A New Total Synthesis of the Marine Antitumor Alkaloid (-)- Agelastatin A

Mathias M. Domostoj, Ed Irving, Feodor Scheinmann, and Karl J. Hale*

Supporting Information □ Part 1

Experimental Procedures

(10 Pages Inclusive of Title Page)

Experimental Procedures for the Synthesis of (-)-Agelastatin A from Oxazolidinone 3

The preparation of (-)-**3** is described in the Supplementary Information of the following paper:
Hale, K.J.; Domostoj, M.M.; Tocher, D.A.; Irving, E.; Scheinmann, F. *Org. Lett.*, **2003**, 5, 2927.

N-Acyl Oxazolidinone 8

To a stirred solution of (-)-**3** (3.0 g, 9.86 mmol) in dry THF (95 mL) at -78°C under N_2 was added a solution of *n*-BuLi (6.2 mL, 1.6 M in hexanes, 9.92 mmol) dropwise over 5 min, and 15 min later, carbamoyl chloride **5**⁶ (3.6 g, 19.7 mmol) in dry THF (5 mL) was added dropwise over 5 min. The cooling bath was removed, the reaction mixture was allowed to warm to RT over 15 min, and the reaction vessel was then transferred to an oil bath, where it was heated at reflux for 4 h. DABCO (6.6 g, 112.2 mmol) was then added in one portion and the heating at reflux was continued for 18 h. The reactants were then cooled to RT, and sat. aq. NH_4Cl (20 mL) and brine (30 mL) were added, and the organic layer was separated. The aqueous layer was then extracted with EtOAc (2 x 50 mL), and the combined organic layers were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was dissolved in the minimum amount of CH_2Cl_2 needed to fully solubilise it, and applied to a SiO_2 flash column packed with petrol. The product was then gradient eluted with 7:3 Petrol:EtOAc through to 1:1 Petrol:EtOAc to give **8** (4.2 g, 94%) as a white solid.

Data for **8**: $[\alpha]_{\text{D}}^{20} -80.7^\circ$ (*c* 0.5, MeOH); IR (KBr) 2954 (w), 1769 (s), 1685 (s), 1482 (w), 1453 (m), 1420 (w), 1403 (w), 1370 (s), 1324 (s), 1284 (m), 1254 (m), 1203 (s), 1167 (w), 1135 (s), 1111 (m), 1079 (s), 1042 (s), 1003 (w), 987 (w), 945 (w), 892 (m), 856 (s), 840 (s), 809 (m), 795 (m), 752 (m), 733 (s), 718 (w), 697 (s); $^1\text{H-NMR}$ (400 MHz, CDCl_3 , 323K) δ 7.12-6.90 (m, 5 H, Ph), 5.54 (dd, $J = 5.7, 2.4$ Hz, 1 H, H5), 5.40 (ddd, $J = 5.7, 1.6, 1.6$ Hz, 1 H, H6), 4.87 (br ddd, $J = 7.3, 0.9$ Hz, 1 H, H6a), 4.36 (d, $J = 7.3$ Hz, 1 H, H3a), 4.34 (d, $J = 15.4$ Hz, 1H, PhCH_2), 4.28 (d, $J = 15.4$ Hz, 1 H, PhCH_2), 4.26 (s, 1 H, H4), 3.98 (br s, 1 H, NH), 3.02 (m, 2 H, SES), 2.63 (s, 3 H, NMe), 1.01 (m, 2 H, SES), -0.06 (TMS); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3 , 363 K, some resonances overlap and are hidden by the NMR solvent peaks) δ 154.2 (C=O), 152.3 (C=O), 137.2 (arom.), 136.7 (C5), 131.8 (C6), 128.1 (arom), 128.0 (arom.), 81.9 (C6a), 64.9 (C4), 64.4 (C3a), 54.0 (CH_2), 50.8 (SES), 36.0 (NMe), 11.3 (SES), -1.8 (TMS). CI Methane HRMS: Calcd. for $\text{C}_{20}\text{H}_{30}\text{N}_3\text{O}_5\text{SSi}$: ($\text{M}+\text{H}$)⁺ 452.1677. Found: 452.16673.

