# Supplementary Material

# Total Syntheses of (-)-Haemanthidine, (+)-Pretazettine and (+)-Tazettine

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This section contains experimental procedures for the preparation of compounds **6-14** (including intermediate compounds) and **1**, **2**, and **3**, with selected analytical data. In addition pertinent crystallographic information is provided for intermediate **10** (21 pages).

**General methods.** All reactions were conducted under a dry argon atmosphere at room temperature unless otherwise specified. THF was distilled from sodium benzophenone ketyl. Dichloromethane, carbontetrachloride and acetonitrile were distilled from calcium hydride. Benzene and absolute ethanol were stored over 4Å molecular sieves. Solutions of compounds in organic solvents were dried over sodium sulfate prior to rotary evaporation. TLC plates were Kieselgel 60 F254 (Merck Art. 5554). Compounds were visualized on the TLC plate by charring with $H_2SO_4$/EtOH/$H_2O$ (1:10:10). Flash column chromatography was done with silica gel 60 (230-400 mesh, Merck). Optical rotations were determined at the sodium D line with a Perkin-Elmer 241 polarimeter. Mass spectra were recorded on a JEOL JMS-SX102A mass spectrometer operating at 3k resolution for low resolution fast atom bombardment (FAB) mass spectra or a Hewlett-Packard 5988A mass spectrometer using chemical ionization with ammonia as the reagent gas. FAB mass spectra were conducted using a *m*-nitrobenzyl alcohol matrix with xenon as the fast atom. Accurate mass measurements were made using FAB at 10k resolution. $^1$H and $^{13}$C NMR spectra were recorded on a Varian Unity Inova-400 spectrometer. Abbreviations for NMR data are as follows: s= singlet, b= broad, d= doublet, m= multiplet, dd= doublet of doublets, t= triplet, ddd= doublet of doublet of doublets. Coupling constants are reported in Hertz and chemical shifts are in ppm on the delta scale. $^1$H and $^{13}$C chemical shifts are reported relative to internal tetramethylsilane (0.00 ppm). $^1$H integration data reflects the fact that most of the compounds reported herein are rotomeric, hemiaminal or hemiacetal isomer mixtures and is not normalized. Elemental analyses were conducted by Atlantic Microlab, Inc., P.O. Box 2288, Norcross, GA 30091.

**(3*S*,4*R*)-3-Methyl-3,4-*O*-isopropylidene-5-hexenal dimethyl acetal** (**6**). Methyl 6-bromo-2,6-deoxy-3-methyl-α-D-allopyranoside[1] (19.31 g, 75.70 mmol) was dissolved in 2,2-dimethoxypropane (186 mL, 1513 mmol) and treated with *p*-toluenesulfonic acid (360 mg, 1.89 mmol) before heating to 80 °C for 14 h. After cooling to room temperature the reaction was quenched with triethylamine (~1.5 mL). The solution was concentrated and the residue was purified by flash chromatography eluting with 8:92 ethyl acetate/petroleum ether affording the bromo acetonide as an oil (21.90 g, 98%). The bromo acetonide (7.280 g, 24.66 mmol) was dissolved in methyl ethyl ketone (150 mL) before adding NaI (21.70 g, 144.8 mmol) and $NaHCO_3$ (60 mg, 0.71 mmol). The reaction was heated to 80 °C for 15 h and then concentrated. The syrup was dissolved in ethyl acetate (200 mL) and washed with 10% aqueous $Na_2S_2O_3$ (150 mL) back extracting the aqueous portion with ethyl acetate (2 × 75 mL). The resultant organic solution was concentrated (not dried) and the iodide dissolved in ethanol (158 mL, 95%). Activated Zn (17.00 g, 260.1 mmol) was added to the solution and the temperature was elevated to 80 °C for 87 min. The reaction mixture was filtered through Celite® 545 and concentrated affording the aldehyde which was protected immediately. To the aldehyde was added $CH(OCH_3)_3$ (42.00 mL, 383.9 mmol) and Amberylyst® 15 resin (980 mg). The reaction stirred 15 h and was concentrated *in vacuo*. The acetal was purified by flash chromatography eluting with 10:90 ethyl acetate/petroleum ether affording **6** as an oil (4.716 g, 83% for three steps); $[\alpha]^{21}_D$ –49.5° (*c* 6.40, $CCl_4$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 5.80 (ddd, *J* = 6.8, 10.6, 17.1 Hz, 1H), 5.40 (dd, *J* = 1.2, 17.3 Hz, 1H), 5.28 (dd *J* = 1.0, 10.6 Hz, 1H), 4.67 (dd *J* = 2.1, 7.7 Hz, 1H), 4.18 (d, *J* = 6.7 Hz, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 1.83 (dd, *J* = 1.7, 14.0 Hz, 1H), 1.53 (dd, *J* = 7.7, 14.2 Hz, 1H), 1.48 (s, 3H), 1.39 (s, 3H), 1.31 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 132.0, 118.5, 107.6, 101.9, 86.0, 80.9, 52.9, 51.5, 38.3, 28.0, 26.7, 23.0; HRMS (FAB) Calcd for $(M-H)^+$ $C_{12}H_{21}O_4$: 229.1440, Found 229.1444; Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.57; H, 9.63. Found: C, 62.66; H, 9.72.

**(3*S*,4*R*)-3,4-*O*-Isopropylidene-3-methyl-5-(1,3-benzodioxol-5-yl)-pentan-5-one-1-al dimethyl acetal** (**7**). $O_3$ was bubbled through a solution of **6** (5.052 g, 21.94 mmol) and $NaHCO_3$ (16.70 g, 198.7 mmol) in 2:1 $CH_2Cl_2$/methanol (100 mL) at -78 °C for 19 min until a dark blue color persisted. Bubbling continued for an additional 40 min and then the $O_3$ was purged from the vessel with $O_2$. Dimethyl sulfide (20.0 mL, 272.3 mmol) was added to the solution at -78 °C and the solution stirred 17 h warming to room temperature. The solution was filtered through Celite® 545 and concentrated. Purification of the aldehyde was accomplished *via* flash chromatography eluting with 35:65 ethyl acetate/petroleum ether affording the aldehyde as an oil (4.170 g, 82%). The aldehyde (4.160 g, 17.91 mmol) in tetrahydrofuran (50 mL) was canulated into a solution of freshly prepared aryl Grignard {Mg (916 mg, 37.7 mmol) in tetrahydrofuran (19 mL) was treated to 4-bromo-1,2,-(methylenedioxybenzene) (5.13 mL, 42.60 mmol) and stirred until all of the Mg metal had been dissolved (70 min)}at 0 °C. The Grignard reaction was stirred 100 min warming to room temperature before being quenched with saturated aqueous $NH_4Cl$ solution (20 mL). The solution was diluted with ethyl acetate and the layers were separated. The remaining aqueous portion was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with saturated aqueous $NH_4Cl$ solution (50 mL) back extracting the aqueous phase with ethyl acetate (50 mL). The resultant organic solution was concentrated *in vacuo*. The residue was then dissolved in $CH_2Cl_2$ (100 mL) before adding 4Å sieves (10.7 g), acetic anhydride (3.95 mL, 41.9 mmol) and pyridinium dichromate (7.88 g, 20.9 mmol). The reaction mixture was stirred 6 h, diluted with ethyl acetate (100 mL) and then filtered through Celite® 545. After washing the solution with saturated aqueous $NaHCO_3$ (2 × 100 mL), and back extracting the aqueous portions (2 × 75 mL), the solvent was removed *in vacuo*. The aryl ketone was purified by flash chromatography eluting with 20:80 ethyl acetate/petroleum ether affording **7**[2] (3.441 g, 70% for two steps); $[\alpha]^{21}_{D}$ –31.5° (*c* 0.78, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.67 (dd, *J* = 1.7, 8.2 Hz, 1H), 7.51 (d, *J* = 1.7 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 6.05 (dd, *J* = 1.4, 1.9 Hz, 2H), 4.88 (s, 1H), 4.61 (dd, *J* = 2.4, 7.5 Hz, 1H), 3.27 (s, 3H), 3.20 (s, 3H), 1.87 (dd, *J* = 1.9, 14.2 Hz, 1H), 1.59 (s, 3H), 1.50 (s, 3H), 1.47 (s, 3H), 1.45 (dd, *J* = 7.5, 14.2 Hz, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 193.0, 152.0, 148.0, 131.0, 125.4, 108.7, 107.7, 101.8, 101.7, 86.6, 81.5, 53.1, 51.7, 38.7, 28.0, 26.8, 25.1; HRMS (FAB) Calcd for $(M-H)^+$ $C_{18}H_{23}O_7$: 351.1444, Found 351.1435; Anal. Calcd for $C_{18}H_{24}O_7$: C, 61.35; H, 6.86. Found: C, 61.43; H, 6.84.

