

Supplementary information for the manuscript

Reversal of facial selectivity in complex Diels-Alder reactions

Jacques-Alexis Funel,^a Louis Ricard^b and Joëlle Prunet*^a

^a *Laboratoire de Synthèse Organique, UMR CNRS 7652, Ecole Polytechnique, DCSO, 91128 Palaiseau Cedex, France. Fax: 33 1 69 33 38 51; Tel: 33 1 69 33 48 73; E-mail: joelle.prunet@polytechnique.fr*

^b *Laboratoire Hétéroéléments et Coordination, UMR CNRS 7653, Ecole Polytechnique, DCPH, 91128 Palaiseau Cedex, France. Fax: 33 1 69 33 39 90; Tel: 33 1 69 33 45 72; E-mail: louis.ricard@polytechnique.fr*

Content

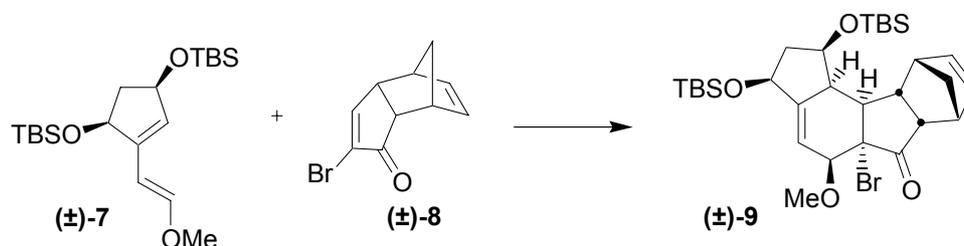
| | |
|---|-------|
| General considerations | S1 |
| Synthesis of (±)- 9 | S2 |
| Synthesis of (±)- 12 | S2-S3 |
| Synthesis of (±)- 13 | S3 |
| Synthesis of (±)- 15 | S4 |
| Synthesis of (±)- 16 and (±)- 17 | S4-S5 |
| Synthesis of <i>anti</i> (±)- 18 and <i>syn</i> (±)- 18 | S5 |
| Crystal-structure data for (±)- 9a | S6 |
| Crystal-structure data for (±)- 12 | S6-S7 |

General considerations

Melting points are uncorrected. Infrared spectra are reported in terms of frequency of absorption (ν , cm^{-1}). ^1H NMR spectra were recorded on a 400 MHz instrument. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Data are reported as follows: δ , chemical shift; multiplicity (recorded as br, broad; s, singlet; d, doublet; t, triplet; q, quadruplet; hex, hexuplet; hept, heptuplet; oct, octuplet and m, multiplet), coupling constants (J in Hertz, Hz), and integration. ^{13}C NMR spectra were recorded on the same instruments 100.6 MHz respectively. The chemical shifts are expressed in parts per million (ppm), reported from the central peak of deuteriochloroform (77.00 ppm). Mass spectra were obtained by either direct introduction or GC/MS coupling with a chromatograph. Ionization was obtained either by electronic impact (EI) or chemical ionisation with ammonia (CI, NH_3) or methane (CI, CH_4). Mass spectral data are reported as m/z . Thin Layer Chromatography (TLC) was performed on precoated plate of silica gel 60F 254 or aluminium oxide 60F 254. Flash chromatography was performed on silica gel 60, 230-400 mesh.

X-ray data were collected on a Nonius KappaCCD diffractometer, ϕ and ω scans, $\text{MoK}\alpha$

radiation ($\lambda = 0.71069 \text{ \AA}$), graphite monochromator, $T = 150 \text{ K}$, structure solution with SIR97,¹ and refined in SHELXL-97² by full matrix least-squares using anisotropic thermal displacement parameters for all non-hydrogen atoms.



A degassed (freeze-thaw-pump cycles) solution of diene (\pm)-7 (629 mg, 1.64 mmol) and bromo enone (\pm)-8 (405 mg, 1.80 mmol, 1.0 equiv) in toluene (8 mL) was refluxed for 40 h under argon. The mixture was concentrated and directly purified by flash chromatography on silica gel (petroleum ether/ether 40:1) to yield 716 mg (72%) of (\pm)-9 as a colorless oil.

mp 131-132°C.

