

Palladium-Catalyzed [3 + 3] Cycloaddition of Trimethylenemethane with Azomethine Imines

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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.

Toluene and THF were purified by passing through a neutral alumina column under nitrogen. 1,2-Dichloroethane and CH₂Cl₂ were distilled over CaH₂ under nitrogen. MeOH was distilled over Mg turnings under nitrogen.

p-Tolualdehyde (Wako Chemicals), *m*-chlorobenzaldehyde (Wako Chemicals), *o*-tolualdehyde (TCI), 3-pyridinecarboxaldehyde (Wako Chemicals), pivaldehyde (Aldrich), benzaldehyde (Wako Chemicals), *p*-trifluoromethylbenzaldehyde (Wako Chemicals), methyl crotonate (TCI), hydrazine monohydrate (Wako Chemicals), triphenylphosphine (Wako Chemicals), and Pd(OAc)₂ (Furuya Metal) were used as received.

(2-(Acetoxymethyl)-2-propenyl)trimethylsilane (**1**),¹ (2-(1'-acetoxyethyl)-2-propenyl)trimethylsilane (**4**),² (2-(acetoxymethyl)-1-buten-3-yl)trimethylsilane (**5**),² pyrazolidin-3-one,³ 4,4-dimethylpyrazolidin-3-one,³ 1-benzylidene-3-oxopyrazolidin-1-ium-2-ide (**2a**),⁴ 1-(*p*-trifluoromethylbenzylidene)-3-oxopyrazolidin-1-ium-2-ide (**2c**),⁴ 1-(*o*-fluorobenzylidene)-3-oxopyrazolidin-1-ium-2-ide (**2e**),⁴ 1-(1-cyclohexenylmethylidene)-3-oxopyrazolidin-1-ium-2-ide (**2h**),⁴ 1-benzylidene-4,4-dimethyl-3-oxopyrazolidin-1-ium-2-ide (**2j**),⁴ Pd(PPh₃)₄,⁵ and CpPd(η³-C₃H₅)⁶ were

¹ Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315.

² Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1981**, *103*, 5972.

³ Perri, S. T.; Slater, S. C.; Toske, S. G.; White, J. D. *J. Org. Chem.* **1990**, *55*, 6037.

⁴ Shintani, R.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 10778.

⁵ Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.

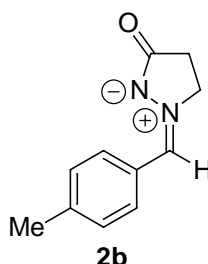
synthesized following the literature procedures.

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.

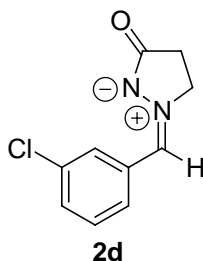
1-(*p*-Methylbenzylidene)-3-oxopyrazolidin-1-ium-2-ide (**2b**) (CAS 62516-59-0)



p-Tolualdehyde (245 μ L, 2.08 mmol) was added to a solution of pyrazolidin-3-one (179 mg, 2.08 mmol) in MeOH (0.50 mL). The mixture was stirred for 1 h at room temperature and then diluted with Et₂O (2.0 mL). The precipitate was collected by filtration, washed with Et₂O, and dried under vacuum to afford compound **2b** as a pale yellow solid (240 mg, 1.27 mmol; 61% yield).

¹H NMR (DMSO-*d*₆): δ 8.17 (d, ³*J*_{HH} = 8.0 Hz, 2H), 7.59 (s, 1H), 7.34 (d, ³*J*_{HH} = 8.1 Hz, 2H), 4.52 (t, ³*J*_{HH} = 8.0 Hz, 2H), 2.55 (t, ³*J*_{HH} = 8.1 Hz, 2H), 2.36 (s, 3H). ¹³C NMR (DMSO-*d*₆): δ 184.8, 141.8, 132.9, 131.3, 129.6, 127.4, 57.3, 29.5, 21.4.

1-(*m*-Chlorobenzylidene)-3-oxopyrazolidin-1-ium-2-ide (**2d**) (CAS 61283-27-0)



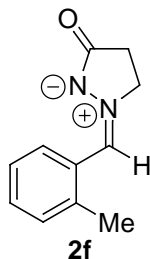
This was synthesized from *m*-chlorobenzaldehyde, following the procedure for compound **2b**. White solid, 63% yield.

¹H NMR (DMSO-*d*₆): δ 8.55 (s, 1H), 8.07-8.05 (m, 1H), 7.66 (s, 1H), 7.58-7.54 (m,

⁶ Parker, G.; Werner, H. *Helv. Chim. Acta* **1973**, *56*, 2819.

2H), 4.59 (t, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 2.58 (t, $^3J_{\text{HH}} = 8.1$ Hz, 2H). ^{13}C NMR (DMSO- d_6): δ 184.6, 133.3, 131.8, 130.53, 130.46, 129.9, 129.53, 129.46, 57.7, 29.0.

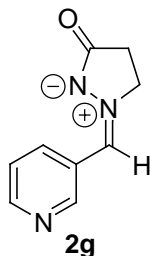
1-(*o*-Methylbenzylidene)-3-oxopyrazolidin-1-ium-2-ide (2f)



This was synthesized from *o*-tolualdehyde, following the procedure for compound **2b**. White solid, 61% yield.

^1H NMR (DMSO- d_6): δ 8.93 (d, $^3J_{\text{HH}} = 8.1$ Hz, 1H), 7.68 (s, 1H), 7.39-7.31 (m, 3H), 4.60 (t, $^3J_{\text{HH}} = 8.4$ Hz, 2H), 2.56 (t, $^3J_{\text{HH}} = 8.2$ Hz, 2H), 2.47 (s, 3H). ^{13}C NMR (DMSO- d_6): δ 184.5, 138.4, 130.8, 130.5, 130.2, 129.4, 128.3, 126.0, 57.8, 29.1, 19.4. HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 189.1022, found 189.1030.