**(2*E*,4*R*,5*S*)-3-(1,3-benzodioxole-5-yl)-7,7-dimethoxy-4,5-*O*-isopropylidene-5-methyl-2-heptenoate** (**8**) To freshly prepared lithium diisopropylamide {diisopropylamine (955 μL, 6.80 mmol) in tetrahydrofuran (15 mL) treated with *n*-butyllithium (2.72 mL, 2.5 M in hexanes, 6.80 mmol) at -78 °C dropwise and stirred for 15 min} was added ethyl (trimethylsilyl)acetate (1.25 mL, 6.80 mmol) dropwise at -78 °C. The reaction was stirred 15 min before **7** (1.840 g, 5.228 mmol) in tetrahydrofuran (18 mL) was added dropwise over 30 min at -78 °C. The reaction warmed to -50 °C over 3 h and was then quenched with saturated aqueous $NH_4Cl$ (30 mL). The solution volume was diluted to 100 mL with ethyl acetate and the layers were separated. After extracting the aqueous portion with ethylacetate (4 × 30 mL), the combined organic portions were concentrated, and the product was purified *via* flash chromatography eluting with 18:82 ethyl acetate/petroleum ether affording the alkenes as a clear viscous oil (2.110 g, 96%, 1.5:1 Z/E).

Typical Isomerization: A mixture of alkenes (1.343 g, 3.180 mmol, 2.8:1 Z/E) in benzene (10 mL) was degassed before adding 2,2'azobisisobutyronitrile (AIBN) (261 mg, 1.59 mmol) and thiophenol (163 μL, 1.59 mmol). The reaction was heated to 80 °C for 11.5 h at which point the benzene was removed *in vacuo*, and the residue was purified *via* flash chromatography eluting with 15→25% ethyl acetate/petroleum ether affording the Z-alkene (99.9 mg, 7.4%) and the E-Alkene **8** (1.173 g, 87.3%) [1:11.7 Z/E isomerized ratio of alkenes)

Average throughput: By executing two Peterson olefinations as above on **7** (5.390 g, 15.30 mmol total) and three isomerizations (total) afforded **8** (6.042 g, 93%); $[\alpha]^{21}_D$ +20.6° (*c* 0.94, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.65-6.77 (m, 3H), 6.29 (d, *J* = 1.7 Hz, 1H), 5.98 (dd, *J* = 1.4, 3.1 Hz, 2H), 4.61 (approx. dd, *J* = 1.7, 8.0 Hz, 2H), 3.99-4.11 (m, 2H), 3.32 (s, 3H), 3.27 (s, 3H), 1.87 (dd, *J* = 1.0, 14.0 Hz, 1H), 1.52 (s, 3H), 1.46 (dd, *J* = 7.9, 14.0 Hz, 1H), 1.43 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 3H), 0.87 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 165.7, 150.1, 147.8, 147.3, 129.6, 121.9, 118.0, 108.8, 108.0, 107.3, 102.3, 101.2, 86.6, 80.6, 59.9, 53.1, 52.6, 37.9, 28.2, 27.0, 24.3, 14.0; HRMS (FAB) Calcd for $(M-H)^+$ $C_{22}H_{29}O_8$: 421.1862, Found 421.1853; Anal. Calcd for $C_{22}H_{30}O_8$: C, 62.55; H, 7.16. Found: C, 62.45; H, 7.09.

**(3b*R*,6a*S*)-Hexahydro-5,5-dimethyl-*N*-[(*S*)-α-methylbenzyl]-6a-methyl-3a-(1,3-benzodioxole-5-yl)-3-carboethoxy-[1,3]dioxolo[3,4]cyclopent[1,2-c]isoxazole** (**9**). The E-alkene **8** (400.0 mg, 0.9468 mmol) in acetone (25 mL, containing 0.4% $H_2O$) was treated to Amberlyst® 15 resin (80 mg) for 12 h at 42 °C at which point the reaction was complete as determined by $^{1}H$ NMR analysis of a small aliquot. The acetone was removed *in vacuo*, and the residue was purified *via* flash chromatography eluting with 20:80 ethyl acetate/petroleum ether affording the aldehyde as a sticky foam (322.1 mg, 90%). To the aldehyde (345.0 mg, 0.9166 mmol) in benzene (10 mL) was added (S)-α-methylbenzyl hydroxylamine oxylate[3] (229 mg, 1.01 mmol) and anhydrous $K_2CO_3$ (253 mg, 1.83 mmol). The reaction was stirred 18 h and was filtered through Celite® 545. The concentrated filtrate was then dissolved in benzene 10 mL and heated to 55 °C for 12 h and then 80 °C for an additional 5 h. The benzene was removed *in vacuo*, and the residue was purified *via* flash chromatography eluting with 15:85 ethyl acetate/petroleum ether affording **9**, the major component of a 12:1 mixture, as a white foam (340.5 mg, 75%); $[\alpha]^{21}_{D}$ –65.4° (*c* 0.98, $CHCl_3$); $^{1}H$ NMR (400 MHz, DMSO-$d_6$, 100 °C) δ 7.46-7.50 (m, 2H), 7.20-7.34 (m, 3H), 6.92-7.00 (m, 2H), 6.79 (d, *J* = 8.2 Hz, 1H), 5.94 (dd, *J* = 1.0, 11.1 Hz, 2H), 4.70 (s, 1H), 4.40 (s, 1H), 4.27 (dd, *J* = 4.7, 7.5 Hz, 1H), 3.94-4.64 (m, 1H), 3.61-3.72 (m, 1H), 2.03 (dd, *J* = 7.7, 14.2 Hz, 1H), 1.86 (dd, *J* = 4.4, 14.4 Hz, 1H), 1.59 (s, 3H), 1.38 (d, *J* = 6.5 Hz, 3H), 1.31 (s, 3H), 1.09 (s, 3H), 0.98 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, 53 °C) δ 168.9, 146.7, 146.2, 142.9, 132.1, 128.3, 127.5, 127.4, 122.9, 110.5, 109.9, 107.5, 107.1, 101.0, 100.8, 89.5, 88.7, 83.4, 69.4, 60.6, 29.7, 27.9, 27.1, 26.7, 22.2, 13.8; HRMS (FAB) Calcd for $M^+$ $C_{28}H_{33}NO_7$: 495.2257, Found 495.2249; Anal. Calcd for $C_{28}H_{33}NO_7$: C, 67.86; H, 6.71; N, 2.83. Found: C, 67.70; H, 6.75; N, 2.74.

**Lactam** (**10**). To a Fisher-Porter tube was added **9** (3.397 g, 6.855 mmol) in 1:1 tetrahydrofuran/methanol (35 mL) which was degassed before adding 10 % Pd/C (3 g). The vessel was evacuated and pressurized with $H_2$ at 55 psi (6×). The reaction stirred 1 week and was then filtered through Celite® 545. The concentrated residue was purified *via* flash chromatography eluting with 10:90 methanol/$CH_2Cl_2$ affording **10** as a white solid (2.269 g, 95%); $[\alpha]^{21}_{D}$ +86.6° (*c* 0.50, $CHCl_3$); $^{1}H$ NMR (400 MHz, $CDCl_3$) δ 6.93 (d, *J* = 1.5 Hz, 1H), 6.74-6.82 (m, 2H), 6.56 (s, 1H), 5.95 (dd, *J* = 1.5, 2.4 Hz, 2H), 4.90 (s, 1H), 4.46 (dd, *J* = 3.1, 6.0 Hz, 1H), 4.40 (s, 1H), 4.17 (bs, 1H), 2.55 (dd, *J* = 6.2, 14.5 Hz, 1H), 2.05 (dd, *J* = 3.3, 14.4 Hz, 1H), 1.53 (s, 3H), 1.30 (s, 3H), 0.97 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 176.4, 147.5, 146.2, 134.4, 120.2, 112.2, 109.0, 107.6, 101.0, 90.3, 87.2, 77.7, 61.8, 61.4, 46.8, 28.0, 27.5, 27.2; HRMS (FAB) Calcd for $M^+$ $C_{18}H_{21}NO_6$: 347.1369, Found 347.1376;  Anal. Calcd for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.09; N, 4.03.  Found: C, 62.27; H, 6.17; N, 4.03.

A sample for x-ray analysis was recrystallized from THF/hexane to afford long colorless needles, mp 238-42°C.