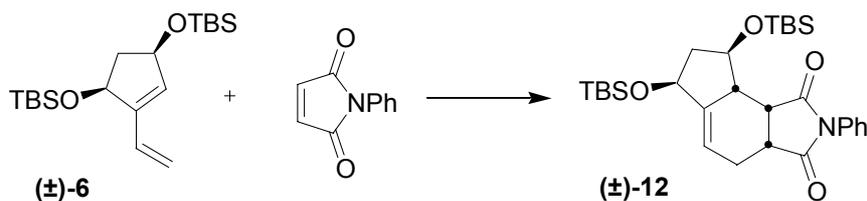
IR (CCl_4) 2955, 2928, 2856, 1756, 1710, 1471, 1257 cm^{-1} .

¹H NMR (CDCl_3 , 400 MHz) δ 6.26 (dd, $J = 5.5, 2.8 \text{ Hz}$, 1H), 6.09 (dd, $J = 5.5, 2.8 \text{ Hz}$, 1H), 5.70-5.69 (m, 1H), 4.58-4.51 (m, 2H, H-9), 4.19-4.18 (m, 1H), 3.46 (s, 3H), 3.19 (br s, 1H), 3.15 (br s, 1H), 2.99 (dd, $J = 11.0, 4.5 \text{ Hz}$, 1H), 2.70-2.69 (m, 1H), 2.55 (ddd, $J = 11.0, 7.6, 3.9 \text{ Hz}$, 1H), 2.30 (dt, $J = 11.3, 6.7 \text{ Hz}$, 1H), 2.11 (dd, $J = 7.6, 4.1 \text{ Hz}$, 1H), 1.73 (q, $J = 11.2 \text{ Hz}$, 1H), 1.53 (d, $J = 8.4 \text{ Hz}$, 1H), 1.36 (d, $J = 8.4 \text{ Hz}$, 1H), 0.95 (s, 9H), 0.93 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H).

¹³C NMR (CDCl_3 , 100 MHz) δ 206.3, 149.2, 138.3, 135.4, 119.2, 85.1, 78.6, 71.4, 70.5, 59.8, 54.1, 51.1, 50.4, 45.6, 44.2, 44.1, 43.2, 41.9, 26.2, 25.9, 18.7, -4.7.

MS (GC, CI NH_3) m/z 628-626 ($\text{M}+\text{NH}_4^+$), 611-609 ($\text{M}+\text{H}^+$), 546-544 ($\text{M}-\text{C}_5\text{H}_5+\text{H}^+$), 499-497 ($\text{M}-\text{OTBS}+\text{NH}_4^+$), 326, 253.

Anal. Calcd for $\text{C}_{30}\text{H}_{49}\text{BrO}_4\text{Si}_2$: C, 59.09; H, 8.10. Found: C, 58.73; H, 8.29.



A solution of diene (\pm)-6 (100 mg, 0.28 mmol) and *N*-phenyl maleimide (51 mg, 0.29 mmol, 1.05 equiv) in toluene (1.5 mL) was heated at 50°C overnight. The mixture was then cooled down and flash chromatography (petroleum ether/ether 8:1) afforded 133 mg (89%) of the expected compound (\pm)-12 as a glass-like oil that turned into a white solid upon dilution in ether

(1) A. Altomare, M. C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A. G. G. Moliterni, G. Polidori and R. Spagna, SIR97, an integrated package of computer programs for the solution and refinement of crystal structures using single crystal data.

(2) G. M. Sheldrick: SHELXL-97, Universität Göttingen, Göttingen, Germany, 1997.

and concentration *in vacuo*. An analytical sample was obtained after recrystallization from hexanes.

mp 129-131°C.