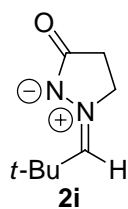
1-(3-Pyridylmethylidene)-3-oxopyrazolidin-1-ium-2-ide (2g) (CAS 84198-94-7)



This was synthesized from 3-pyridinecarboxaldehyde, following the procedure for compound **2b**. Pale yellow solid, 58% yield.

^1H NMR (DMSO- d_6): δ 9.19 (d, $^4J_{\text{HH}} = 1.9$ Hz, 1H), 8.82 (dt, $^3J_{\text{HH}} = 8.0$ Hz and $^4J_{\text{HH}} = 1.9$ Hz, 1H), 8.63 (dd, $^3J_{\text{HH}} = 4.7$ Hz and $^4J_{\text{HH}} = 1.7$ Hz, 1H), 7.71 (s, 1H), 7.57 (dd, $^3J_{\text{HH}} = 8.2$ and 4.7 Hz, 1H), 4.61 (t, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 2.59 (t, $^3J_{\text{HH}} = 8.1$ Hz, 2H). ^{13}C NMR (DMSO- d_6): δ 184.6, 151.4, 150.7, 137.0, 128.7, 126.4, 123.8, 57.7, 29.2.

1-(2,2-Dimethylpropylidene)-3-oxopyrazolidin-1-ium-2-ide (2i)



This was synthesized from pivaldehyde, following the procedure for compound **2b**. White solid, 57% yield.

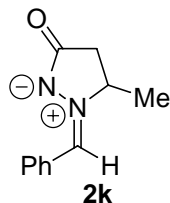
^1H NMR (DMSO- d_6): δ 6.77 (s, 1H), 4.31 (t, $^3J_{\text{HH}} = 8.2$ Hz, 2H), 2.43 (t, $^3J_{\text{HH}} = 8.3$ Hz, 2H), 1.25 (s, 9H). ^{13}C NMR (DMSO- d_6): δ 182.9, 145.2, 56.7, 33.7, 29.5, 25.8. HRMS (ESI) calcd for $\text{C}_8\text{H}_{14}\text{N}_2\text{ONa}$ ($\text{M}+\text{Na}^+$) 177.0998, found 177.1007.

5-Methylpyrazolidin-3-one (CAS 10234-76-1)

This was synthesized from methyl crotonate and hydrazine monohydrate, following the procedure for pyrazolidin-3-one.³ Pale yellow oil, 100% yield.

^1H NMR (CDCl_3): δ 3.83-3.76 (m, 1H), 2.55 (dd, $^2J_{\text{HH}} = 16.2$ Hz and $^3J_{\text{HH}} = 7.1$ Hz, 1H), 2.18 (dd, $^2J_{\text{HH}} = 16.2$ Hz and $^3J_{\text{HH}} = 8.8$ Hz, 1H), 1.29 (d, $^3J_{\text{HH}} = 6.3$ Hz, 3H).

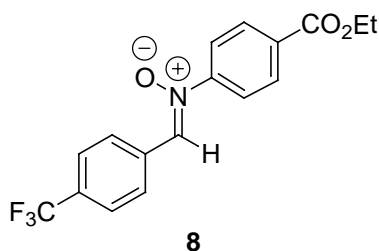
1-Benzylidene-5-methyl-3-oxopyrazolidin-1-ium-2-ide (**2k**) (CAS 14893-83-5)



This was synthesized from benzaldehyde and 5-methylpyrazolidin-3-one, following the procedure for compound **2b**. White solid, 62% yield.

^1H NMR (DMSO- d_6): δ 8.32-8.30 (m, 2H), 7.72 (s, 1H), 7.55-7.50 (m, 3H), 4.84-4.78 (m, 1H), 2.84 (dd, $^2J_{\text{HH}} = 16.3$ Hz and $^3J_{\text{HH}} = 9.1$ Hz, 1H), 2.24 (dd, $^2J_{\text{HH}} = 16.3$ Hz and $^3J_{\text{HH}} = 4.1$ Hz, 1H), 1.55 (d, $^3J_{\text{HH}} = 6.7$ Hz, 3H). ^{13}C NMR (DMSO- d_6): δ 183.2, 132.0, 131.4, 131.2, 130.1, 128.8, 65.7, 37.2, 22.2.

N-(*p*-Ethoxycarbonylphenyl)- α -(*p*-trifluoromethylphenyl)nitron (8)



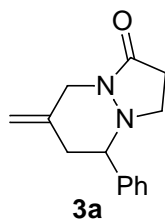
p-Trifluoromethylbenzaldehyde (290 μ L, 2.12 mmol) was added to a solution of ethyl *p*-hydroxylaminobenzoate (385 mg, 2.12 mmol) in EtOH (1.5 mL). The mixture was stirred for 2 h at room temperature and then diluted with MeOH. The precipitate was collected by filtration, washed with MeOH, and dried under vacuum to afford compound **8** as a white solid (185 mg, 0.55 mmol; 26% yield).

^1H NMR (C_6D_6): δ 8.23 (d, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 8.01 (d, $^3J_{\text{HH}} = 8.7$ Hz, 2H), 7.39 (d, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 7.38 (d, $^3J_{\text{HH}} = 8.5$ Hz, 2H), 7.12 (s, 1H), 4.11 (q, $^3J_{\text{HH}} = 7.1$ Hz, 2H), 1.01 (t, $^3J_{\text{HH}} = 7.1$ Hz, 3H). ^{13}C NMR ($\text{DMSO}-d_6$): δ 164.7, 151.2, 134.4, 133.6, 131.3, 130.1, 130.0 (q, $^2J_{\text{CF}} = 32.1$ Hz), 129.4, 125.4 (q, $^3J_{\text{CF}} = 4.1$ Hz), 123.9 (q, $^1J_{\text{CF}} = 272$ Hz), 122.1, 61.2, 14.1. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{15}\text{F}_3\text{NO}_3$ ($\text{M}+\text{H}^+$) 338.0999, found 338.1007.