Pyrrole carboxamide 9

To a vigorously stirred suspension of the lithium carboxylate salt of 5-trimethylsilyl-pyrrole-2-carboxylic acid³ (7.28 g, 38.5 mmol) in dry CH_2Cl_2 (77 mL) under an N_2 atmosphere was added oxalyl chloride (3.4 mL, 38.5 mmol) in one portion followed by 4 drops of dry DMF. The reactants were stirred at RT for 2 h, and then taken up in a syringe, and added via syringe pump (flow rate 20 mL/h) to a solution of **8** (8.69 g, 19.2 mmol) in dry THF (116 mL) containing freshly distilled Et_3N (13.5 mL, 96.0 mmol) and 4-dimethylaminopyridine (235 mg, 1.92 mmol). When the addition of **6** was complete, sat. aq. NaHCO_3 (50 mL) was added. The mixture was then partitioned between brine (150 mL) and CH_2Cl_2 (300 mL). The organic layer was separated, dried over MgSO_4 , filtered and concentrated *in vacuo*. The residue was taken up in the minimum amount of CH_2Cl_2 needed to fully dissolve it, and applied to a SiO_2 flash column packed with petrol. The product was then eluted with a gradient 85:15 to 7:3 Petrol:EtOAc to give **9** (10.5 g, 89%) as a colourless oil.

Data for **9**; $[\alpha]_{\text{D}}^{25} -113^\circ$ (c 0.4, MeOH); IR (NaCl neat film) 3335 (w), 2955 (w), 1777 (s), 1680 (s), 1537 (w), 1484 (w), 1452 (w), 1404 (w), 1351 (s), 1251 (s), 1173 (s), 1149 (s), 1054 (m), 952 (w), 918 (w), 842 (s), 803 (w), 757 (m), 700 (w), 631 (w); $^1\text{H-NMR}$ (400 MHz, C_6D_6 , 343 K) δ 9.51 (br s, 1 H, NH pyrrole), 7.35 (dd, $J = 3.8, 2.2$ Hz, 1 H, pyrrole), 7.24-7.18 (m, 4 H, Ph), 7.06 (m, 1 H, Ph), 6.35 (dd, $J = 3.8, 2.5$ Hz, 1 H, pyrrole), 5.54 (ddd, $J = 5.7, 1.8, 1.8$ Hz, 1 H, H5), 5.51-5.43 (m, 3 H, H6 + H3a + H6a), 5.28 (m, 1 H, H4), 4.48 (d, $J = 15.0$ Hz, 1H, PhCH_2), and 4.40 (d, $J = 15.5$ Hz, 1 H, PhCH_2), 3.79-3.71 (m, 1 H, SES), 3.59-3.49 (m, 1 H, SES), 2.73 (s, 3 H, NMe), 1.27-1.17 (m, 2 H, SES), 0.05 (s, 9 H, TMS), -0.08 (s, 9 H, TMS); $^{13}\text{C-NMR}$ (100 MHz, C_6D_6 , 343 K, some resonances overlap and are hidden by the NMR solvent peaks) δ 162.9 (C=O), 154.4 (C=O), 152.8 (C=O), 141.3 (C6), 137.1 (C5), 134.1 (arom), 133.1 (alkene), 130.6 (pyrrole), 129.0 (arom.), 121.7 (pyrrole), 119.6 (pyrrole), 83.4 (C6a), 70.9 (C4), 62.2 (C3a), 53.7 (CH_2), 52.0 (SES), 35.7 (NMe), 10.6 (SES), -1.6 (TMS), -2.1 (TMS). Electrospray HRMS: Calcd. for $\text{C}_{28}\text{H}_{40}\text{N}_4\text{O}_6\text{SSi}_2\text{Na}$: $(\text{M}+\text{Na})^+$ 639.2114. Found: 639.21130.

Pyrrole carboxamide **10**

To a degassed solution of the sulfonamide **9** (5.00 g, 8.11 mmol) in freshly distilled toluene (42 mL) under N_2 was added Bu_3SnH (3.4 mL, 12.6 mmol) and the mixture was brought to reflux. AIBN (4.40 g, 26.7 mmol) was then added in 32 equal portions [137 mg, (0.1 equiv)] approx. every 15 min over 8 h. The mixture was allowed to cool to RT, and the solvent was removed *in vacuo*. The organotin by-products were removed by gradient elution SiO_2 flash chromatography with 9:1 to 8:2 Petrol/EtOAc. The product **10** (2.20 g, 60%) eluted with 7:3 Petrol/EtOAc and was obtained as a yellow oil.