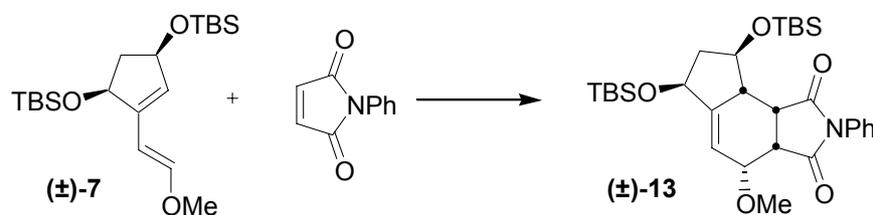
IR (CCl₄) 3062, 2972, 1732 (br), 1640, 1183 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 7.47-7.36 (m, 3H), 7.18-7.14 (m, 2H), 5.84 (ddd, *J* = 9.2, 6.0, 2.8 Hz, 1H), 4.96 (ddd, *J* = 10.4, 8.0, 6.4 Hz, 1H), 4.43-4.39 (m, 1H), 3.43 (dd, *J* = 8.8, 6.8 Hz, 1H), 3.32 (ddd, *J* = 8.8, 7.6, 1.2 Hz, 1H), 2.90 (dd, *J* = 15.6, 6.8 Hz, 1H), 2.62 (ddd, *J* = 10.4, 6.4, 3.2 Hz, 1H), 2.27 (dt, *J* = 11.6, 6.4 Hz, 1H), 2.23-2.18 (m, 1H), 1.72 (q, *J* = 10.8 Hz, 1H), 0.92 (s, 9H), 0.91 (s, 9H) 0.16 (s, 3H), 0.13 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 178.9, 177.2, 147.8, 131.9, 129.1, 128.6, 126.5, 117.9, 70.8, 68.7, 48.3, 45.2, 41.0, 40.2, 26.2, 25.8, 18.2, 17.9, -4.5, -4.6, -4.7, -4.8.

MS (GC, CI NH₃) *m/z* 546 (M+NH₄⁺), 529 (M+H⁺), 471, 395 (M-OTBS+H⁺), 299 (M-2OTBS+2NH₄⁺), 281 (M-2OTBS+NH₄⁺), 264 (M-2OTBS+H⁺).

HRMS Calcd for C₂₉H₄₆O₄NSi₂+H⁺: 528.2958. Found: 528.2965.



A solution of diene (±)-7 (52 mg, 0.14 mmol) and *N*-phenyl maleimide (52 mg, 0.14 mmol) in toluene (1 mL) was heated at 50°C overnight. The mixture was then cooled down and flash chromatography (petroleum ether/ CH₂Cl₂ 3:1) afforded 56 mg (75%) of the expected compound (±)-13 as a glass-like oil that turned into a white solid upon dilution in ether and concentration *in vacuo*. An analytical sample was obtained after recrystallization from hexanes.

mp 144-145°C.

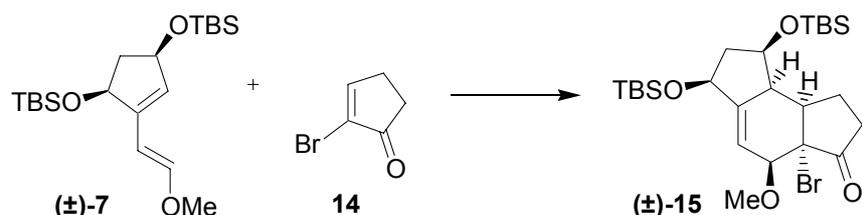
IR (CCl₄) 2956, 2929, 2857, 1714 (br), 1382, 1097 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 7.48-7.41 (m, 3H), 7.18-7.16 (m, 2H), 5.88-5.86 (m, 1H), 5.09 (ddd, *J* = 10.4, 6.4, 1.6 Hz, 1H), 4.45-4.38 (m, 1H), 4.10-4.06 (m, 1H), 3.67 (t, *J* = 8.0 Hz, 1H), 3.61 (s, 3H), 3.39 (dd, *J* = 8.4, 6.4 Hz, 1H), 2.58-2.52 (m, 1H), 2.30 (dt, *J* = 11.6, 6.4 Hz, 1H), 1.74 (q, *J* = 10.8, 1H), 0.91 (s, 9H), 0.90 (s, 9H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 176.5, 173.4, 146.7, 131.7, 129.1, 128.6, 126.5, 121.3, 77.2, 70.1, 68.8, 58.0, 48.1, 45.3, 43.7, 39.2, 25.7, 18.2, 17.9, -4.6, -4.7, -4.9.