III. Catalytic Reactions

General Procedure for Table 2 and Equations 2–3.

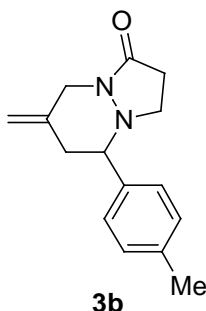
A solution of $\text{Pd}(\text{PPh}_3)_4$ (18.5 mg, 16.0 μ mol), (2-(acetoxymethyl)-2-propenyl)trimethylsilane **1** (74.5 mg, 0.400 mmol), and azomethine imine **2** (0.200 mmol) in CH_2Cl_2 (1.0 mL) was stirred for 48 h at 40 $^\circ\text{C}$, and the reaction mixture was directly passed through a pad of silica gel with EtOAc. After removing the solvent under vacuum, the residue was purified by silica gel preparative TLC to afford compound **3**.



Entry 1. White solid. 81% yield.

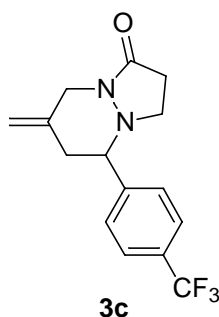
^1H NMR (CDCl_3): δ 7.39–7.30 (m, 5H), 5.01 (s, 1H), 4.89 (s, 1H), 4.59 (d, $^2J_{\text{HH}} = 13.8$

Hz, 1H), 3.65 (d, $^2J_{\text{HH}} = 13.5$ Hz, 1H), 3.36 (dd, $^2J_{\text{HH}} = 11.3$ Hz and $^3J_{\text{HH}} = 2.8$ Hz, 1H), 3.21 (td, $J_{\text{HH}} = 10.1$ Hz and $^3J_{\text{HH}} = 5.0$ Hz, 1H), 2.66 (q, $J_{\text{HH}} = 9.6$ Hz, 1H), 2.59-2.38 (m, 4H). ^{13}C NMR (CDCl_3): δ 170.0, 140.2, 138.7, 129.0, 128.5, 127.7, 111.9, 71.6, 48.5, 47.6, 42.4, 30.7. Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}$: C, 73.66; H, 7.06. Found: C, 73.54; H, 7.26.



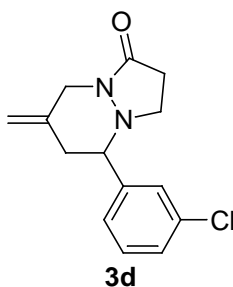
Entry 2. Colorless oil. 74% yield.

^1H NMR (CDCl_3): δ 7.25 (d, $^3J_{\text{HH}} = 7.8$ Hz, 2H), 7.17 (d, $^3J_{\text{HH}} = 7.9$ Hz, 2H), 5.00 (s, 1H), 4.88 (s, 1H), 4.59 (d, $^2J_{\text{HH}} = 14.2$ Hz, 1H), 3.65 (d, $^2J_{\text{HH}} = 14.4$ Hz, 1H), 3.32 (d, $^2J_{\text{HH}} = 11.0$ Hz, 1H), 3.20 (td, $J_{\text{HH}} = 10.1$ Hz and $^3J_{\text{HH}} = 5.0$ Hz, 1H), 2.66 (q, $J_{\text{HH}} = 9.5$ Hz, 1H), 2.59-2.51 (m, 2H), 2.48-2.34 (m, 2H), 2.36 (s, 3H). ^{13}C NMR (CDCl_3): δ 170.0, 138.8, 138.2, 137.1, 129.7, 127.5, 111.8, 71.3, 48.4, 47.5, 42.4, 30.6, 21.3. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}$: C, 74.35; H, 7.49. Found: C, 74.19; H, 7.50.



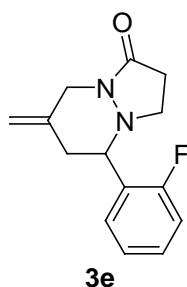
Entry 3. White solid. 92% yield.

^1H NMR (CDCl_3): δ 7.64 (d, $^3J_{\text{HH}} = 8.3$ Hz, 2H), 7.51 (d, $^3J_{\text{HH}} = 8.0$ Hz, 2H), 5.04 (s, 1H), 4.91 (s, 1H), 4.61 (d, $^2J_{\text{HH}} = 13.9$ Hz, 1H), 3.65 (d, $^2J_{\text{HH}} = 13.9$ Hz, 1H), 3.44 (dd, $^2J_{\text{HH}} = 10.7$ Hz and $^3J_{\text{HH}} = 3.7$ Hz, 1H), 3.24 (td, $J_{\text{HH}} = 10.2$ Hz and $^3J_{\text{HH}} = 4.8$ Hz, 1H), 2.66-2.42 (m, 5H). ^{13}C NMR (CDCl_3): δ 169.9, 144.3, 138.0, 130.7 (q, $^2J_{\text{CF}} = 32.6$ Hz), 128.0, 126.0 (q, $^3J_{\text{CF}} = 4.1$ Hz), 124.1 (q, $^1J_{\text{CF}} = 271.7$ Hz), 112.3, 71.1, 48.6, 47.5, 42.4, 30.6. Anal. Calcd for $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_2\text{O}$: C, 60.81; H, 5.10. Found: C, 60.73; H, 5.40.



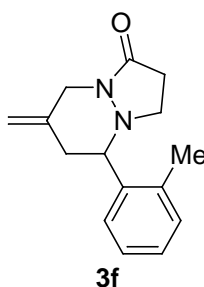
Entry 4. Colorless oil. 90% yield.