Data for **10**: $[\alpha]_{\text{D}}^{25} -289^\circ$ (*c* 1, MeOH); IR (KBr) 2956 (m), 2362 (w), 1779 (s), 1696 (s), 1621 (m), 1577 (m), 1549 (w), 1521 (m), 1481 (w), 1455 (m), 1401 (w), 1354 (s), 1251 (m), 1194 (s), 1147 (w), 1051 (s), 992 (w), 960 (w), 842 (s), 800 (m), 760 (m); $^1\text{H-NMR}$ (500 MHz, CDCl_3 , 328 K) δ 9.19 (br s, 1 H, NH pyrrole), 7.34-7.24 (m, 5 H, Ph), 6.54 (dd, $J = 3.5, 2.4$ Hz, 1 H, pyrrole), 6.35 (dd, $J = 3.3, 3.0$ Hz, 1 H, pyrrole), 6.13 (d, $J = 7.3$ Hz, 1 H, NHCO of urea), 6.07 (br s, 2 H, H5 + H6), 5.65 (d, $J = 7.5$ Hz, 1 H, H6a), 4.89 (apparent d, $J = 7.3$ Hz, 1H, H3a), 4.73 (d, $J = 15.3$ Hz, 1 H, CH_2Ph), 4.51 (d, $J = 15.3$ Hz, 1H, CH_2Ph), 2.96 (s, 3 H, NMe), 0.25 (s, 9 H, TMS); $^{13}\text{C-NMR}$ (125 MHz, CDCl_3 , 328 K) δ 160.8 (C=O), 153.6 (C=O), 153.0 (C=O), 136.5 (arom.), 136.4 (arom.), 136.1 (alkene), 131.7 (alkene), 128.8 (arom.), 128.7 (arom.), 127.8 (arom.), 127.6 (arom.), 118.4 (pyrrole), 110.1 (pyrrole), 82.8 (C6a), 63.8 (C3a), 61.7 (C4), 53.7 (CH_2), 36.1 (NMe), -1.2 (TMS). FAB HRMS: Calcd. for $\text{C}_{23}\text{H}_{29}\text{N}_4\text{O}_4\text{Si}$: ($\text{M}+\text{H}$) $^+$ 453.19592. Found: 453.19528.

Cyclopentenol **12**

To a vigorously stirred solution of oxazolidinone **10** (3.55 g, 7.84 mmol) in THF:H₂O (9:1) (100 mL) at RT was added LiOH.H₂O (3.29 g, 78.5 mmol) in one portion, and the solution stirred at RT for 128 h. The solvents were then removed *in vacuo*, and the residue was partitioned between EtOAc (100 mL) and H₂O (100 mL). The layers were separated, and the aqueous layer was further extracted with EtOAc (2 x 100 mL). The combined organic layer was washed with H₂O (50 mL), sat. aq. NH₄Cl (50 mL), brine (50 mL), and dried over MgSO₄; it was then filtered and concentrated *in vacuo*. The residue was then purified by SiO₂ flash chromatography using EtOAc as eluent to give **12** (1.32 g, 40%) as a white foam, as well as some recovered **10** (1.72 g, yield of the reaction based upon recovered **10** = 77 %).