**Formamide (11).**[4]  To **10** (1.060 g, 3.052 mmol) in tetrahydrofuran (40 mL) was added $LiAlH_4$ in THF (12.2 mL, 1.0 M) the reaction was then heated to 60 °C for 2 h.  After cooling the reaction to room temperature it was quenched with $H_2O$ (1 mL), aqueous NaOH (1 mL, 6 M) and $H_2O$ (2 mL).  The solution was then decanted from the precipitate, and the salts were washed with tetrahydrofuran (4 × 65 mL).  The combined organic portions were concentrated *in vacuo*.  The amine was dissolved in tetrahydrofuran (35 mL) and then canulated into a freshly prepared solution of acetic formic anhydride {To acetic anhydride (2.30 mL, 24.4 mmol) was added formic acid (1.11 mL, 29.3 mmol) the reaction was heated to 60 °C for 2 h and then diluted with tetrahydrofuran (3 mL)} at -60 °C.  The reaction was stirred 15 min, warming to -20 °C, at which point it was quenched with methanol (3 mL).  The solution was concentrated and the residue was dissolved in $CH_2Cl_2$ (120 mL) and washed with aqueous NaOH (2 × 50 mL, 1 M).  The combined aqueous phases were back extracted with $CH_2Cl_2$ (2 × 50 mL).  The resultant organic solution was concentrated and the residue was dissolved in pyridine (21 mL) before adding 4-dimethylaminopyridine (460 mg, 3.77 mmol) and pivaloylchloride (7.50 mL, 61.0 mmol).  The solution was heated to 80 °C for 24 h and then concentrated.  The residue was dissolved in $CH_2Cl_2$ (100 mL) and washed with aqueous HCl (2 × 30 mL, 2.5%) back extracting the aqueous phase with $CH_2Cl_2$ (2 × 15 mL).  The resultant organic solution was washed with aqueous NaOH (45 mL, 1 M) back extracting the aqueous phase with $CH_2Cl_2$ (2 × 15 mL).  The combined organic portions were concentrated and purified *via* flash chromatography eluting with 65:35 ethyl acetate/petroleum ether affording **11** as a white foam (1.016 g, 75%); $[\alpha]^{21}_D$ +30.6° (*c* 1.03, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 0.57H), 8.21 (s, 0.36H), 6.60-6.78 (m, 3H), 5.96-5.97 (m, 2H), 5.25 (d, *J* = 4.6 Hz, 0.51H), 5.17 (d, *J* = 4.4 Hz, 0.35H), 5.08 (t, *J* = 8.5

Hz, 0.41H), 4.92 (dd, $J = 7.7, 9.6$ Hz, 0.6H), 4.69 (d, $J = 2.2$ Hz, 0.84H), 3.77 (dd, $J = 4.4, 12.7$ Hz, 0.42H), 3.63 (dd, $J = 4.3, 14.7$ Hz, 0.55H), 3.52 (dd, $J = 6.2, 14.6$ Hz, 0.86H), 2.90 (dd, $J = 7.4, 13.7$ Hz, 0.4H), 2.59 (dd, $J = 7.5, 13.3$ Hz, 0.58H), 2.00 (dd, $J = 9.9, 13.3$ Hz, 0.64H), 1.77 (dd, $J = 9.7, 13.5$ Hz, 0.4H), 1.60 (2s, 3H), 1.35 and 1.40 (2s, 3H), 1.27 and 1.26 (2s, 9H), 0.86 and 0.83 (2s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 177.8, 177.6, 160.5, 160.4, 147.7, 147.6, 146.6, 146.5, 133.3, 133.0, 120.6, 120.2, 111.0, 109.3, 109.2, 107.8, 107.7, 101.1 (2C), 91.3, 91.0, 85.6, 85.4, 81.2, 80.8, 63.7, 63.5, 61.9, 52.3, 50.8, 44.3, 42.4, 38.9, 38.8, 29.3 (2C), 27.4 (2C), 27.1 (2C), 24.6, 24.4; HRMS (FAB) Calcd for $MH^+$ $C_{24}H_{32}NO_7$: 446.2179, Found 446.2193.

**Ketoaldehyde (12)**. To **11** (1.107 g, 2.485 mmol) was added trifluoroacetic acid (12 mL) and $H_2O$ (0.84 mL). The reaction was stirred 10 h and the trifluoroacetic acid was removed *in vacuo*. The residue was dissolved in $CH_2Cl_2$ (2 mL) and triethylamine (0.5 mL) was added dropwise before applying this solution directly to a silica gel column eluting with 60→75% ethyl acetate/petroleum ether affording the diol as a white foam (964.2 mg, 96%). The diol (117.0 mg, 0.2886 mmol) in 2:1 THF/$H_2O$ (3 mL) was treated to $NaIO_4$ (198 mg, 0.926 mmol) for 22 h before diluting the solution with ethyl acetate (20 mL). The solution was decanted from the salts and the salts were washed with ethyl acetate (3 × 10 mL). The combined organic solution was concentrated and the residue was purified *via* flash chromatography eluting with 25:75 ethyl acetate/$CH_2Cl_2$ affording **12** as a white foam (108.9 mg, 94%); $[\alpha]^{21}_{D}$ +104.1° (*c* 0.91, $CHCl_3$); $^1$H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 0.27H), 9.39 (s, 0.73H), 8.19 (s, 0.73H), 8.14 (s, 0.27H), 6.77-6.92 (m, 3H), 6.06 (d, $J = 5.6$ Hz, 0.82H), 6.00 (d, $J = 1.9$ Hz, 2H), 5.78 (d, $J = 2.8$ Hz, 0.27H), 5.34 (dd, $J = 3.8, 7.4$ Hz, 0.3H), 5.05 (dd, $J = 4.3, 7.5$ Hz, 0.76H), 4.50 (dd, $J = 5.8, 14.5$ Hz, 0.82H), 3.84 (dd, $J = 5.1, 11.8$ Hz, 0.28H), 3.60 (dd, $J = 1.5, 11.8$ Hz, 0.28H), 3.45 (dd, $J = 4.4, 18.3$, 0.73H), 3.35 (d, $J = 14.5$ Hz, 0.76H), 3.22 (dd, $J = 8.0, 17.8$ Hz, 0.27H), 3.11 (dd, $J = 3.6, 17.4$ Hz, 0.27H), 2.92 (dd, $J = 7.9, 18.5$ Hz, 0.75H), 2.23 (s, 3H), 1.25 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 205.7, 205.3, 194.9, 193.9, 177.2, 177.0, 161.8, 160.7, 149.0, 148.9, 148.2, 148.0, 127.9, 126.8, 120.9, 109.1, 109.0, 107.7, 107.4, 101.7, 101.6, 75.9, 74.7, 65.8, 64.8, 59.3, 56.2, 50.1, 49.0, 45.6, 44.3, 38.7, 30.5, 29.9, 26.9 (2C); HRMS (FAB) Calcd for $MH^+$ $C_{21}H_{26}NO_7$: 404.1709, Found 404.1722.

**(3*R*,3a*S*,7a*S*)-*N*-Formal-3-(pivaloyloxy)-3a-[3,4-(methylenedioxy)phenyl]-2,3,3a,6,7,7a-hexahydroindol-6-one** (**13**). A solution of **12** (105.0 mg, 0.2603 mmol) in benzene (1.5 mL) was treated with acetic acid (14.9 μL, 0.2603 mmol) and pyrrolidine (21.7 μL, 0.2603 mmol). The solution was stirred for 11 h and was applied directly to a silica gel column eluting with 50:50 ethyl acetate/$CH_2Cl_2$ providing **12** (58.0 mg, 58%); $[\alpha]^{21}_D$ +152.4° (*c* 0.97, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 0.5H), 8.21 (s, 0.5H), 6.80-6.94 (m, 4H), 6.27 (dd, *J* = 10.4, 14.4 Hz, 1H), 6.00 and 5.99 (2s, 2H), 5.71 (dd, *J* = 5.0, 6.7 Hz, 0.5H), 5.57 (t, *J* = 6.7 Hz, 0.5H), 4.67 (t, *J* = 5.3 Hz, 0.5H), 4.53 (dd, *J* = 5.3, 8 Hz, 0.5H), 4.14 (dd, *J* = 6.7, 13.2 Hz, 0.5H), 4.04 (dd, *J* = 6.5, 10.8 Hz, 0.5H), 3.34-3.42 (m, 1H), 3.15 (dd, *J* = 6.3, 17.3 Hz, 0.5H), 2.98 (dd, *J* = 8.0, 16.8 Hz, 0.5H), 2.84 (dd, *J* = 3.3, 5.0 Hz, 0.5H), 2.79 (dd, *J* = 3.9, 5.1 Hz, 0.5H), 1.16 and 1.15 (2s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 196.1, 195.3, 177.6, 177.4, 161.7, 160.2, 148.8, 147.7, 146.6, 146.1, 131.4, 131.0, 130.4, 119.9, 108.8, 108.7, 106.8, 101.6 (2C), 75.3, 75.1, 61.2, 59.2, 53.6, 52.5, 49.0, 48.1, 40.7, 38.8, 38.7, 37.3, 27.0; HRMS (FAB) Calcd for $M^+$ $C_{21}H_{23}NO_6$: 385.1525, Found 385.1537.