^1H NMR (CDCl_3): δ 7.39 (s, 1H), 7.31-7.29 (m, 2H), 7.27-7.24 (m, 1H), 5.02 (s, 1H), 4.90 (s, 1H), 4.59 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.63 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.34 (dd, $^2J_{\text{HH}} = 10.8$ Hz and $^3J_{\text{HH}} = 3.9$ Hz, 1H), 3.25 (td, $J_{\text{HH}} = 10.0$ Hz and $^3J_{\text{HH}} = 5.0$ Hz, 1H), 2.65 (q, $J_{\text{HH}} = 9.3$ Hz, 1H), 2.59-2.40 (m, 4H). ^{13}C NMR (CDCl_3): δ 169.9, 142.3, 138.1, 134.9, 130.3, 128.6, 127.7, 125.8, 112.1, 70.9, 48.6, 47.5, 42.3, 30.6. Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{ClN}_2\text{O}$: C, 64.00; H, 5.75. Found: C, 63.71; H, 5.80.



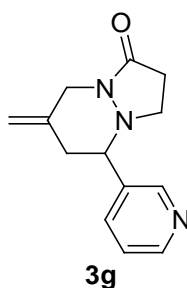
Entry 5. Pale yellow oil. 88% yield.

^1H NMR (CDCl_3): δ 7.54 (t, $^3J_{\text{HH}} = 7.3$ Hz, 1H), 7.32-7.27 (m, 1H), 7.18 (t, $^3J_{\text{HH}} = 7.5$ Hz, 1H), 7.07 (t, $^3J = 9.2$ Hz, 1H), 5.03 (s, 1H), 4.92 (s, 1H), 4.61 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 3.85 (d, $^2J_{\text{HH}} = 10.3$ Hz, 1H), 3.66 (d, $^2J_{\text{HH}} = 13.3$ Hz, 1H), 3.27 (td, $J_{\text{HH}} = 9.9$ Hz and $^3J_{\text{HH}} = 5.4$ Hz, 1H), 2.70 (q, $J_{\text{HH}} = 9.4$ Hz, 1H), 2.62-2.39 (m, 4H). ^{13}C NMR (CDCl_3): δ 170.0, 160.5 (d, $^1J_{\text{CF}} = 246.5$ Hz), 138.2, 129.6 (d, $^3J_{\text{CF}} = 8.3$ Hz), 128.6, 126.9 (d, $^2J_{\text{CF}} = 13.0$ Hz), 124.9 (d, $^3J_{\text{CF}} = 3.0$ Hz), 115.8 (d, $^2J_{\text{CF}} = 22.2$ Hz), 112.1, 62.9, 48.3, 47.5, 40.8, 30.5. Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{FN}_2\text{O}$: C, 68.28; H, 6.14. Found: C, 68.07; H, 6.16.



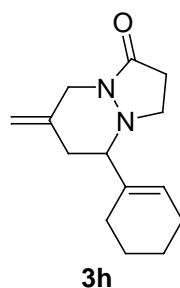
Entry 6. Colorless oil. 70% yield.

^1H NMR (CDCl_3): δ 7.52 (bs, 1H), 7.23 (t, $^3J_{\text{HH}} = 7.3$ Hz, 1H), 7.20-7.15 (m, 2H), 5.00 (s, 1H), 4.89 (s, 1H), 4.61 (d, $^2J_{\text{HH}} = 14.0$ Hz, 1H), 3.68-3.64 (m, 2H), 3.31-3.26 (m, 1H), 2.62-2.52 (m, 2H), 2.48-2.39 (m, 3H), 2.35 (s, 3H). ^{13}C NMR (CDCl_3): δ 170.0, 138.8, 138.3, 135.4, 130.8, 127.6, 126.8, 111.7, 66.6, 48.2, 47.5, 41.4, 30.7, 19.7. Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}$: C, 74.35; H, 7.49. Found: C, 74.10; H, 7.51.



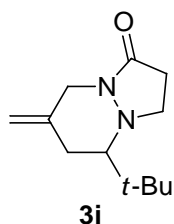
Entry 7. Pale yellow oil. 75% yield.

^1H NMR (CDCl_3): δ 8.62 (s, 1H), 8.60 (d, $^3J_{\text{HH}} = 4.6$ Hz, 1H), 7.77 (d, $^3J_{\text{HH}} = 7.7$ Hz, 1H), 7.35 (dd, $^3J_{\text{HH}} = 7.8$ and 4.7 Hz, 1H), 5.05 (s, 1H), 4.92 (s, 1H), 4.61 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.65 (d, $^2J_{\text{HH}} = 13.4$ Hz, 1H), 3.43 (d, $^2J_{\text{HH}} = 8.8$ Hz, 1H), 3.22 (td, $J_{\text{HH}} = 10.0$ Hz and $^3J_{\text{HH}} = 4.7$ Hz, 1H), 2.67-2.41 (m, 5H). ^{13}C NMR (CDCl_3): δ 169.9, 150.0, 149.3, 137.8, 135.8, 135.2, 124.1, 112.4, 69.0, 48.7, 47.5, 42.2, 30.6. HRMS (ESI) calcd for $\text{C}_{13}\text{H}_{16}\text{N}_3\text{O}$ ($\text{M}+\text{H}^+$) 230.1288, found 230.1299.



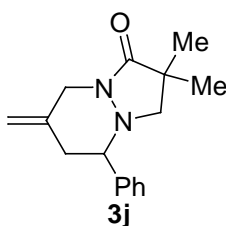
Entry 8. White solid. 71% yield.