Data for **12**: $[\alpha]_D^{25}$ -204.1 ° (*c* 1, MeOH); IR (neat) 3312 (m), 2956 (w), 1633 (s), 1555 (m), 1527 (s), 1453 (w), 1389 (w), 1339 (w), 1250 (m), 1203 (m), 1148 (w), 1049 (w), 950 (w), 841 (m), 758 (w), 699 (w); ¹H-NMR (500 MHz, CDCl₃, 298 K) δ 9.51 (br s, 1H, pyrrole NH), 7.50 (d, *J* = 5.9 Hz, 1 H, pyrrole CONH), 7.31-7.20 (m, 5 H, Ph), 6.83 (dd, *J* = 3.6, 2.3 Hz, 1 H, pyrrole), 6.41 (dd, *J* = 3.6, 2.6 Hz, 1 H, pyrrole), 6.18 (dd, *J* = 6.1, 1.4 Hz, H3), 6.07 (ddd, *J* = 5.1, 2.4, 2.4 Hz, 1 H, H2), 5.87 (d, *J* = 7.0 Hz, urea NH), 5.08 (m, 1 H, H4), 4.66 (br s, 1 H, H1), 4.51 (d, *J* = 15.9 Hz, CH₂Ph), 4.47 (d, *J* = 15.9 Hz, 1H, CH₂Ph), 4.19 (dd, *J* = 13.2, 7.1 Hz, 1 H, H5), 3.58 (br s, 1 H, OH), 2.84 (s, 3 H, NMe), 0.30 (s, 9 H, TMS); ¹³C-NMR (125 MHz, CDCl₃, 298 K) δ 162.3 (C=O), 159.0 (C=O), 137.6 (arom.), 137.2 (C3), 135.8 (arom.), 133.1 (C2), 129.2 (arom.), 128.6 (arom.), 127.4 (arom.) 127.2 (arom.), 118.5 (pyrrole), 111.1 (pyrrole), 96.1 (pyrrole C with Me₃Si), 73.2 (C1), 60.0 (C4), 59.9 (C5), 52.2 (CH₂), 34.0 (NMe), -1.1 (TMS). FAB HRMS: Calcd. for C₂₂H₃₁N₄O₃Si: (M+H)⁺ 427.2167. Found: 427.21697.

Cyclopentenone 2

To a stirred solution of alcohol **12** (1.32 g, 3.10 mmol) in DMF (31 mL) was added pyridinium dichromate (5.82 g, 15.5 mmol) and the mixture was stirred at RT for 2 h. The mixture was then partitioned between EtOAc (500 mL) and H₂O (100 mL), and the organic layer was separated and washed successively with H₂O (6 x 50 mL) and brine (50 mL). After being dried over MgSO₄, the organic fraction was filtered and the solvent was removed *in vacuo*. The residue was then purified by SiO₂ flash chromatography using EtOAc to give **2** (0.95 g, 73%) as a colorless oil.

Data for **2**: $[\alpha]_D^{25} -242^\circ$ (*c* 1, MeOH); IR (NaCl neat film) 2956 (m), 1725 (s), 1835 (s), 1553 (s), 1535 (s), 1452 (w), 1388 (w), 1335 (m), 1250 (m), 1199 (m), 1148 (w), 1117 (w), 1080 (w), 1049 (w), 979 (w), 842 (s), 798 (w), 759 (m), 699 (w); ¹H-NMR (500 MHz, CDCl₃, 298 K) δ 9.33 (br s, 1 H, NH pyrrole), 7.88 (d, *J* = 6.0 Hz, 1 H, H3), 7.76 (m, 1 H, pyrrole CONH), 7.31-7.18 (m, 5 H, Ph), 6.77 (dd, *J* = 3.3, 2.4 Hz, 1 H, pyrrole), 6.38 (dd, *J* = 3.4, 2.7 Hz, 1 H, pyrrole), 6.29 (d, *J* = 6.1 Hz, 1 H, H2), 5.32 (d, *J* = 4.4 Hz, 1 H, urea NH), 4.71 (br s, 1 H, H4), 4.54 (d, *J* = 15.8 Hz, 1H, CH₂Ph), 4.41 (d, *J* = 15.8 Hz, CH₂Ph), 4.37 (dd, *J* = 4.3, 4.3 Hz, 1 H, H5), 2.87 (s, 3 H, NMe), 0.24 (s, 9 H, TMS); ¹³C-NMR (125 MHz, CDCl₃, 298 K) δ 201.3 (C=O ketone), 162.3 (C=O), 160.7 (C3), 158.9 (C=O), 137.1 (arom.), 136.1 (arom.), 131.4 (C2), 128.9 (arom.), 128.8 (arom.), 127.5 (arom.), 127.3 (arom.), 118.5 (pyrrole), 111.1 (pyrrole.), 62.7 (C5), 59.2 (C4), 52.3 (CH₂), 34.3 (NMe), -1.1 (TMS). FAB HRMS: Calcd. for C₂₂H₂₉N₄O₃Si: (M+H)⁺ 425.2011. Found: 425.20174.