**(3*R*,3a*S*,6*S*,7a*S*,)-*N*-Formyl-3-(pivaloyloxy)-3a-[3,4-(methylenedioxy)phenyl]-6-methoxy-2,3,3a,6,7,7a-hexhydroindole** (**14**). To **13** (219.0 mg, 0.5682 mmol) in methanol (10 mL) was added $CeCl_3 \cdot 7H_2O$ (211.7 mg, 0.5682 mmol) before cooling the solution to -78 °C and adding $NaBH_4$ (53.0 mg, 1.40 mmol).[5] After stirring for 8 min, the reaction was quenched with $H_2O$ (0.5 mL) and warmed to room temperature. The solution was concentrated, and the residue was dissolved in $CH_2Cl_2$ (50 mL) and washed with $H_2O$ (25 mL) back extracting the aqueous phase with $CH_2Cl_2$ (3 × 15 mL). The combined organic portions were concentrated and the residue was purified *via* flash chromatography eluting with ethyl acetate affording a 6:1 (β:α) mixture of allylic alcohols (209.9 mg, 95%). To the alcohols (207.0 mg, 0.5343 mmol) in THF (4 mL) was added triethylamine (427.0 μL, 3.065 mmol) and methanesulfonic anhydride (534.0 mg, 3.065 mmol) in THF (3.5 mL) at 0 °C. After completion of the mesylation (30 min), the reaction temperature was lowered to -78 °C before adding anhydrous methanol (42 mL) dropwise. The reaction was warmed to -22 °C and proceeded for 105 h before warming again to 0 °C. The reaction continued for an additional 62 h at which point it was quenched with saturated aqueous $NaHCO_3$ (2 mL) and concentrated. The residue was dissolved in $CH_2Cl_2$ (50 mL) and washed with aqueous NaOH (15 mL, 1 M) back extracting the aqueous phase with $CH_2Cl_2$ (3 × 15 mL). The combined organic portions were concentrated and the residue was purified *via* flash chromatography eluting with 70:30 ethyl acetate/petroleum ether affording a 1:12 (β:α) mixture of allylic methyl ethers as a white foam (109.3 mg, 51%); $[\alpha]^{21}_{D}$ +99.3° (*c* 1.00, $CHCl_3$); $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 0.62H), 8.24 (s, 0.38H), 6.74-6.92 (m, 3H), 6.20 (dd, *J*= 2.4, 10.4 Hz, 0.38H), 6.16 (dd, *J*= 4.1, 10.3 Hz, 0.62H), 5.96 and 5.95 (2s, 2H), 5.86 (dd, *J*= 0.7, 10.3 Hz, 0.62H), 5.66 (dd, *J*= 4.1, 6.4 Hz, 0.55H), 5.48 (t, *J*= 6.8 Hz, 0.42H), 4.36 (dd, *J*= 3.1, 6.3Hz, 0.45H), 4.32 (dd, *J*= 4.3, 9.6 Hz, 0.55H), 3.98-4.07 (m, 1H), 3.82-3.89 (m, 1H), 3.41 and 3.40 (2s, 3H), 2.60-2.68 (m, 0.38H), 2.22-2.30 (m, 1H), 2.02-2.10 (m, 1H), 1.80-1.88 (m, 0.62H), 1.15 and 1.14 (2s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 177.8, 177.4, 161.5, 160.6, 148.2, 148.1, 146.9, 134.4, 133.9, 131.5, 130.5, 128.3 (2C), 120.0, 119.7, 108.3, 108.2, 107.3, 101.3, 101.2, 75.0, 74.9, 71.5, 71.1, 59.0, 58.6, 56.5, 56.4, 53.3, 51.9, 48.7, 47.9, 38.8, 38.6, 31.7, 27.1, 27.0, 26.5; HRMS (FAB) Calcd for $M^+$ $C_{22}H_{27}NO_6$: 401.1838, Found 401.1838.

**11-*O*-Pivaloylhaemanthidine**. To **14** (108.8 mg, 0.2710 mmol) in a 5 mL round bottom flask was added $POCl_3$ (1.14 mL, 12.2 mmol) at which point the flask was sealed with glass stopper and heated to 80 °C for 6h. The reaction was then cooled to room temperature and the $POCl_3$ was removed *in vacuo*. The residue was treated with 1:1 tetrahydrofuran/$H_2O$ (4 mL) for 24 h at which point the THF was removed *in vacuo*. The residue was dissolved in $CH_2Cl_2$ (40 mL) and washed with aqueous NaOH (20 mL, 1 M) back extracting the aqueous phase with $CH_2Cl_2$ (3 × 10 mL). The combined organic portions were concentrated and the residue was purified *via* flash chromatography eluting with 5:95 methanol/ $CH_2Cl_2$ affording 11-*O*-pivaloylhaemanthidine as a white foam (96.7 mg, 89%); $[\alpha]^{21}_{D}$ –28.1° (*c* 0.97, $CHCl_3$); $^1H$ NMR

(400 MHz, $CDCl_3$) δ 6.98 (s, 0.38H), 6.90 (s, 0.40H), 6.88 (s, 0.36H), 6.84 (s, 0.41H), 6.30 (d, *J* = 10.3 Hz, 1 H), 6.16 (ddd, *J* = 1.9, 5.0, 10.1 Hz, 1H), 5.90-5.94 (m, 2H), 5.72 (s, 0.52H), 5.09 (s, 0.55H), 4.84-4.89 (m, 1H), 4.23 (dd, *J* = 7.4, 14.5 Hz, 0.49H), 3.95 (dd, *J* = 5.0, 13.3 Hz, 0.59H), 3.79-3.85 (m, 1H), 3.60 (approx. dd, *J* = 7.5, 10.1 Hz, 0.50H), 3.38 and 3.34 (2s, 3H), 3.25-3.42 (m, 1H), 2.95 (dd, *J* = 2.9, 14.7 Hz, 0.51H), 1.97-2.17 (m, 2H), 1.14 (s, 9H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 177.4, 177.3, 147.9, 147.6, 146.8, 146.7, 134.8, 133.6, 129.8, 129.4, 128.8, 127.4, 127.2, 126.8, 109.2, 107.8, 103.5, 103.4, 101.1, 101.0, 88.3, 85.8, 79.0, 78.2, 72.3, 72.2, 61.6, 56.7, 56.4, 56.3, 55.1, 49.8, 49.4, 49.2, 38.3, 2C, 27.9, 27.5, 27.2, 27.0; HRMS (FAB) Calcd for $MH^+$ $C_{22}H_{28}NO_6$: 402.1917, Found 402.1919.

**Haemanthidine** (**3**). 11-O-Pivaloylhaemanthidine (20.0 mg, 0.0498 mmol) was treated with methanolic LiOH (3 mL, 1.4 M) for 31 h before removing the methanol *in vacuo*. The residue was dissolved in $H_2O$ (4 mL), and the solution was extracted with $CH_2Cl_2$ (4 × 4 mL). The concentrated organic solution was purified *via* flash chromatography eluting with 14:86 methanol/ $CH_2Cl_2$ affording **3** as an opaque film (11.2 mg, 71%); $[\alpha]^{21}_D$ –24.9° (*c* 0.78, $CHCl_3$); {lit.[6] $[\alpha]^{22}_D$ $-41^0$ (*c* 1, $CHCl_3$)}; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 0.41H), 6.82 (s, 0.48H), 6.80 (s, 0.56H), 6.77 (s, 0.45H), 6.34-6.43 (m, 2H), 5.88-5.94 (m, 2H), 5.72 (s, 0.39H), 5.08 (s, 0.53H), 4.21 (dd, *J* = 6.8, 14.4 Hz, 0.52H), 3.84-3.94 (m, 3.47H), 3.61 (dd, *J* = 4.8, 13.4 Hz, 0.53H), 3.37 and 3.35 (2s, 3H), 3.22-3.37 (m, 1H), 2.96 (dd, *J* = 2.6, 14.4 Hz 0.42H), 2.34 (td, *J* = 4.3, 13.5 Hz, 0.46H), 2.19 (td, *J* = 4.5, 13.5 Hz, 0.54H), 2.00-2.14 (m, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 147.8, 147.6, 146.7, 146.5, 135.6, 134.2, 132.9, 132.4, 128.4, 127.4, 126.3, 126.1, 109.5, 108.3, 102.9, 102.8, 101.1, 88.4, 85.8, 78.8, 78.1, 72.4, 72.2, 61.7, 57.8, 56.9, 56.6, 56.3, 51.8, 50.7, 50.3, 27.5, 27.4; HRMS (FAB) Calcd for $M^+$ $C_{17}H_{19}NO_5$: 317.1263, Found 317.1263.

**Pretazettine** (**1**). To **3** (8.5 mg, 0.027 mmol) in methanol (1.6 mL) was added methyl iodide (0.47 mL, 7.6 mmol). The reaction was stirred for 6 h before removing the methanol *in* *vacuo* at which point the residue was treated with aqueous HCl (2 mL, 0.01 M) for 1 min and the pH of the solution was adjusted to pH 8 with saturated aqueous $NaHCO_3$ (ca. 5 drops). The solution was extracted with $CH_2Cl_2$ (7 × 4 mL), and the organic portions were combined, filtered and concentrated. Purification of the product was carried out *via* flash chromatography eluting with 30:3:67 methanol/triethylamine/$CH_2Cl_2$ affording **1** as a white film (8.4 mg, 95%); $[\alpha]^{21}_D$ +178.5° (*c* 0.65, $CHCl_3$); {lit.[7] $[\alpha]^{24}_D$ $+180^0$ (*c* 0.2, $CHCl_3$)}; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 6.77 (s, 1H), 6.12 (s, 1H), 5.93 (s, 2H), 5.89 (bd, *J* = 10.4 Hz, 1H), 5.52 (dt, *J* = 1.7, 10.4 Hz, 1H), 4.34 (dd, *J* = 8.1, 11.6 Hz, 1H), 4.12-4.19 (m, 1H), 3.44 (s, 3H), 2.93-3.02 (m, 2H), 2.64 (dd, *J* = 7.7, 9.7 Hz 1H), 2.50 (s, 3H), 2.48-2.53 (m, 1H), 1.77 (ddd, *J* = 1.9, 9.4, 13.3 Hz 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 147.7, 146.5, 135.3, 129.1, 128.8, 127.4, 108.1, 104.8, 101.2, 93.9, 73.8, 73.1, 64.1, 56.1, 54.0, 46.2, 43.3, 30.2; HRMS (FAB) Calcd for $M^+$ $C_{18}H_{21}NO_5$: 331.1420, Found 331.1410.