MS (GC, CI NH₃) *m/z* 559 (M+H⁺), 527, 501, 428 (M-OTBS+H⁺), 393, 294 (M-2OTBS+NH₄⁺).

Anal. Calcd for C₃₀H₄₇NO₅Si₂: C, 64.59; H, 8.49. Found: C, 64.58; H, 8.53.



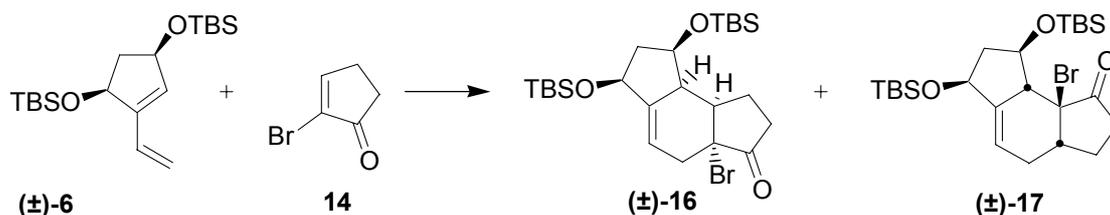
A solution of (*E*)-diene **(±)-7** (60 mg, 0.16 mmol) and 2-bromocyclopentenone (25 mg, 0.24 mmol, 1.5 equiv) in toluene (1 mL) was refluxed under argon for 4h. The mixture was concentrated *in vacuo*. Flash chromatography on silica gel (petroleum ether/ether 20:1) afforded 19 mg (22%, unoptimized) of **(±)-15** as a light yellow oil.

IR (CCl₄) 2957, 2929, 2858, 1760, 1717, 1462, 1360, 1261, 1218 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 5.67-5.66 (m, 1H), 4.57-4.48 (m, 2H), 4.16-4.14 (m, 1H), 3.37 (s, 3H), 2.95-2.90 (m, 1H), 2.51 (dt, *J* = 12.0, 5.6 Hz, 1H), 2.46-2.38 (m, 1H), 2.27 (dt, *J* = 11.4, 6.4 Hz, 1H), 2.23-2.11 (m, 2H, H-11), 1.93-1.82 (m, 1H), 1.51 (q, *J* = 11.4 Hz, 1H), 0.97 (s, 9H), 0.93 (s, 9H), 0.21 (s, 3H), 0.18 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz) δ 209.7, 145.0, 113.2, 82.3, 71.2, 70.8, 69.8, 59.2, 45.2, 44.9, 38.4, 35.9, 25.7, 25.6, 22.1, 17.9, -4.7, -4.8, -5.0, -5.2.

MS (GC, CI NH₃) *m/z* 564-562 (M+NH₄⁺), 546-544 (M+H⁺), 514-512 (M-OCH₃+H⁺), 465 (M-Br+H⁺), 433 (M-OCH₃-Br+H⁺).



A solution of diene **(±)-6** (300 mg, 0.84 mmol) and 2-bromocyclopentenone **14** (204 mg, 1.26 mmol, 1.5 equiv) in toluene (6 mL) was refluxed under Ar for 4 days. The mixture was concentrated *in vacuo*. Flash chromatography on silica gel (petroleum ether/ether 60:1) afforded 45 mg (15%) of unreacted diene **(±)-6**, 75 mg (17%, unoptimized) of **(±)-17** as a sole diastereomer and 28 mg (6%, unoptimized) of regioadduct **(±)-16** as a 3.5:1 mixture of diastereomers.

(±)-16: data for the major diastereomer

IR (CCl₄) 2957, 2929, 2856, 1746, 1472, 1461, 1255, 1089 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 5.35 (br s, 1H), 4.43-4.39 (m, 2H), 2.88 (br s, 1H), 2.72-2.67 (m, 2H), 2.55-2.50 (m, 1H), 2.43-2.23 (m, 1H), 2.19-2.14 (m, 2H), 1.92-1.74 (m, 1H), 1.52-1.44 (m, 1H), 1.41 (q, *J* = 10.8 Hz, 1H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H).

¹³C NMR (CDCl₃, 100 MHz) δ 211.7, 145.2, 112.7, 71.4, 70.4, 48.0, 45.2, 39.6, 33.4, 30.8, 26.0, 25.9, 20.6, 18.2, -4.1, -4.5.