^1H NMR (CDCl_3): δ 5.70 (s, 1H), 4.93 (s, 1H), 4.83 (s, 1H), 4.48 (d, $^2J_{\text{HH}} = 12.5$ Hz, 1H), 3.48 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.32 (td, $J_{\text{HH}} = 10.0$ Hz and $^3J_{\text{HH}} = 5.2$ Hz, 1H), 2.78 (q, $J_{\text{HH}} = 9.6$ Hz, 1H), 2.72 (dd, $^2J_{\text{HH}} = 11.7$ Hz and $^3J_{\text{HH}} = 2.5$ Hz, 1H), 2.54 (ddd, $^2J_{\text{HH}} = 16.6$ Hz and $^3J_{\text{HH}} = 9.0$ and 5.1 Hz, 1H), 2.50-2.37 (m, 2H), 2.24 (d, $^2J_{\text{HH}} = 13.6$ Hz, 1H), 2.06-1.94 (m, 4H), 1.70-1.50 (m, 4H). ^{13}C NMR (CDCl_3): δ 169.8, 139.2, 136.5, 126.9, 111.5, 73.8, 47.8, 47.3, 38.4, 30.7, 25.3, 24.2, 22.9, 22.7. Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{O}$: C, 72.38; H, 8.68. Found: C, 72.27; H, 8.79.



Entry 9. Pale yellow oil. 20% yield.

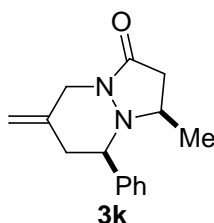
^1H NMR (CDCl_3): δ 4.91 (s, 1H), 4.88 (s, 1H), 4.56 (d, $^2J_{\text{HH}} = 14.6$ Hz, 1H), 3.66 (td, $J_{\text{HH}} = 9.6$ Hz and $^3J_{\text{HH}} = 3.5$ Hz, 1H), 3.50 (d, $^2J_{\text{HH}} = 14.4$ Hz, 1H), 2.85 (q, $J_{\text{HH}} = 9.8$ Hz, 1H), 2.59 (ddd, $^2J_{\text{HH}} = 16.6$ Hz and $^3J_{\text{HH}} = 8.8$ and 3.6 Hz, 1H), 2.52-2.43 (m, 2H), 2.33 (dd, $^3J_{\text{HH}} = 8.6$ and 4.1 Hz, 1H), 2.26 (dd, $^2J_{\text{HH}} = 13.5$ Hz and $^3J_{\text{HH}} = 9.0$ Hz, 1H), 1.02 (s, 9H). ^{13}C NMR (CDCl_3): δ 169.5, 139.4, 110.9, 74.0, 53.0, 47.2, 34.9, 34.0, 31.4, 28.5. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{21}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 209.1648, found 209.1658.



Equation 2. White solid. 94% yield.

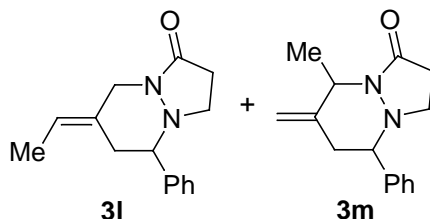
^1H NMR (CDCl_3): δ 7.39-7.30 (m, 5H), 5.02 (d, $^2J_{\text{HH}} = 1.5$ Hz, 1H), 4.90 (d, $^2J_{\text{HH}} = 1.3$ Hz, 1H), 4.57 (dd, $^2J_{\text{HH}} = 13.9$ Hz and $^4J_{\text{HH}} = 1.4$ Hz, 1H), 3.63 (d, $^2J_{\text{HH}} = 13.8$ Hz, 1H), 3.24 (dd, $^3J_{\text{HH}} = 12.4$ Hz and 2.9 Hz, 1H), 2.97 (d, $^2J_{\text{HH}} = 9.7$ Hz, 1H), 2.56 (dd, $^2J_{\text{HH}} = 13.1$ Hz and $^3J_{\text{HH}} = 12.4$ Hz, 1H), 2.47 (d, $^2J_{\text{HH}} = 13.5$ Hz, 1H), 2.35 (d, $^2J_{\text{HH}} = 9.8$ Hz, 1H), 1.17 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (CDCl_3): δ 174.5, 140.1, 138.8, 129.0, 128.3, 127.7, 111.8, 72.4, 63.7, 48.0, 42.6, 41.2, 23.5, 23.4. Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}$: C, 74.97;

H, 7.86. Found: C, 74.77; H, 7.80.



Equation 3. White solid. 87% yield, dr = 96/4. Recrystallization from Et₂O afforded single crystals suitable for X-ray analysis, and the relative configuration of the major diastereomer was determined to be *syn*.

Major diastereomer: ¹H NMR (CDCl₃): δ 7.40-7.30 (m, 5H), 4.97 (d, ²J_{HH} = 1.5 Hz, 1H), 4.83 (d, ²J_{HH} = 1.3 Hz, 1H), 4.68 (dd, ²J_{HH} = 14.0 Hz and ⁴J_{HH} = 1.4 Hz, 1H), 3.68 (d, ²J_{HH} = 13.9 Hz, 1H), 3.52 (dd, ³J_{HH} = 11.4 and 3.1 Hz, 1H), 3.16 (dq, ³J_{HH} = 9.0, 6.7, and 3.4 Hz, 1H), 2.85 (d, ²J_{HH} = 16.9 Hz and ³J_{HH} = 8.8 Hz, 1H), 2.63-2.57 (m, 1H), 2.47 (dt, ²J_{HH} = 13.8 Hz and J_{HH} = 2.4 Hz, 1H), 2.03 (ddd, ²J_{HH} = 16.9 Hz and ³J_{HH} = 3.3 Hz and ⁴J_{HH} = 1.3 Hz, 1H), 0.98 (d, ³J_{HH} = 6.6 Hz, 3H). ¹³C NMR (CDCl₃): δ 169.0, 141.0, 139.1, 129.0, 128.4, 127.6, 111.3, 70.5, 52.8, 46.8, 42.9, 36.8, 22.0. Anal. Calcd for C₁₅H₁₈N₂O: C, 74.35; H, 7.49. Found: C, 74.11; H, 7.49.