**Tazettine** (**2**). To **1** (19.2 mg, 0.0579 mmol) in methanol (1.5 mL) was added aqueous NaOH (1 mL, 0.1 M). The reaction was stirred for 30 min before removing the methanol *in vacuo*. The aqueous portion was extracted with $CH_2Cl_2$ (7 × 5 mL), and the organic portions were combined, filtered and concentrated. Purification of the product was carried out *via* flash chromatography eluting with 15:85 methanol/ $CH_2Cl_2$ affording tazettine (**2**) as a white film (17.5 mg, 91%); $[\alpha]^{21}_D$ +142.5° (*c* 0.98, $CHCl_3$); {lit.[8] $[\alpha]^{16}_D$ $+150^0$ ($CHCl_3$)}; $^1H$ NMR (400 MHz, $CDCl_3$) δ $^1H$ 6.86 (s, 1H), 6.50 (s, 1H), 6.14 (dt, *J* = 1.4, 10.4 Hz, 1H), 5.90 (s, 2H), 5.61 (dt, *J* = 1.8, 10.4 Hz, 1H), 4.96 (dd, *J* = 0.5, 14.7, 1H), 4.63 (d, *J* = 14.7 Hz, 1H), 4.11-4.17 (m, 1H), 3.46 (s, 3H), 3.30 (d, *J* = 10.6 Hz, 1H), 2.85-2.89 (m, 1H), 2.68 (d, *J* = 10.6 Hz, 1H), 2.40 (s, 3H), 2.19-2.27 (m, 1H), 1.63 (ddd, *J* = 2.2, 10.1, 13.7, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 146.6, 146.4, 130.6, 128.7, 128.0, 125.5, 109.3, 104.0, 102.0, 100.9, 72.9, 70.0, 65.5, 62.0, 56.1, 49.9, 42.0, 26.7; HRMS (FAB) Calcd for $M^+$ $C_{18}H_{21}NO_5$: 331.1420, Found 331.1421.

**References and Notes**:

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1. The preparation of diol **5** could be accomplished by scale-up of the chemistry reported in the following references. Starting with α-methyl-D-mannopyranoside, **5** could be prepared in five steps in 55% overall yield. (a) Horton, D.; Weckerle, W. *Carbohydr. Res.* **1975**, *44*, 227. (b) Thiem, J.; Elvers, J. *Chem. Ber.* **1981**, *114*, 1442. (c) Krohn, K.; Broser, E.; Heins, H. *Carbohydr. Res.* **1987**, *164*, 59.
2. Ketone **7** is particularly sensitive to even mildly acidic conditions and is best used directly after preparation.
3. Wovkulich, P. M.; Uskokovic, M. R. *Tetrahedron* **1985**, *41*, 3455. An improved preparation of this material will be reported in the full paper.
4. The NMR spectra of compounds **11-14**, and all intermediate materials, were complicated by the presence of amide rotational isomers (~3/2).
5. (a) Luche, J. L.; Rodrigues, H. L.; Cragge, P. *J. Chem. Soc., Chem. Commun*. **1978**, 601. (b) Luche, J. L. *J. Am. Chem. Soc*. **1978**, *100*, 2226.
6. Boit, H.-G. *Chem. Ber.* **1954**, *87*, 1339.
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8. Späth, E.; Kahovec, L. *Chem. Ber*. **1934**, *67*, 1501.

# Total Syntheses of (-)-Haemanthidine, (+)-Pretazettine and (+)-Tazettine

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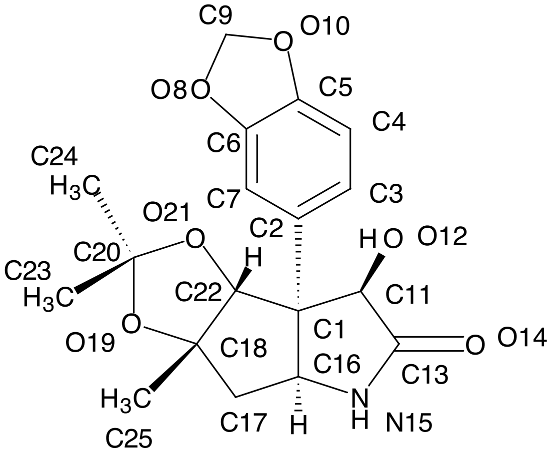
# Crystallographic Data for Compound 10



$C_{18}H_{21}NO_6$

Colorless fine needles from THF/hexane. mp. 238-42°C. ;

Anal. Calcd for $C_{18}H_{21}NO_6$: C, 62.24; H, 6.09; N, 4.03.

Found: C, 62.27; H, 6.17; N, 4.03.

Space Group and Cell Dimensions   Orthorhombic  $P\ 2_12_12_1$

a   6.7137(4)   b  12.4163(7)   c  20.0684(11)
Volume  1672.89(17)A**3
Empirical formula : $C_{18}H_{21}NO_6$
Cell dimensions were obtained from 5613 reflections with 2_ angle
in the range   3.00 -  50.00 degrees.
Crystal dimensions :  0.35  X  0.15  X  0.15  mm
FW =    347.36     Z =    4     F(000) =     736.52
Dcalc  1.379Mg.m-3, mu   0.10mm-1, lambda 0.71073A, $2\_{max}$  50.0
The intensity data were collected on a Siemens SMART diffractometer,
using the omega scan mode.
The h,k,l ranges used during structure solution and refinement are :--
Hmin,max   -7   8;  Kmin,max  -14  14;  Lmin,max -23  23
No. of reflections measured                    16308
No. of unique reflections                       2955
No. of reflections with Inet > 3.0sigma(Inet)  2760
Merging R-value on intensities  0.023
No correction was made for absorption

The last least squares cycle was calculated with
46 atoms, 311 parameters and 2756 out of 2955 reflections.
Weights based on counting-statistics were used.
The residuals are as follows :--
For significant reflections,  RF 0.037, Rw 0.032 GoF  2.47
For all reflections,          RF 0.042, Rw 0.033.
where RF = Sum(Fo-Fc)/Sum(Fo),
Rw = Sqrt[Sum(w(Fo-Fc)**2)/Sum(wFo**2)] and
GoF = Sqrt[Sum(w(Fo-Fc)**2)/(No. of reflns - No. of params.)]
The maximum shift/sigma ratio was  0.001.
In the last D-map, the deepest hole was  -0.190e/A**3,
and the highest peak   0.210e/A**3.
Secondary ext. coeff.    0.6212microns     sigma    0.0840

The following references are relevant to the NRCVAX System.

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   Gabe, E.J., Le Page, Y., Charland,.J.-P., Lee, F.L. and White, P.S. (1989) J. Appl. Cryst., 22, 384-387.
2. Scattering Factors from Int. Tab. Vol. 4 :
   International Tables for X-ray Crystallography, Vol. IV, (1974) Kynoch Press, Birmingham, England.

   The following references may also be relevant.

3. ORTEP Plotting :
   Johnson, C.K., (1976) ORTEP - A Fortran Thermal Ellipsoid Plot Program, Technical Report ORNL-5138, Oak Ridge
4. Pluto Plotting :
   S. Motherwell, University Chemical Laboratory, Cambridge, 1978
5. Missing Symmetry Treatment by MISSYM :
   Le Page, Y., (1988) J. Appl. Cryst., 21, 983-984.
6. Grouping of Equivalent Reflections in DATRD2 :
   Le Page, Y. and Gabe, E.J., (1979) J. Appl. Cryst., 12, 464-466.
7. Extinction Treatment :
   Larson, A.C., (1970) p.293, Crystallographic Computing, Munksgaard, Copenhagen.

