\alpha]_D^{20} +21.2$ (c 1.37, CHCl₃). The relative and absolute configurations were assigned by analogy with entry 6.

¹H NMR (CDCl₃): δ 7.95 (d, ³J_{HH} = 8.7 Hz, 2H), 7.55 (d, ³J_{HH} = 8.3 Hz, 2H), 7.44 (d, ³J_{HH} = 8.4 Hz, 2H), 7.31 (d, ³J_{HH} = 8.8 Hz, 2H), 7.15 (d, ³J_{HH} = 8.8 Hz, 2H), 6.87 (d, ³J_{HH} = 8.8 Hz, 2H), 5.71 (s, 1H), 4.72 (s, 1H), 4.65 (d, ²J_{HH} = 14.4 Hz, 1H), 4.48 (d, ²J_{HH} = 14.4 Hz, 1H), 4.33 (q, ³J_{HH} = 7.1 Hz, 2H), 4.25 (s, 1H), 3.81 (s, 3H), 3.74 (d, ²J_{HH} = 13.6 Hz, 1H), 3.19 (s, 3H), 2.93 (d, ²J_{HH} = 13.8 Hz, 1H), 1.36 (t, ³J_{HH} = 7.1 Hz, 3H). ¹³C NMR (CDCl₃): δ 174.1, 166.3, 158.5, 152.5, 142.1, 139.8, 135.8, 131.2, 130.6, 130.2 (q, ²J_{CF} = 32.6 Hz), 128.0, 124.7 (q, ³J_{CF} = 3.6 Hz), 124.0 (q, ¹J_{CF} = 272 Hz), 123.7, 115.1, 114.4, 113.7, 76.9, 71.2, 60.7, 58.4,

55.3, 51.9, 42.2, 14.5. Anal. Calcd for C₃₁H₃₀F₃NO₆: C, 65.37; H, 5.31. Found: C, 65.66; H, 5.42.

3ed

Entry 4. Colorless oil, solidified on standing. 98% yield, dr = 80/20. The ee of the major diastereomer was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 90/10, flow = 0.7 mL/min. Retention times: 10.5 min [minor enantiomer], 23.6 min [major enantiomer]. 96% ee. $[\alpha]^{20}_{\text{D}} -37.7$ (*c* 1.17, CHCl₃). The relative and absolute configurations were assigned by analogy with entry 6.

3eb

Entry 5. The reaction was conducted with 10 mol % catalyst for 48 h. Colorless oil. 99% yield, dr = 70/30. The ee of the major diastereomer was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 90/10, flow = 0.5 mL/min. Retention times: 13.1 min [minor enantiomer], 17.3 min [major enantiomer]. 89% ee. $[\alpha]^{20}_{\text{D}} -33.5$ (*c* 1.45, CHCl₃). The relative and absolute configurations were assigned by analogy with entry 6.

3ec

Entry 7. Colorless oil, solidified on standing. 89% yield, dr = 72/28. The ee of the major diastereomer was determined on a Daicel Chiralcel OD-H column with hexane/2-propanol = 90/10, flow = 0.5 mL/min. Retention times: 16.3 min [minor enantiomer], 31.5 min [major enantiomer]. 88% ee. $[\alpha]^{20}_{\text{D}} -32.6$ (*c* 0.74, CHCl₃). The relative and absolute configurations were determined by X-ray crystallographic analysis.

IV. X-ray Crystal Structure of Compound **3ec**

Data Collection

A colorless hexane/Et₂O solution of compound **3ec** was prepared. Crystals suitable for X-ray analysis were obtained by keeping the solution in a freezer.

A colorless prism crystal of C₃₃H₃₀ClNO₅ 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-K α 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 primitive monoclinic cell with dimensions:

$$\begin{aligned} a &= 9.509(4) \text{ \AA} \\ b &= 12.566(6) \text{ \AA} \quad \beta = 106.781(18)^\circ \\ c &= 12.510(8) \text{ \AA} \\ V &= 1431.1(12) \text{ \AA}^3 \end{aligned}$$

For $Z = 2$ and F.W. = 556.06, the calculated density is 1.290 g/cm³. Based on the systematic absences of:

$$0k0: k \pm 2n$$

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

$$P2_1 (\#4)$$

The data were collected at a temperature of -150 ± 1 °C to a maximum 2θ value of 54.9°. 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 $\chi = 45.0^\circ$ and $\phi = 0.0^\circ$. The exposure rate was 80.0 [sec./°]. A second sweep of data was performed using ω scans from 0.0 to 160.0° in 5.0° step, at $\chi = 45.0^\circ$ and $\phi = 180.0^\circ$. The exposure rate was 80.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 13548 reflections that were collected, 6335 were unique ($R_{\text{int}} = 0.050$).