17:

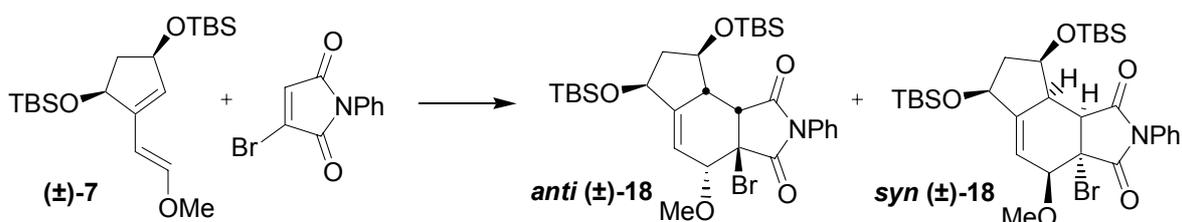
IR (CCl₄) 2957, 2929, 2856, 1746, 1472, 1461, 1255, 1089 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz) δ 5.60 (br s, 1H), 5.08 (dt, *J* = 13.6, 6.9 Hz, 1H), 4.3 (br s, 1H), 3.27-3.24 (br s, 1H), 2.81-2.77 (m, 1H), 2.70-2.48 (m, 3H), 2.22 (dt, *J* = 12.6, 6.3 Hz, 1H), 2.10

(ddd, $J = 18.4, 8.8, 6.8$ Hz, 1H), 1.99-1.94 (m, 1H), 1.68-1.60 (m, 2H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.06 (s, 6H).

^{13}C NMR (CDCl₃, 100 MHz) δ 210.2, 144.0, 120.5, 71.6, 70.0, 68.0, 54.3, 44.6, 44.0, 33.4, 30.8, 26.6, 25.2, 23.1, 18.2, 17.8, -4.5.

MS (GC, CI NH₃) m/z 517-515 (M+H⁺).



A solution of diene (±)-7 (60 mg, 0.19 mmol) and Br-*N*-phenyl maleimide (39 mg, 0.19 mmol, 1.0 equiv) in toluene (2 mL) was heated at reflux for 4 h. The mixture was then cooled down and flash chromatography (petroleum ether/CH₂Cl₂ 2:1) afforded 69 mg (70%) of a 2.5:1 mixture of diastereomers *anti* (±)-18 and *syn* (±)-18 (as a yellow oil).

***anti* (±)-18:**

IR (CCl₄) 2058, 2929, 1736, 1264 cm⁻¹.

^1H NMR (CDCl₃, 400 MHz) δ 7.51-7.41 (m, 3H), 7.31-7.25 (m, 2H), 5.86-5.85 (m, 1H), 5.09-5.03 (m, 1H), 4.48-4.45 (m, 1H), 4.32-4.31 (m, 1H), 3.73 (s, 3H), 3.54 (d, $J = 7.2$ Hz, 1H), 2.84 (br s, 1H), 2.39 (dt, $J = 12.2, 6.4$ Hz, 1H), 1.83 (d, $J = 10.8$ Hz, 1H), 0.96 (s, 9H), 0.95 (s, 9H) 0.17 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H).

^{13}C NMR (CDCl₃, 100 MHz) δ 173.0, 170.1, 149.3, 131.5, 129.1, 128.9, 126.4, 120.7, 85.6, 70.6, 69.2, 60.7, 60.5, 52.1, 47.0, 45.0, 25.8, 25.6, 18.2, 18.0, -4.5, -4.6, -4.8.

MS (GC, CI NH₃) m/z 638-636 (M+H⁺), 504-502 (M-OTBS+H⁺), 473-471 (M-OTBS-OCH₃+H⁺).

***syn* (±)-18:**

IR (CCl₄) 2058, 2929, 1736, 1264 cm⁻¹.