15-Nov-1997

Table . Atomic Parameters x,y,z and Biso.
E.S.Ds. refer to the last digit printed.

| | x | y | z | Biso |
|---|---|---|---|---|
| C1 | 0.1238 ( 3) | 0.00922(14) | 0.93039( 9) | 1.98( 8) |
| C2 | 0.1806 ( 3) | -0.10855(15) | 0.92348( 9) | 2.03( 8) |
| C3 | 0.3728 ( 3) | -0.14129(16) | 0.94017( 9) | 2.29( 8) |
| C4 | 0.4341 ( 3) | -0.24907(17) | 0.93686( 9) | 2.44( 9) |
| C5 | 0.2939 ( 3) | -0.32233(15) | 0.91668( 9) | 2.23( 8) |
| C6 | 0.1038 ( 3) | -0.29138(15) | 0.89975( 9) | 2.26( 8) |
| C7 | 0.0425 ( 3) | -0.18630(16) | 0.90203(10) | 2.26( 9) |
| O8 | -0.00999(21) | -0.38103(11) | 0.88551( 7) | 3.08( 6) |
| C9 | 0.1310 ( 3) | -0.46758(17) | 0.87963(11) | 2.90( 9) |
| O10 | 0.31094(21) | -0.43346(10) | 0.91274( 6) | 2.94( 6) |
| C11 | 0.1747 ( 3) | 0.05729(15) | 0.99958( 9) | 2.15( 8) |
| O12 | 0.37300(20) | 0.08935(11) | 1.01054( 7) | 2.52( 6) |
| C13 | 0.0235 ( 3) | 0.14851(15) | 1.00647(10) | 2.22( 8) |
| O14 | 0.03846(19) | 0.22823(10) | 1.04392( 7) | 2.65( 6) |
| N15 | -0.12614(25) | 0.12918(14) | 0.96502( 8) | 2.52( 7) |
| C16 | -0.1037 ( 3) | 0.03113(16) | 0.92486(10) | 2.28( 8) |
| C17 | -0.1489 ( 3) | 0.05137(19) | 0.85189(10) | 2.71( 9) |
| C18 | 0.0386 ( 3) | 0.10476(17) | 0.82343( 9) | 2.48( 8) |
| O19 | 0.10433(21) | 0.04550(13) | 0.76619( 7) | 3.90( 7) |
| C20 | 0.3150 ( 3) | 0.03487(19) | 0.76834(10) | 3.21( 9) |
| O21 | 0.36470(19) | 0.03801(13) | 0.83723( 7) | 3.30( 6) |
| C22 | 0.2068 ( 3) | 0.08409(17) | 0.87383(10) | 2.19( 8) |
| C23 | 0.4214 ( 4) | 0.1251 ( 3) | 0.73262(15) | 4.82(15) |
| C24 | 0.3718 ( 5) | -0.0761 ( 3) | 0.7430 ( 3) | 7.35(21) |
| C25 | 0.0057 ( 5) | 0.22268(22) | 0.80709(17) | 4.51(13) |
| H3 | 0.466 ( 3) | -0.0864 (13) | 0.9530 ( 8) | 2.3 ( 4) |
| H4 | 0.565 ( 3) | -0.2700 (13) | 0.9497 ( 8) | 1.9 ( 4) |
| H7 | -0.090 ( 3) | -0.1673 (14) | 0.8905 ( 9) | 2.3 ( 4) |
| H9a | 0.080 ( 3) | -0.5332 (15) | 0.9017 ( 9) | 2.3 ( 4) |
| H9b | 0.167 ( 3) | -0.4796 (14) | 0.8297 ( 9) | 2.5 ( 4) |
| H11 | 0.1465 (24) | 0.0018 (12) | 1.0348 ( 8) | 0.9 ( 3) |
| H12 | 0.402 ( 4) | 0.1472 (18) | 0.9880 (11) | 4.0 ( 6) |
| H15 | -0.234 ( 3) | 0.1743 (17) | 0.9621 (11) | 3.6 ( 5) |
| H16 | -0.179 ( 3) | -0.0274 (14) | 0.9439 ( 8) | 1.3 ( 3) |
| H17a | -0.176 ( 3) | -0.0165 (15) | 0.8304 ( 9) | 2.0 ( 4) |
| H17b | -0.269 ( 3) | 0.0967 (16) | 0.8451 ( 9) | 3.3 ( 5) |
| H22 | 0.249 ( 3) | 0.1539 (15) | 0.8922 ( 8) | 1.8 ( 4) |
| H23a | 0.380 ( 5) | 0.1262 (24) | 0.6889 (15) | 8.0 ( 8) |
| H23b | 0.564 ( 4) | 0.1099 (18) | 0.7311 (10) | 4.0 ( 5) |
| H23c | 0.390 ( 5) | 0.196 ( 3) | 0.7511 (14) | 7.3 ( 9) |
| H24a | 0.302 ( 6) | -0.129 ( 3) | 0.7750 (16) | 9.5 (10) |
| H24b | 0.324 ( 4) | -0.0613 (22) | 0.6948 (14) | 6.3 ( 8) |
| H24c | 0.518 ( 6) | -0.0836 (23) | 0.7386 (15) | 8.2 ( 8) |
| H25a | -0.082 ( 4) | 0.2275 (22) | 0.7726 (13) | 6.5 ( 7) |
| H25b | -0.046 ( 4) | 0.2600 (17) | 0.8475 (11) | 4.2 ( 6) |
| H25c | 0.139 ( 4) | 0.2651 (19) | 0.7978 (10) | 5.0 ( 6) |

Biso is the Mean of the Principal Axes of the Thermal Ellipsoid

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                 Table of u(i,j) or U values  *100.
               E.S.Ds. refer to the last digit printed

              u11(U)     u22        u33        u12        u13        u23

   C1        1.82( 9)   2.75(11)   2.95(10)  -0.17( 8)  -0.24( 9)   0.13( 8)
   C2        2.33(10)   3.04(11)   2.33( 9)  -0.25( 9)   0.09( 8)   0.19( 8)
   C3        2.45(11)   3.19(12)   3.05(11)  -0.29(10)  -0.19( 9)   0.05( 9)
   C4        2.45(12)   3.89(13)   2.93(11)   0.17(10)  -0.19( 9)   0.28( 9)
   C5        3.44(12)   2.82(11)   2.23(10)   0.17( 9)   0.01( 9)   0.20( 8)
   C6        3.31(12)   3.12(11)   2.16(10)  -0.94( 9)  -0.07( 9)  -0.19( 8)
   C7        2.21(11)   3.45(12)   2.94(11)  -0.17( 9)  -0.12( 9)   0.15( 9)
   O8        3.71( 9)   3.21( 8)   4.78( 9)  -0.53( 7)  -0.27( 7)  -0.53( 7)
   C9        4.04(13)   2.96(12)   4.03(13)  -0.49(11)   0.45(11)  -0.28(10)
   O10       4.41( 8)   2.67( 8)   4.11( 8)   0.04( 7)  -0.53( 7)  -0.06( 6)
   C11       2.21(10)   2.80(11)   3.14(10)  -0.13( 8)  -0.21( 9)   0.51( 9)
   O12       2.53( 8)   3.24( 8)   3.81( 8)  -0.20( 7)  -0.81( 6)   0.21( 7)
   C13       2.38(11)   2.93(11)   3.14(11)  -0.33( 9)   0.34( 9)   0.47( 9)
   O14       2.93( 8)   3.07( 8)   4.08( 8)  -0.05( 7)   0.21( 6)  -0.48( 6)
   N15       1.96( 9)   3.42(10)   4.21(10)   0.24( 9)  -0.10( 8)  -0.45( 8)
   C16       1.89(10)   2.84(11)   3.93(11)  -0.38( 9)   0.00( 9)  -0.14( 9)
   C17       2.26(11)   4.04(14)   4.00(12)   0.14(10)  -0.53(10)  -0.15(10)
   C18       2.53(11)   3.99(13)   2.90(11)   0.11(10)  -0.48( 8)   0.28( 9)
   O19       3.04( 8)   8.27(12)   3.53( 8)  -0.99( 8)  -0.35( 7)  -1.41( 8)
   C20       2.86(12)   5.45(14)   3.88(12)  -0.94(11)   0.30(10)  -1.25(11)
   O21       2.55( 7)   6.34(10)   3.66( 8)   0.88( 8)   0.74( 7)   1.76( 7)
   C22       2.19(10)   2.80(11)   3.34(11)  -0.07( 9)  -0.27( 9)   0.16( 9)
   C23       3.99(17)   9.8 ( 3)   4.56(16)  -0.63(16)   0.26(13)   3.00(18)
   C24       4.72(19)   9.0 ( 3)  14.2 ( 4)  -2.16(19)   3.03(23)  -6.9 ( 3)
   C25       4.60(18)   5.21(16)   7.32(21)   0.55(14)  -1.50(17)   2.26(15)
   H3        2.9( 5)
   H4        2.4( 5)
   H7        3.0( 5)
   H9a       2.9( 5)
   H9b       3.2( 5)
   H11       1.2( 4)
   H12       5.1( 7)
   H15       4.6( 7)
   H16       1.6( 4)
   H17a      2.6( 5)
   H17b      4.2( 6)
   H22       2.3( 5)
   H23a     10.1(11)
   H23b      5.1( 7)
   H23c      9.2(12)
   H24a     12.1(13)
   H24b      7.9(10)
   H24c     10.4(10)
   H25a      8.2( 9)
   H25b      5.3( 7)
   H25c      6.4( 7)

       Anisotropic Temperature Factors are of the form
Temp=-2*Pi*Pi*(h*h*u11*astar*astar+---+2*h*k*u12*astar*bstar+---)
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         DISANG -- The NRCVAX Distance and Angle Program
The Space Group is  P 21 21 21    NonCentrosymmetric
The Equivalent Positions are:
  1)     x      y      z    2) 1/2+x  1/2-y     -z
  3)    -x  1/2+y  1/2-z    4) 1/2-x     -y  1/2+z
The Lattice is Primitive. There are no Centering Vectors