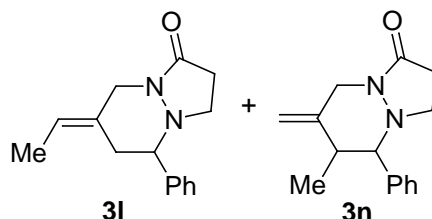
Procedure for Equation 4.

A solution of Pd(PPh₃)₄ (18.5 mg, 16.0 μmol), (2-(1'-acetoxyethyl)-2-propenyl)trimethylsilane **4** (80.1 mg, 0.400 mmol), and azomethine imine **2a** (34.8 mg, 0.200 mmol) in CH₂Cl₂ (1.0 mL) was stirred for 48 h at 40 °C, and the reaction mixture was directly passed through a pad of silica gel with EtOAc. After removing the solvent under vacuum, the residue was purified by silica gel preparative TLC with EtOAc/hexane = 1/1 to afford compound **3l** as a colorless oil (27.6 mg, 0.114 mmol; 57% yield) and compound **3m** as a white solid (7.3 mg, 30 μmol; 15% yield).

3l: ¹H NMR (CDCl₃): δ 7.40-7.31 (m, 5H), 5.54 (q, ³J_{HH} = 6.8 Hz, 1H), 4.49 (d, ²J_{HH} = 13.7 Hz, 1H), 3.65 (d, ²J_{HH} = 13.7 Hz, 1H), 3.29 (d, ²J_{HH} = 11.5 Hz, 1H), 3.20 (td, J_{HH} =

10.0 Hz and $^3J_{\text{HH}} = 5.0$ Hz, 1H), 2.77 (d, $^2J_{\text{HH}} = 14.1$ Hz, 1H), 2.66 (q, $J_{\text{HH}} = 8.1$ Hz, 1H), 2.54 (ddd, $^2J_{\text{HH}} = 16.5$ Hz and $^3J_{\text{HH}} = 8.9$ and 5.0 Hz, 1H), 2.44-2.37 (m, 1H), 2.28 (t, $J_{\text{HH}} = 12.9$ Hz, 1H), 1.61 (d, $^3J_{\text{HH}} = 6.8$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 169.8, 140.5, 129.5, 129.0, 128.4, 127.7, 121.0, 71.1, 48.7, 48.6, 36.0, 30.6, 13.0. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 243.1492, found 243.1482.

3m: ^1H NMR (CDCl_3): δ 7.39-7.31 (m, 5H), 4.97 (s, 1H), 4.87 (q, $^3J_{\text{HH}} = 6.8$ Hz, 1H), 4.82 (s, 1H), 3.35 (dd, $^2J_{\text{HH}} = 11.8$ Hz and $^3J_{\text{HH}} = 3.0$ Hz, 1H), 3.18 (td, $J_{\text{HH}} = 9.9$ Hz and $^3J_{\text{HH}} = 4.8$ Hz, 1H), 2.76 (dd, $^2J_{\text{HH}} = 14.1$ Hz and $^3J_{\text{HH}} = 12.2$ Hz, 1H), 2.61 (q, $J_{\text{HH}} = 9.5$ Hz, 1H), 2.54 (ddd, $^2J_{\text{HH}} = 16.1$ Hz and $^3J_{\text{HH}} = 8.8$ and 4.9 Hz, 1H), 2.42-2.33 (m, 2H), 1.46 (d, $^3J_{\text{HH}} = 6.8$ Hz, 3H). ^{13}C NMR (CDCl_3): δ 169.4, 143.2, 140.5, 129.0, 128.4, 127.6, 110.9, 72.1, 53.0, 48.6, 39.2, 31.0, 17.9. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}$ ($\text{M}+\text{H}^+$) 243.1492, found 243.1483.

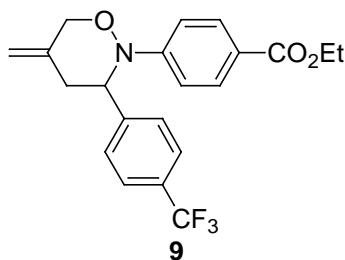


Procedure for Equation 5.

A solution of $\text{Pd}(\text{PPh}_3)_4$ (18.5 mg, 16.0 μmol), (2-(acetoxymethyl)-1-buten-3-yl)trimethylsilane **5** (80.1 mg, 0.400 mmol), and azomethine imine **2a** (34.8 mg, 0.200 mmol) in CH_2Cl_2 (1.0 mL) was stirred for 72 h at 40 $^\circ\text{C}$, and the reaction mixture was directly passed through a pad of silica gel with EtOAc. After removing the solvent under vacuum, the residue was purified by silica gel preparative TLC with EtOAc/hexane = 1/1 to afford a mixture of compounds **3l–3n** as a colorless oil (32.1 mg, 0.132 mmol; 66% yield).

3n (mixture of *cis/trans* ~ 46/54): ^1H NMR (CDCl_3): δ 7.39-7.27 (m, 5H), 5.10 (s, 0.54H), 5.00 (bs, 0.46H), 4.924 (s, 0.54H), 4.918 (s, 0.46H), 4.63 (d, $^2J_{\text{HH}} = 13.7$ Hz, 0.54H), 4.47 (bs, 0.46H), 3.83 (bs, 0.46H), 3.72 (d, $^2J_{\text{HH}} = 13.7$ Hz, 0.54H), 3.65 (bs, 0.46H), 3.38 (bs, 0.46H), 3.07 (td, $J_{\text{HH}} = 10.0$ Hz and $^3J_{\text{HH}} = 4.6$ Hz, 0.54H), 2.94 (d, $^3J_{\text{HH}} = 10.3$ Hz, 0.54H), 2.63-2.35 (m, 4H), 0.99 (d, $^3J_{\text{HH}} = 6.0$ Hz, 1.38H), 0.80 (d, $^3J_{\text{HH}} = 6.6$ Hz, 1.62H). ^{13}C NMR (CDCl_3): δ 169.8, 169.4, 143.3, 139.0, 128.9, 128.54, 128.52, 127.9, 111.0, 110.1, 78.0, 77.5, 49.0, 48.6, 43.9, 41.7, 30.7, 30.6, 14.0, 13.5. Anal. Calcd for

C₁₅H₁₈N₂O: C, 74.35; H, 7.49. Found: C, 74.06; H, 7.61



Procedure for Equation 6.