^1H NMR (CDCl₃, 400 MHz) δ 7.47-7.37 (m, 3H), 7.31-7.28 (m, 2H), 5.75-5.74 (m, 1H), 4.66-4.60 (m, 2H), 4.43-4.42 (m, 1H), 3.74 (s, 3H), 3.65 (d, $J = 4.0$ Hz, 1H), 2.86-2.85 (m, 1H), 2.48 (q, $J = 10.5$ Hz), 2.26 (dt, $J = 11.6, 6.8$ Hz, 1H), 0.95 (s, 9H), 0.94 (s, 9H) 0.15 (s, 6H), 0.11 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (CDCl₃, 100 MHz) δ 170.4, 170.0, 150.7, 132.0, 129.2, 129.0, 128.6, 126.6, 126.0, 119.2, 87.1, 70.9, 69.3, 61.5, 60.3, 54.4, 42.1, 40.6, 25.9, 25.8, 18.2, 18.1, -4.4, -4.5, -4.9.

MS (GC, CI NH₃) m/z 638-636 (M+H⁺), 504-502 (M-OTBS+H⁺), 473-471 (M-OTBS-OCH₃+H⁺).

Crystal-structure data for (\pm)-**9a**

| | |
|--|--|
| Molecular formula | C ₁₈ H ₂₁ BrO ₄ |
| Molecular weight | 381.26 |
| Crystal habit | colorless needle |
| Crystal dimensions(mm) | 0.22x0.18x0.08 |
| Crystal system | monoclinic |
| Space group | P2 ₁ /c |
| a(Å) | 9.1750(10) |
| b(Å) | 15.3160(10) |
| c(Å) | 11.4560 (10) |
| β (°) | 102.2600(10) |
| V(Å ³) | 1573.1(2) |
| Z | 4 |
| d(g-cm ⁻³) | 1.610 |
| F000 | 784 |
| μ (cm ⁻¹) | 2.632 |
| Absorption corrections | multi-scan; 0.5952 min, 0.8171 max |
| Maximum θ (°) | 30.01 |
| HKL ranges | -12 12; -19 21; -16 16 |
| Reflections measured | 7595 |
| Unique data | 4570 |
| Rint | 0.023 |
| Reflections used | 3526 |
| Criterion | >2sigma(I) |
| Refinement type | Fsqd |
| Hydrogen atoms | mixed |
| Parameters refined | 215 |
| Reflections/parameter | 16 |
| wR2 | 0.0965 |
| R1 | 0.0342 |
| Weights a, b | 0.0467; 0.0744 |
| GoF | 1.058 |
| difference peak/hole (eÅ ⁻³) | 0.572(0.077)/-0.560(0.077) |

Crystal-structure data for (\pm)-**12**

| | |
|------------------------|---|
| Molecular formula | C ₂₉ H ₄₅ NO ₄ Si ₂ |
| Molecular weight | 527.84 |
| Crystal habit | colorless needle |
| Crystal dimensions(mm) | 0.22x0.06x0.04 |
| Crystal system | triclinic |
| Space group | Pbar1 |
| a(Å) | 11.2940(10) |
| b(Å) | 16.4190(10) |
| c(Å) | 17.5230(10) |

Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2005

| | |
|--|-------------------------------------|
| $\alpha(^{\circ})$ | 101.6800(10) |
| $\beta(^{\circ})$ | 102.9000(10) |
| $\gamma(^{\circ})$ | 89.8000(10) |
| $V(\text{\AA}^3)$ | 3098.8(4) |
| Z | 4 |
| $d(\text{g}\cdot\text{cm}^{-3})$ | 1.131 |
| F000 | 1144 |
| $\mu(\text{cm}^{-1})$ | 0.146 |
| Absorption corrections | multi-scan ; 0.9686 min, 0.9942 max |
| Maximum θ | 22.98 |
| HKL ranges | -12 12; -17 18; -19 19 |
| Reflections measured | 15402 |
| Unique data | 8593 |
| Rint | 0.0412 |
| Reflections used | 5458 |
| Criterion | >2sigma(I) |
| Refinement type | Fsqd |
| Hydrogen atoms | mixed |
| Parameters refined | 669 |
| Reflections / parameter | 8 |
| wR2 | 0.1223 |
| R1 | 0.0453 |
| Weights a, b | 0.0651; 0.0000 |
| GoF | 0.948 |
| difference peak/hole ($\text{e}\text{\AA}^{-3}$) | 0.182(0.045)/-0.309(0.045) |