C(1)-C(2)   1.518(3)            N(15)-H(15)   0.918(23)
C(1)-C(11)  1.550(3)            C(16)-C(17)   1.517(3)
C(1)-C(16)  1.555(3)            C(16)-H(16)   0.964(18)
C(1)-C(22)  1.569(3)            C(17)-C(18)   1.533(3)
C(2)-C(3)   1.393(3)            C(17)-H(17a)  0.963(19)
C(2)-C(7)   1.406(3)            C(17)-H(17b)  0.992(23)
C(3)-C(4)   1.402(3)            C(18)-O(19)   1.4339(25)
C(3)-H(3)   0.959(18)           C(18)-C(22)   1.538(3)
C(4)-C(5)   1.370(3)            C(18)-C(25)   1.517(3)
C(4)-H(4)   0.950(19)           O(19)-C(20)   1.421(3)
C(5)-C(6)   1.376(3)            C(20)-O(21)   1.4228(25)
C(5)-O(10)  1.3868(23)          C(20)-C(23)   1.510(4)
C(6)-C(7)   1.369(3)            C(20)-C(24)   1.518(4)
C(6)-O(8)   1.3799(23)          O(21)-C(22)   1.4107(24)
C(7)-H(7)   0.949(21)           C(22)-H(22)   0.983(19)
O(8)-C(9)   1.437(3)            C(23)-H(23a)  0.92(3)
C(9)-O(10)  1.442(3)            C(23)-H(23b)  0.98(3)
C(9)-H(9a)  0.989(19)           C(23)-H(23c)  0.98(3)
C(9)-H(9b)  1.043(19)           C(24)-H(24a)  1.03(4)
C(11)-O(12) 1.4068(23)          C(24)-H(24b)  1.03(3)
C(11)-C(13) 1.527(3)            C(24)-H(24c)  0.99(4)
C(11)-H(11) 1.005(16)           C(25)-H(25a)  0.91(3)
O(12)-H(12) 0.872(23)           C(25)-H(25b)  0.996(24)
C(13)-O(14) 1.2469(24)          C(25)-H(25c)  1.05(3)
C(13)-N(15) 1.326(3)            H(23a)-H(23b) 1.51(4)
N(15)-C(16) 1.468(3)            H(23a)-H(23c) 1.52(4)



C(2)-C(1)-C(11)   113.42(15)          C(17)-C(16)-H(16)     113.7(9)
C(2)-C(1)-C(16)   114.14(15)          C(16)-C(17)-C(18)     105.46(16)
C(2)-C(1)-C(22)   114.54(15)          C(16)-C(17)-H(17a)    108.9(10)
C(11)-C(1)-C(16)  102.31(14)          C(16)-C(17)-H(17b)    112.9(11)
C(11)-C(1)-C(22)  109.97(15)          C(18)-C(17)-H(17a)    111.4(11)
C(16)-C(1)-C(22)  101.16(14)          C(18)-C(17)-H(17b)    111.7(12)
C(1)-C(2)-C(3)    119.46(16)          H(17a)-C(17)-H(17b)   106.4(16)
C(1)-C(2)-C(7)    121.58(17)          C(17)-C(18)-O(19)     109.22(17)
C(3)-C(2)-C(7)    118.94(18)          C(17)-C(18)-C(22)     106.62(16)
C(2)-C(3)-C(4)    122.61(19)          C(17)-C(18)-C(25)     112.24(20)
C(2)-C(3)-H(3)    117.3(10)           O(19)-C(18)-C(22)     102.43(15)
C(4)-C(3)-H(3)    120.0(10)           O(19)-C(18)-C(25)     111.53(19)
C(3)-C(4)-C(5)    116.51(19)          C(22)-C(18)-C(25)     114.22(20)
C(3)-C(4)-H(4)    121.3(10)           C(18)-O(19)-C(20)     109.24(14)
C(5)-C(4)-H(4)    122.2(10)           O(19)-C(20)-O(21)     105.09(15)
C(4)-C(5)-C(6)    121.66(18)          O(19)-C(20)-C(23)     112.81(21)
C(4)-C(5)-O(10)   128.38(18)          O(19)-C(20)-C(24)     108.93(20)
C(6)-C(5)-O(10)   109.89(17)          O(21)-C(20)-C(23)     109.27(20)
C(5)-C(6)-C(7)    122.48(18)          O(21)-C(20)-C(24)     106.9(3)
C(5)-C(6)-O(8)    109.85(17)          C(23)-C(20)-C(24)     113.3(3)
C(7)-C(6)-O(8)    127.53(19)          C(20)-O(21)-C(22)     109.93(15)
C(2)-C(7)-C(6)    117.79(19)          C(1)-C(22)-C(18)      108.28(16)
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| | |
|---|---|
| C(2)-C(7)-H(7) | 121.4(10) |
| C(6)-C(7)-H(7) | 120.7(10) |
| C(6)-O(8)-C(9) | 104.81(15) |
| O(8)-C(9)-O(10) | 107.11(15) |
| O(8)-C(9)-H(9a) | 110.5(11) |
| O(8)-C(9)-H(9b) | 109.9(10) |
| O(10)-C(9)-H(9a) | 109.2(10) |
| O(10)-C(9)-H(9b) | 106.8(11) |
| H(9a)-C(9)-H(9b) | 113.2(14) |
| C(5)-O(10)-C(9) | 104.45(15) |
| C(1)-C(11)-O(12) | 117.24(15) |
| C(1)-C(11)-C(13) | 102.72(15) |
| C(1)-C(11)-H(11) | 108.9(8) |
| O(12)-C(11)-C(13) | 113.90(15) |
| O(12)-C(11)-H(11) | 105.2(9) |
| C(13)-C(11)-H(11) | 108.6(9) |
| C(11)-O(12)-H(12) | 111.4(15) |
| C(11)-C(13)-O(14) | 126.12(17) |
| C(11)-C(13)-N(15) | 108.21(16) |
| O(14)-C(13)-N(15) | 125.66(18) |
| C(13)-N(15)-C(16) | 114.62(17) |
| C(13)-N(15)-H(15) | 121.9(13) |
| C(16)-N(15)-H(15) | 123.5(13) |
| C(1)-C(16)-N(15) | 101.94(15) |
| C(1)-C(16)-C(17) | 107.14(16) |
| C(1)-C(16)-H(16) | 110.8(10) |
| N(15)-C(16)-C(17) | 111.85(17) |
| N(15)-C(16)-H(16) | 110.7(10) |
| C(1)-C(22)-O(21) | 113.78(16) |
| C(1)-C(22)-H(22) | 110.7(10) |
| C(18)-C(22)-O(21) | 106.08(15) |
| C(18)-C(22)-H(22) | 108.0(10) |
| O(21)-C(22)-H(22) | 109.7(10) |
| C(20)-C(23)-H(23a) | 108.6(19) |
| C(20)-C(23)-H(23b) | 109.6(13) |
| C(20)-C(23)-H(23c) | 112.6(18) |
| H(23a)-C(23)-H(23b) | 105.7(22) |
| H(23a)-C(23)-H(23c) | 106(3) |
| H(23b)-C(23)-H(23c) | 113.3(23) |
| C(20)-C(24)-H(24a) | 104.6(19) |
| C(20)-C(24)-H(24b) | 94.3(15) |
| C(20)-C(24)-H(24c) | 111.4(17) |
| H(24a)-C(24)-H(24b) | 123.8(25) |
| H(24a)-C(24)-H(24c) | 116(3) |
| H(24b)-C(24)-H(24c) | 103.7(23) |
| C(18)-C(25)-H(25a) | 108.8(17) |
| C(18)-C(25)-H(25b) | 108.9(13) |
| C(18)-C(25)-H(25c) | 113.5(12) |
| H(25a)-C(25)-H(25b) | 111.1(21) |
| H(25a)-C(25)-H(25c) | 112.4(21) |
| H(25b)-C(25)-H(25c) | 102.0(17) |
| C(23)-H(23a)-H(23b) | 38.5(15) |
| C(23)-H(23a)-H(23c) | 38.0(17) |
| H(23b)-H(23a)-H(23c) | 65.1(19) |
| C(23)-H(23b)-H(23a) | 35.8(14) |
| C(23)-H(23c)-H(23a) | 35.5(16) |