The linear absorption coefficient, μ , for Mo-K α radiation is 1.756 cm^{-1} . The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods⁹ and expanded using Fourier techniques.¹⁰ The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement¹¹ on F was based on 10085 observed reflections ($I > 2.00\sigma(I)$) and 392 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.0520$$

$$R_w = [\sum w (|F_o| - |F_c|)^2 / \sum w F_o^2]^{1/2} = 0.0597$$

The standard deviation of an observation of unit weight¹² was 0.91. A Sheldrick weighting scheme was used. Plots of $\sum w (|F_o| - |F_c|)^2$ versus $|F_o|$, reflection order in data collection, $\sin \theta/\lambda$ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.76 and $-1.08 \text{ e}^-/\text{\AA}^3$, respectively. The absolute structure was deduced based on Flack parameter $-0.01(6)$.¹³

Neutral atom scattering factors were taken from Cromer and Waber.¹⁴ Anomalous dispersion effects were included in F_{calc} ; the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.¹⁶ The values for the mass attenuation coefficients are those of Creagh and Hubbell.¹⁷ All calculations were performed using the CrystalStructure^{18,19} crystallographic software package.

⁹ **SIR92**: Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, 27, 435.

¹⁰ **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).

¹¹ Least Squares function minimized:

$$\sum w (|F_o| - |F_c|)^2 \quad \text{where } w = \text{Least Squares weights.}$$

¹² Standard deviation of an observation of unit weight:

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

$$\text{where: } N_o = \text{number of observations, } N_v = \text{number of variables}$$

¹³ Flack, H. D. *Acta Cryst. Sect. A* **1983**, 39, 876.

¹⁴ Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

¹⁵ Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, 17, 781.

¹⁶ 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).

¹⁷ 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).

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 649066). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

¹⁸ CrystalStructure 3.8.0: Crystal Structure Analysis Package, Rigaku and Rigaku/MSO (2000-2006). 9009 New Trails Dr. The Woodlands TX 77381 USA.

¹⁹ 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).

Experimental Details

A. Crystal Data

Empirical Formula	$\text{C}_{33}\text{H}_{30}\text{ClNO}_5$
Formula Weight	556.06
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.40 X 0.30 mm
Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	3 oscillations @ 60.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	$a = 9.509(4) \text{ \AA}$ $b = 12.566(6) \text{ \AA}$ $c = 12.510(8) \text{ \AA}$ $\beta = 106.781(18)^\circ$ $V = 1431.1(12) \text{ \AA}^3$
Space Group	$P2_1$ (#4)
Z value	2
D_{calc}	1.290 g/cm^3
F000	584.00
$\mu(\text{MoK}\alpha)$	1.756 cm^{-1}

B. Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID
Radiation	MoK α ($\lambda = 0.71075 \text{ \AA}$) graphite monochromated
Detector Aperture	280 mm x 256 mm
Data Images	44 exposures
ω oscillation Range ($\chi=45.0$, $\phi=0.0$)	130.0 - 190.0°
Exposure Rate	80.0 sec./°
ω oscillation Range ($\chi=45.0$, $\phi=180.0$)	0.0 - 160.0°
Exposure Rate	80.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{\text{max}}$	54.9°
No. of Reflections Measured	Total: 13548 Unique: 6335 ($R_{\text{int}} = 0.050$) Friedel pairs: 2915
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	$\Sigma w (F_o - F_c)^2$
Least Squares Weights	$1 / [0.0010F_o^2 + 3.0000\sigma(F_o^2) + 0.5000]$
$2\theta_{\text{max}}$ cutoff	54.9°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations ($I > 2.00\sigma(I)$)	10085
No. Variables	392
Reflection/Parameter Ratio	25.73
Residuals: R ($I > 2.00\sigma(I)$)	0.0520
Residuals: Rw ($I > 2.00\sigma(I)$)	0.0597
Goodness of Fit Indicator	0.909
Flack Parameter	-0.01(6)
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	$0.76 \text{ e}^-/\text{\AA}^3$
Minimum peak in Final Diff. Map	$-1.08 \text{ e}^-/\text{\AA}^3$

V. X-ray Crystal Structure of Compound 8

Data Collection

A colorless Et₂O solution of compound **8** was prepared. Crystals suitable for X-ray analysis were obtained by keeping the solution in a freezer.