Tricyclic Pyrrolocyclopentanone **4** Via **18**

To a solution of the α,β -unsaturated ketone **2** (680 mg, 1.61 mmol) in dry THF (16 mL) at 0 °C was added *N*-bromosuccinimide (NBS) (572 mg, 3.21 mmol) in one portion. The mixture was stirred for 2 h at 0 °C and then at RT for 1 h. To the reaction mixture was then added Hünig's base (1.4 mL, 8.03 mmol) dropwise, and the stirring continued overnight (18 h). Sat. aq. NH_4Cl (20 mL) was then added, and the solution was multiply extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with brine (10 mL) and dried over MgSO_4 . After filtration and removal of the solvents *in vacuo* a residue was obtained that was used directly for the next step; the residue was a mixture of components that contained **18** as the major product, along with other di- and mono-bromopyrroles.

A solution of the above product mixture containing **18** was dissolved in MeOH (16 mL) and solid NaOAc (396 mg, 4.83 mmol) was added followed by 10% Pd on C (wet) (339 mg, *ca.* 0.161 mmol). The mixture was hydrogenated under an atmosphere of H_2 at 1 atm for 2 h. The suspension was then filtered through Celite, and the filtrate concentrated *in vacuo*. The residue was taken up in EtOAc (50 mL), washed with H_2O (5 mL) and brine (5 mL), dried over MgSO_4 , filtered, and concentrated *in vacuo*. Purification of the residue by SiO_2 flash chromatography using EtOAc:MeOH 95:5 removed the faster-moving undesired products followed by **4** (195 mg, 35% over 3 steps) as a colorless oil.

Data for **4**: $[\alpha]_D -79.3^\circ$ (*c* 0.3, MeOH); IR (NaCl neat film) 3320 (s), 2922 (m), 1756 (s), 1665 (s), 1533 (s), 1470 (m), 1420 (m), 1391 (m), 1358 (m), 1317 (m), 1267 (m), 1235 (m), 1199 (m), 1139 (m), 1065 (m), 910 (s), 731 (s), 648 (m); $^1\text{H-NMR}$ (500 MHz, CDCl_3 , 298 K) δ 7.72 (br s, 1 H, pyrrole CONH), 7.30-7.15 (m, 5 H, arom.), 6.86 (dd, $J = 3.8, 1.4$ Hz, 1 H, pyrrole), 6.78 (dd, $J = 2.5, 1.6$ Hz, 1 H,

pyrrole), 6.25 (dd, $J = 3.8, 2.7$ Hz, 1 H, pyrrole), 6.10 (d, $J = 5.8$ Hz, 1 H, CONH urea), 4.84 (dd, $J = 5.7, 5.7$ Hz, 1 H, H4), 4.55 (m, 1 H, H3), 4.47 (d, $J = 16.0$ Hz, 1 H, $-\text{CH}_2\text{Ph}$), 4.30 (d, $J = 16.0$ Hz, 1 H, $-\text{CH}_2\text{Ph}$), 3.59 (m, 1 H, H2), 3.16 (dd, $J = 18.8, 6.1$ Hz, 1 H, H5), 3.01 (d, $J = 18.8$, 1 H, H5), 2.77 (s, 3 H, N-CH₃); ¹³C-NMR (125 MHz, CDCl₃ 298 K) δ 207.5 (C=O ketone), 159.9 (C=O), 157.7 (C=O), 137.0 (arom.), 128.7 (arom.), 127.4 and 127.1 (arom.), 123.4 (pyrrole), 122.8 (pyrrole), 115.2 (pyrrole), 111.2 (pyrrole), 62.3 (C2), 55.8 (C3), 52.1 (CH₂), 50.6 (C4), 42.3 (C5), 34.2 (N-CH₃); FAB HRMS: Calcd. for C₁₉H₂₁N₄O₃: (M+H)⁺ 353.16136. Found: 353.16339.

TLC picture at the end of each step in this one-pot reaction sequence (anisaldehyde stain):

NBS Step

Hunig's Cyclisation

Hydrogenation

(-)-Debromoagelastatin A (20)

To a solution of **4** (165 mg, 0.468 mmol) in freshly distilled THF (4.7 mL) was added 20% Pd(OH)₂ on carbon (65 mg). The mixture was hydrogenated under a atmosphere of H₂ (1 atm) for 23 h at RT, then diluted with methanol (20 mL) and filtered through Celite. The filter pad was washed with MeOH to remove all of the products, and the combined filtrate was concentrated *in vacuo*. The residue was purified by SiO₂ flash chromatography, eluting with an 85:15 mixture of EtOAc/MeOH to give **20** (81 mg, 66%) as a white solid.