A solution of Pd(PPh₃)₄ (11.6 mg, 10.0 μmol), (2-(acetoxymethyl)-2-propenyl)trimethylsilane **1** (46.6 mg, 0.25 mmol), and nitrone **8** (33.8 mg, 0.10 mmol) in CH₂Cl₂ (0.50 mL) was stirred for 43 h at 40 °C, and the reaction mixture was directly passed through a pad of silica gel with EtOAc. After removing the solvent under vacuum, the residue was purified by silica gel preparative TLC with EtOAc/hexane = 1/4.5 to afford **9** as a colorless oil (35.7 mg, 91.2 μmol; 91% yield).

¹H NMR (CDCl₃): δ 7.88 (d, ³J_{HH} = 8.9 Hz, 2H), 7.51 (d, ³J_{HH} = 8.8 Hz, 2H), 7.49 (d, ³J_{HH} = 8.8 Hz, 2H), 6.94 (d, ³J_{HH} = 8.9 Hz, 2H), 5.04 (dd, ³J_{HH} = 6.0 and 4.7 Hz, 1H), 4.99 (s, 1H), 4.94 (s, 1H), 4.68 (d, ²J_{HH} = 12.8 Hz, 1H), 4.57 (d, ²J_{HH} = 12.7 Hz, 1H), 4.31 (q, ³J_{HH} = 7.1 Hz, 2H), 3.09 (dd, ²J_{HH} = 14.0 Hz and ³J_{HH} = 6.3 Hz, 1H), 2.72 (dd, ²J_{HH} = 13.9 Hz and ³J_{HH} = 4.4 Hz, 1H), 1.35 (t, ³J_{HH} = 7.1 Hz, 3H). ¹³C NMR (CDCl₃): δ 166.6, 152.0, 144.1, 139.3, 131.0, 129.8 (q, ²J_{CF} = 32.6 Hz), 128.3, 125.5 (q, ³J_{CF} = 3.6 Hz), 124.3 (q, ¹J_{CF} = 272 Hz), 123.1, 114.4, 111.8, 74.3, 63.3, 60.7, 37.5, 14.6. HRMS (ESI) calcd for C₂₁H₂₁F₃NO₃ (M+H⁺) 392.1468, found 392.1463.

V. X-ray Crystal Structure of **3k**

Data Collection

A colorless Et₂O solution of **3k** was prepared. Crystals suitable for X-ray analysis were obtained by slow evaporation of Et₂O at room temperature.

A colorless prism crystal of C₁₅H₁₈N₂O having approximate dimensions of 0.52 x 0.30 x 0.10 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:

$$a = 7.076(5) \text{ \AA} \quad \alpha = 77.94(3)^\circ$$

$$b = 7.693(5) \text{ \AA} \quad \beta = 84.96(3)^\circ$$

$$c = 12.82(1) \text{ \AA} \quad \gamma = 75.35(3)^\circ$$

$$V = 659.7(8) \text{ \AA}^3$$

For $Z = 2$ and F.W. = 242.32, the calculated density is 1.22 g/cm^3 . Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be:

$$P\bar{1} \text{ (\#2)}$$

The data were collected at a temperature of $-150 \pm 1 \text{ }^\circ\text{C}$ 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 $110.0 \text{ [sec./}^\circ\text{]}$. 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 $110.0 \text{ [sec./}^\circ\text{]}$. The crystal-to-detector distance was 127.40 mm. Readout was performed in the 0.100 mm pixel mode.

Data Reduction

A total of 3001 reflections was collected.

The linear absorption coefficient, μ , for Mo-K α radiation is 0.8 cm^{-1} . The data were corrected for Lorentz and polarization effects.

Structure Solution and Refinement

The structure was solved by direct methods⁷ and expanded using Fourier techniques.⁸ The non-hydrogen atoms were refined anisotropically. Hydrogen atoms

⁷ SIR92: Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994**, *27*, 435.

were refined using the riding model. The final cycle of full-matrix least-squares refinement⁹ on F was based on 2539 observed reflections ($I > 3.00\sigma(I)$) and 181 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma | |F_o| - |F_c| | / \Sigma |F_o| = 0.046$$

$$R_w = [\Sigma w (|F_o| - |F_c|)^2 / \Sigma w F_o^2]^{1/2} = 0.064$$

The standard deviation of an observation of unit weight¹⁰ was 1.34. A Sheldrick weighting scheme was used. 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 0.22 and $-0.39 \text{ e}^-/\text{\AA}^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.¹¹ Anomalous dispersion effects were included in F_{calc} ;¹² the values for $\Delta f'$ and $\Delta f''$ were those of Creagh and McAuley.¹³ The values for the mass attenuation coefficients are those of Creagh and Hubbell.¹⁴ All calculations were performed using the CrystalStructure^{15,16} crystallographic software package.

⁸ 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).

⁹ Least Squares function minimized: (SHELXL97)

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

¹⁰ 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

¹¹ Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).

¹² Ibers, J. A.; Hamilton, W. C. *Acta Crystallogr.* **1964**, *17*, 781.