A colorless prism crystal of C₂₄H₂₃F₃N₂O₃ having approximate dimensions of 0.50 x 0.50 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-K α 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 primitive monoclinic cell with dimensions:

$$\begin{aligned} a &= 10.979(4) \text{ \AA} \\ b &= 14.520(6) \text{ \AA} \quad \beta = 108.120(14)^\circ \\ c &= 14.534(6) \text{ \AA} \\ V &= 2202.0(15) \text{ \AA}^3 \end{aligned}$$

For $Z = 4$ and F.W. = 444.45, the calculated density is 1.341 g/cm³. The systematic absences of:

$$\begin{aligned} h0l: & h \pm 2n \\ 0k0: & k \pm 2n \end{aligned}$$

uniquely determine the space group to be:

$$P2_1/a \text{ (\#14)}$$

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 $\chi = 45.0^\circ$ and $\phi = 0.0^\circ$. The exposure rate was 150.0 [sec./°]. A second sweep was performed using ω scans from 0.0 to 160.0° in 5.0° step, at $\chi = 45.0^\circ$ and $\phi = 180.0^\circ$. The exposure rate was 150.0 [sec./°]. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

Of the 5010 reflections that were collected, 5010 were unique ($R_{\text{int}} = 0.053$).

The linear absorption coefficient, μ , for Mo-K α radiation is 1.055 cm⁻¹. The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods⁹ and expanded using Fourier techniques.¹⁰ The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The final cycle of full-matrix least-squares refinement¹¹ on F was based on 4057 observed reflections ($I > 2.00\sigma(I)$) and 312 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma ||F_o| - |F_c|| / \Sigma |F_o| = 0.0680$$

$$R_w = [\Sigma w (|F_o| - |F_c|)^2 / \Sigma w F_o^2]^{1/2} = 0.0829$$

The standard deviation of an observation of unit weight¹² was 1.07. A Chebychev polynomial weighting scheme was used.²⁰ Plots of $\Sigma w (|F_o| - |F_c|)^2$ versus $|F_o|$, reflection order in data collection, $\sin \theta/\lambda$ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 1.04 and -0.82 e⁻/Å³, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.¹⁴ Anomalous dispersion effects were included in Fcalc;¹⁵ the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.¹⁶ The values for the mass attenuation coefficients are those of Creagh and Hubbell.¹⁷ All calculations were performed using the CrystalStructure^{18,19} crystallographic software package.

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 647861). The data can be obtained free of charge via the Internet at www.ccdc.cam.ac.uk/conts/retrieving.html.

²⁰ Carruthers, J. R.; Watkin, D. J. *Acta Cryst.* **1979**, A35, 698.

Experimental Details

A. Crystal Data

Empirical Formula	$\text{C}_{24}\text{H}_{23}\text{F}_3\text{N}_2\text{O}_3$
Formula Weight	444.45
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.50 X 0.50 X 0.30 mm
Crystal System	monoclinic
Lattice Type	Primitive
Indexing Images	3 oscillations @ 60.0 seconds
Detector Position	127.40 mm
Pixel Size	0.100 mm
Lattice Parameters	$a = 10.979(4) \text{ \AA}$ $b = 14.520(6) \text{ \AA}$ $c = 14.534(6) \text{ \AA}$ $\beta = 108.120(14)^\circ$ $V = 2202.0(15) \text{ \AA}^3$
Space Group	$P2_1/a$ (#14)
Z value	4
D_{calc}	1.341 g/cm^3
F000	928.00
$\mu(\text{MoK}\alpha)$	1.055 cm^{-1}

B. Intensity Measurements

Diffractometer	Rigaku RAXIS-RAPID
Radiation	MoK α ($\lambda = 0.71075 \text{ \AA}$) graphite monochromated
Detector Aperture	280 mm x 256 mm
Data Images	44 exposures
ω oscillation Range ($\chi=45.0$, $\phi=0.0$)	130.0 - 190.0°
Exposure Rate	150.0 sec./°
ω oscillation Range ($\chi=45.0$, $\phi=180.0$)	0.0 - 160.0°
Exposure Rate	150.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{\text{max}}$	55.0°
No. of Reflections Measured	Total: 5010 Unique: 5010 ($R_{\text{int}} = 0.053$)
Corrections	Lorentz-polarization

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SIR92)
Refinement	Full-matrix least-squares on F
Function Minimized	$\Sigma w (F_o - F_c)^2$
Least Squares Weights	Chebyshev polynomial with 3 parameters 132.5550, 173.5960, 47.4727
$2\theta_{\text{max}}$ cutoff	55.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations ($I > 2.00\sigma(I)$)	4057
No. Variables	312
Reflection/Parameter Ratio	13.00
Residuals: R ($I > 2.00\sigma(I)$)	0.0680
Residuals: R_w ($I > 2.00\sigma(I)$)	0.0829
Goodness of Fit Indicator	1.070
Max Shift/Error in Final Cycle	0.003
Maximum peak in Final Diff. Map	$1.04 \text{ e}^-/\text{\AA}^3$
Minimum peak in Final Diff. Map	$-0.82 \text{ e}^-/\text{\AA}^3$