Data for **20**: $[\alpha]_D^{25}$ -64.8 ° (*c* 0.48, MeOH); IR (KBr) 3286 (br s), 1652 (br s), 1553 (m), 1474 (m), 1419 (m), 1377 (m), 1302 (m), 1266 (w), 1210 (w), 1133 (w), 1072 (w), 753 (w); ¹H-NMR (500 MHz, CD₃OD, 298 K) δ 7.02 (dd, *J* = 2.6, 1.6 Hz, 1 H, H1), 6.88 (dd, *J* = 3.9, 1.6 Hz, 1 H, H3), 6.22 (dd, *J* = 3.9, 2.6 Hz, 1 H, H2), 4.65 (apparent dt, *J* = 9.7, 6.1 Hz, 1 H, H9a), 4.00 (d, *J* = 5.4 Hz, 1 H, H5a), 3.80 (s, 1 H, H5b), 2.79 (3H, NMe), 2.61 (dd, *J* = 13.3, 6.4 Hz, 1 H, H9), 2.27 (dd, *J* = 13.3, 10.3 Hz, 1 H, H9); ¹³C-NMR (125 MHz, CD₃OD, 298 K) δ 162.1 (C7), 161.3 (C4), 125.6 (C1), 122.9 (C3a), 115.4 (C3), 111.1 (C2), 95.8 (C8a), 68.0 (C5b), 62.9 (C5a), 55.6 (C9a), 41.6 (C9), 24.2 (N-Me). Electrospray HRMS: Calcd. for C₁₂H₁₅N₄O₃: (M+H)⁺ 263.1145. Found: 263.11333.

(-)-Agelastatin A

To a stirred solution of **20** (69 mg, 0.263 mmol) in MeOH (5 mL) and freshly distilled THF (10 mL) at 0°C was added recrystallised *N*-bromosuccinimide (NBS) (23.4 mg, 0.132 mmol). The cold bath was removed immediately after the addition, and the reaction mixture was allowed to warm to RT with stirring. After 2 h, a sample of the reaction mixture was concentrated and analyzed by ¹H NMR; this showed a 56% conversion of (-)-debromoagelastatin A (**20**) to (-)-agelastatin A (**1**). The mixture was recooled to 0°C, and more NBS (18.4 mg, 0.103 mmol) was added. The ice bath was removed and the reactants were stirred for a further 2 h at RT. The solution was then concentrated *in vacuo*, and the residue was purified by SiO₂ flash chromatography, eluting with 8:2 EtOAc/MeOH, to give (-)-agelastatin A (75.4 mg, 84%) as a white solid.

Data for (-)-agelastatin A: $[\alpha]_D^{25} -84.2^{\circ}$ (*c* 1, MeOH); IR (KBr) 3280 (m), 1652 (s), 1554 (m), 1424 (s), 1377 (m), 1304 (w), 1269 (w), 1196 (w), 1139 (w), 1091 (w), 935 (w), 749 (w), 663 (w); ¹H-NMR (500 MHz, CD₃OD, 298 K) δ 6.90 (d, *J* = 4.1 Hz, 1 H, H3), 6.31 (d, *J* = 4.1 Hz, 1 H, H2), 4.58 (m, 1 H, H9a), 4.07 (d, *J* = 5.5 Hz, 1 H, H5a), 3.88 (s, 1 H, H5b), 2.80 (s, 3 H, N-Me), 2.63 (dd, *J* = 13.0, 6.5 Hz, 1 H, H9), 2.09 (dd, *J* = 12.6, 12.6 Hz, 1 H, H9); ¹³C-NMR (125 MHz, CD₃OD, 298 K) δ 161.4 (C7), 161.1 (C4), 124.1 (C3a), 116.0 (C3), 113.8 (C2), 107.2 (C1), 95.6 (C8a), 67.4 (C5b), 62.2 (C5a), 54.3 (C9a), 40.0 (C9), 24.2 (N-Me). CI Methane HRMS: Calcd. for C₁₂H₁₄N₄O₃Br (M+H)⁺ 341.0251. Found: 341.0251.