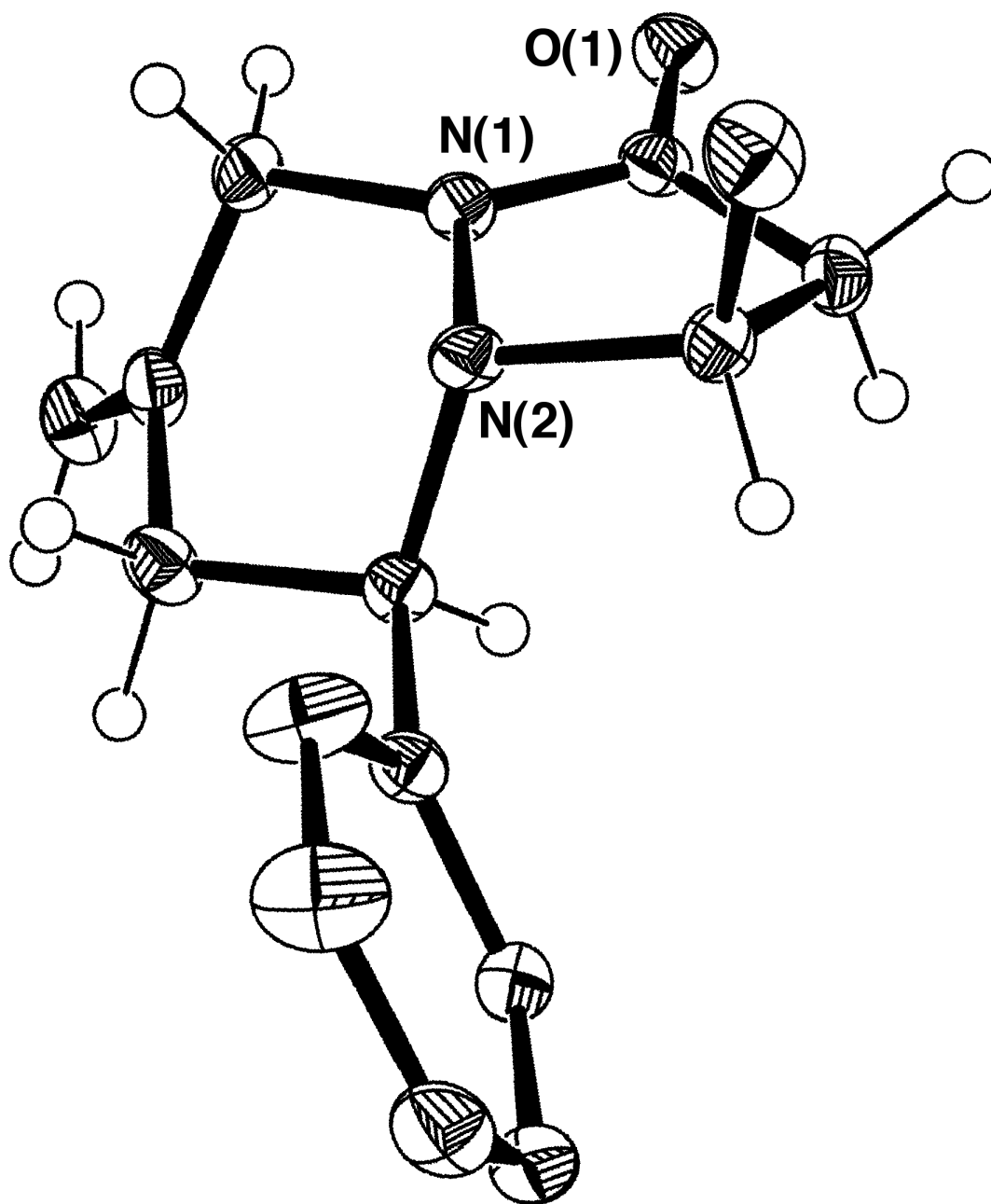
¹³ Creagh, D. C.; McAuley, W. J. "International Tables for Crystallography", Vol C, (Wilson, A. J. C., ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219–222 (1992).

¹⁴ 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).

¹⁵ CrystalStructure 3.6.0: Crystal Structure Analysis Package, Rigaku and Rigaku/MSO (2000-2004). 9009 New Trails Dr. The Woodlands TX 77381 USA.

¹⁶ CRYSTALS Issue 10: Watkin, D. J.; Prout, C. K.; Carruthers, J. R.; Betteridge, P. W. Chemical Crystallography Laboratory, Oxford, UK. (1996).

The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (deposition number: CCDC 297116). 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 ₁₅ H ₁₈ N ₂ O
Formula Weight	242.32
Crystal Color, Habit	colorless, prism
Crystal Dimensions	0.52 X 0.30 X 0.10 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 = 7.076(5) Å b = 7.693(5) Å c = 12.82(1) Å α = 77.94(3)° β = 84.96(3)° γ = 75.35(3)° V = 659.7(8) Å ³
Space Group	P-1 (#2)
Z value	2
D _{calc}	1.220 g/cm ³
F ₀₀₀	260.00
μ(MoKα)	0.77 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 ($\chi=45.0$, $\phi=30.0$)	130.0 - 190.0°
Exposure Rate	110.0 sec./°
ω oscillation Range ($\chi=45.0$, $\phi=180.0$)	0.0 - 160.0°
Exposure Rate	110.0 sec./°
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{\text{max}}$	54.9°
No. of Reflections Measured	Total: 3001
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	$w = 1/[0.0010F_o^2 + 3.0000\sigma(F_o^2) + 0.5000]$
2 θ_{\max} cutoff	0.0°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (I>3.00 σ (I))	2539
No. Variables	181
Reflection/Parameter Ratio	14.03
Residuals: R (I>3.00 σ (I))	0.046
Residuals: Rw (I>3.00 σ (I))	0.064
Goodness of Fit Indicator	1.340
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.22 e ⁻ /Å ³
Minimum peak in Final Diff. Map	-0.39 e ⁻ /Å ³