Torsion angles

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| C11 | C1 | C2 | C3 | -51.00(24) | C11 | C1 | C2 | C7 | 127.5( 4) |
| C16 | C1 | C2 | C3 | -167.7( 4) | C16 | C1 | C2 | C7 | 10.85(19) |
| C22 | C1 | C2 | C3 | 76.4( 3) | C22 | C1 | C2 | C7 | -105.1( 3) |
| C2 | C1 | C11 | O12 | 80.6( 3) | C2 | C1 | C11 | C13 | -153.7( 4) |
| C2 | C1 | C11 | H11 | -38.7(15) | C16 | C1 | C11 | O12 | -156.0( 4) |
| C16 | C1 | C11 | C13 | -30.28(20) | C16 | C1 | C11 | H11 | 84.8(16) |
| C22 | C1 | C11 | O12 | -49.10(21) | C22 | C1 | C11 | C13 | 76.6( 3) |
| C22 | C1 | C11 | H11 | -168.4(16) | C2 | C1 | C16 | N15 | 152.3( 4) |
| C2 | C1 | C16 | C17 | -90.1( 3) | C2 | C1 | C16 | H16 | 34.4(17) |
| C11 | C1 | C16 | N15 | 29.38(19) | C11 | C1 | C16 | C17 | 147.0( 4) |
| C11 | C1 | C16 | H16 | -88.5(18) | C22 | C1 | C16 | N15 | -84.2( 3) |
| C22 | C1 | C16 | C17 | 33.45(21) | C22 | C1 | C16 | H16 | 158.0(18) |
| C2 | C1 | C22 | C18 | 100.3( 3) | C2 | C1 | C22 | O21 | -17.32(16) |
| C2 | C1 | C22 | H22 | -141.4(18) | C11 | C1 | C22 | C18 | -130.5( 4) |
| C11 | C1 | C22 | O21 | 111.8( 3) | C11 | C1 | C22 | H22 | -12.3(17) |
| C16 | C1 | C22 | C18 | -22.91(19) | C16 | C1 | C22 | O21 | -140.6( 4) |
| C16 | C1 | C22 | H22 | 95.3(18) | C1 | C2 | C3 | C4 | 178.1( 4) |
| C1 | C2 | C3 | H3 | -3.7(18) | C7 | C2 | C3 | C4 | -0.40(20) |
| C7 | C2 | C3 | H3 | 177.7(19) | C1 | C2 | C7 | C6 | -177.4( 4) |
| C1 | C2 | C7 | H7 | 1.0(19) | C3 | C2 | C7 | C6 | 1.09(19) |
| C3 | C2 | C7 | H7 | 179.5(20) | C2 | C3 | C4 | C5 | -0.55(19) |
| C2 | C3 | C4 | H4 | -178.2(19) | H3 | C3 | C4 | C5 | -178.6(19) |
| H3 | C3 | C4 | H4 | 4. ( 3) | C3 | C4 | C5 | C6 | 0.82(19) |
| C3 | C4 | C5 | O10 | -176.0( 4) | H4 | C4 | C5 | C6 | 178.4(19) |
| H4 | C4 | C5 | O10 | 1.7(18) | C4 | C5 | C6 | C7 | -0.12(21) |
| C4 | C5 | C6 | O8 | -176.2( 4) | O10 | C5 | C6 | C7 | 177.2( 4) |
| O10 | C5 | C6 | O8 | 1.14(14) | C4 | C5 | O10 | C9 | -171.9( 4) |
| C6 | C5 | O10 | C9 | 11.01(21) | C5 | C6 | C7 | C2 | -0.85(19) |
| C5 | C6 | C7 | H7 | -179.3(20) | O8 | C6 | C7 | C2 | 174.4( 4) |
| O8 | C6 | C7 | H7 | -4.0(19) | C5 | C6 | O8 | C9 | -12.84(21) |
| C7 | C6 | O8 | C9 | 171.4( 4) | C6 | O8 | C9 | O10 | 19.46(17) |
| C6 | O8 | C9 | H9a | 138.2(19) | C6 | O8 | C9 | H9b | -96.2(18) |
| O8 | C9 | O10 | C5 | -18.72(18) | H9a | C9 | O10 | C5 | -138.3(19) |
| H9b | C9 | O10 | C5 | 99.0(18) | C1 | C11 | O12 | H12 | 71. ( 3) |
| C13 | C11 | O12 | H12 | -49. ( 3) | H11 | C11 | O12 | H12 | -167. ( 3) |
| C1 | C11 | C13 | O14 | -158.7( 4) | C1 | C11 | C13 | N15 | 20.53(18) |
| O12 | C11 | C13 | O14 | -30.83(18) | O12 | C11 | C13 | N15 | 148.4( 4) |
| H11 | C11 | C13 | O14 | 86.1(16) | H11 | C11 | C13 | N15 | -94.7(16) |
| C11 | C13 | N15 | C16 | -1.18(18) | C11 | C13 | N15 | H15 | 179.0(24) |
| O14 | C13 | N15 | C16 | 178.0( 4) | O14 | C13 | N15 | H15 | -1.8(24) |
| C13 | N15 | C16 | C1 | -18.57(19) | C13 | N15 | C16 | C17 | -132.7( 4) |
| C13 | N15 | C16 | H16 | 99.3(18) | H15 | N15 | C16 | C1 | 161.3(24) |
| H15 | N15 | C16 | C17 | 47.1(24) | H15 | N15 | C16 | H16 | -81. ( 3) |
| C1 | C16 | C17 | C18 | -31.80(20) | C1 | C16 | C17 | H17a | 87.9(19) |
| C1 | C16 | C17 | H17b | -154.1(21) | N15 | C16 | C17 | C18 | 79.1( 3) |
| N15 | C16 | C17 | H17a | -161.2(19) | N15 | C16 | C17 | H17b | -43.2(21) |
| H16 | C16 | C17 | C18 | -154.5(18) | H16 | C16 | C17 | H17a | -35. ( 3) |
| H16 | C16 | C17 | H17b | 83. ( 3) | C16 | C17 | C18 | O19 | 126.3( 4) |
| C16 | C17 | C18 | C22 | 16.33(19) | C16 | C17 | C18 | C25 | -109.4( 4) |
| H17a | C17 | C18 | O19 | 8.3(19) | H17a | C17 | C18 | C22 | -101.7(19) |
| H17a | C17 | C18 | C25 | 132.5(19) | H17b | C17 | C18 | O19 | -110.6(21) |
| H17b | C17 | C18 | C22 | 139.4(21) | H17b | C17 | C18 | C25 | 13.6(21) |
| C17 | C18 | O19 | C20 | -137.5( 4) | C22 | C18 | O19 | C20 | -24.73(21) |
| C25 | C18 | O19 | C20 | 97.9( 4) | C17 | C18 | C22 | C1 | 4.68(18) |
| C17 | C18 | C22 | O21 | 127.2( 4) | C17 | C18 | C22 | H22 | -115.2(18) |
| O19 | C18 | C22 | C1 | -110.0( 3) | O19 | C18 | C22 | O21 | 12.48(15) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| O19 | C18 | C22 | H22 | 130.1(18) | C25 | C18 | C22 | C1 | 129.3( 4) |
| C25 | C18 | C22 | O21 | -108.3( 4) | C25 | C18 | C22 | H22 | 9.4(18) |
| C17 | C18 | C25 | H25a | -67. ( 3) | C17 | C18 | C25 | H25b | 54.3(23) |
| C17 | C18 | C25 | H25c | 167.1(23) | O19 | C18 | C25 | H25a | 56. ( 3) |
| O19 | C18 | C25 | H25b | 177.3(24) | O19 | C18 | C25 | H25c | -69.9(22) |
| C22 | C18 | C25 | H25a | 172. ( 3) | C22 | C18 | C25 | H25b | -67.2(23) |
| C22 | C18 | C25 | H25c | 45.6(22) | C18 | O19 | C20 | O21 | 27.81(19) |
| C18 | O19 | C20 | C23 | -91.1( 4) | C18 | O19 | C20 | C24 | 142.1( 5) |
| O19 | C20 | O21 | C22 | -18.99(18) | C23 | C20 | O21 | C22 | 102.3( 4) |
| C24 | C20 | O21 | C22 | -134.7( 5) | O19 | C20 | C23 | H23a | -59. ( 3) |
| O19 | C20 | C23 | H23b | -173.6(24) | O19 | C20 | C23 | H23c | 59. ( 3) |
| O21 | C20 | C23 | H23a | -175. ( 3) | O21 | C20 | C23 | H23b | 69.9(24) |
| O21 | C20 | C23 | H23c | -57. ( 3) | C24 | C20 | C23 | H23a | 66. ( 3) |
| C24 | C20 | C23 | H23b | -49.2(24) | C24 | C20 | C23 | H23c | -176. ( 3) |
| O19 | C20 | C24 | H24a | -60. ( 3) | O19 | C20 | C24 | H24b | 67. ( 3) |
| O19 | C20 | C24 | H24c | 173. ( 3) | O21 | C20 | C24 | H24a | 53. ( 3) |
| O21 | C20 | C24 | H24b | 180. ( 3) | O21 | C20 | C24 | H24c | -74. ( 3) |
| C23 | C20 | C24 | H24a | 173. ( 3) | C23 | C20 | C24 | H24b | -60. ( 3) |
| C23 | C20 | C24 | H24c | 47. ( 3) | C20 | O21 | C22 | C1 | 122.8( 3) |
| C20 | O21 | C22 | C18 | 3.85(20) | C20 | O21 | C22 | H22 | -112.6(18) |
| C20 | C23 | H23a | H23b | -118. ( 4) | C20 | C23 | H23a | H23c | 122. ( 4) |
| H23b | C23 | H23a | H23b | 0. ( 3) | H23b | C23 | H23a | H23c | -121. ( 5) |
| H23c | C23 | H23a | H23b | 121. ( 6) | H23c | C23 | H23a | H23c | 0. ( 4) |
| C20 | C23 | H23b | H23a | 117. ( 3) | H23a | C23 | H23b | H23a | 0. ( 4) |
| H23c | C23 | H23b | H23a | -116. ( 5) | C20 | C23 | H23c | H23a | -119. ( 4) |
| H23a | C23 | H23c | H23a | 0. ( 4) | H23b | C23 | H23c | H23a | 116. ( 5) |
| C23 | H23a | H23b | C23 | 0.0( 6) | H23c | H23a | H23b | C23 | 36. ( 3) |
| C23 | H23a | H23c | C23 | 0.0( 6) | H23b | H23a | H23c | C23 | -36. ( 3) |