Concise Total Syntheses of (+)-Haplocidine and (+)-Haplocine Via Late-Stage Oxidation of (+)-Fendleridine Derivatives.

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Supporting Information

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks, modified Schlenk (Kjeldahl shape) flasks or glass pressure vessels. The flasks were fitted with rubber septa or Teflon-wrapped glass stoppers, and reactions were conducted under a positive pressure of argon. Cannulae or gas-tight syringes with stainless steel needles were used to transfer air- or moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al.[1] using granular silica gel (60-Å pore size, 40–63 μm, 4–6% H_2O content, Zeochem) or non-activated alumina (80–325 mesh, chromatographic grade). Analytical thin layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm) or basic alumina impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to short wave ultraviolet light (254 nm) and irreversibly stained by treatment with an aqueous solution of ceric ammonium molybdate (CAM) or an aqueous solution of potassium permanganate ($KMnO_4$) followed by heating (~ 1 min) on a hot plate (~ 250 ºC). Organic solutions were concentrated at 29–30 °C on rotary evaporators capable of achieving a minimum pressure of ~2 torr.

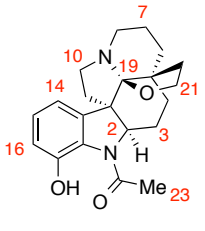
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile, tetrahydrofuran, *N*,*N*-dimethylformamide, and methanol were purchased from J. T. Baker (Cycletainer™) and were purified by the method of Grubbs et al. under positive argon pressure.[2] Diisopropylethylamine and *N*,*N*-diisopropylamine were dried by distillation over calcium hydride under an inert nitrogen atmosphere and used directly. *N*,*N*'-Dimethylpropylene urea was distilled from calcium hydride and stored sealed under argon atmosphere. The molarity of *n*-butyllithium solutions was determined by titration against diphenylacetic acid[3] (average of three titrations). Trifluoromethanesulfonic anhydride was purchased from Oakwood Products, Inc. 1-Decanol, crotonyl chloride, trifluoroacetic acid and thiophenol were purchased from Alfa Aesar. All other solvents and chemicals were purchased from Sigma−Aldrich.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Varian inverse probe INOVA-500, Varian INOVA-500, Bruker Advance 400, or with a Bruker Advance III 400 spectrometer. Chemical shifts are recorded in parts per million on the δ scale and are referenced from the residual protium in the NMR solvent ($CHCl_3$: δ 7.26). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance spectra were recorded with a Varian inverse probe INOVA-500, Varian INOVA-500, Bruker Advance 400, or with a Bruker Advance III 400 spectrometer and are recorded in parts per million on the δ scale and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.16). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Fluorine-19 nuclear magnetic resonance spectra were recorded with a Bruker Advance III 400 spectrometer and are recorded in parts per million on the δ scale and are referenced from the fluorine resonances of trifluoroacetic acid (CF_3CO_2H δ–76.55). Data are

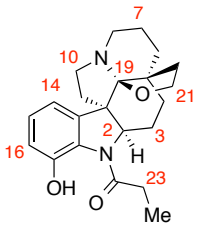
[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. *Organometallics* **1996**, *15*, 1518.
[3] Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant(s) in Hertz, assignment]. Infrared data were obtained with a Perkin−Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad), assignment]. Optical rotations were measured on a Jasco-1010 polarimeter. We thank Dr. Li Li at the Massachusetts Institute of Technology Department of Chemistry instrumentation facility for obtaining mass spectroscopic data. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics APEXIV 4.7 Tesla FT-ICR-MS using a direct analysis in real time (DART) ionization source.

Positional Numbering System. At least two numbering systems exist in the literature for the *aspidosperma* alkaloids. For direct comparison between structures, the system employed by Ban for (+)-fendleridine is optimal and is used throughout this report.[4]



(+)-haplocidine (**1**)



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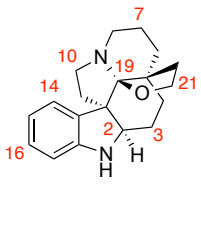
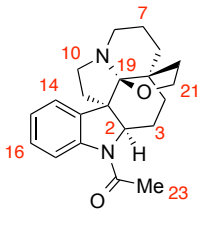
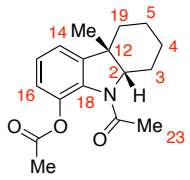


(+)-fendleridine (**3**)



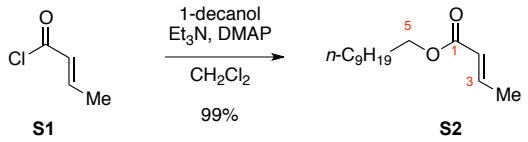
(+)-acetylaspidoalbidine (**4**)

For the tricyclic model system, we have mimicked the numbering system as utilized in the aspidosperma alkaloids for clarity of discussion.



(±)-**23a**

[4] Honma, Y.; Ohnuma, T.; Ban, Y. *Heterocycles* **1976**, *5*, 47.



***n*-Decyl-*E*-but-(2)-enoate S2:**

Triethylamine (13.0 mL, 93.0 mmol, 1.50 equiv) was added via syringe to a solution of 1-decanol (17.7 mL, 93.0 mmol, 1.50 equiv), 4-(dimethylamino)-pyridine (1.51 g, 12.4 mmol, 0.200 equiv), and crotonyl chloride (6.00 mL, 62.0 mmol, 1 equiv), in dichloromethane (300 mL) at 0 °C, and the resulting mixture was warmed to 23 °C after 10 min. After 11 h, saturated aqueous ammonium chloride solution (200 mL) and dichloromethane (200 mL) were sequentially added, and the layers were separated. The aqueous layer was further extracted with dichloromethane (3 × 250 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution (200 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (10 → 20% dichloromethane in hexanes) to afford *n*-decyl-*E*-but-(2)-enoate **S2** (13.9 g, 99.0%) as a colorless oil. Assignments were made using additional information from a gCOSY experiment.

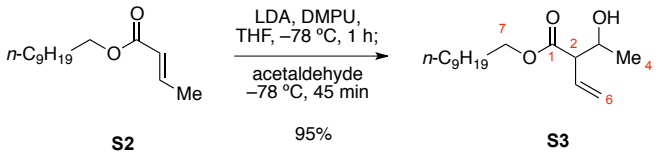
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, 1.5:1 *E*:*Z* mixture, * denotes the *E* isomer): δ 7.05–6.88 (m, 1H, C_3**H***), 5.99–5.87 (m, 1H, C_3**H**), 5.84 (dq, *J* = 15.5, 1.7 Hz, 1H, C_2**H***), 5.21–5.12 (m, 1H, C_2**H**), 4.11 (t, *J* = 6.8 Hz, 2H, C_5**H**$_2$*), 4.08 (t, *J* = 6.8 Hz, 2H, C_5**H**$_2$), 3.09 (app-dt, *J* = 7.0, 1.4 Hz, 3H, C_4**H**$_3$), 1.87 (dd, *J* = 6.9, 1.7 Hz, 3H, C_4**H**$_3$*), 1.77–1.58 (m, 4H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***), 1.44–1.13 (m, 28H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***), 0.88 (t, *J* = 6.9 Hz, 6H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 1.5:1 *E*:*Z* mixture, * denotes the *E* isomer): δ 171.7 (**C**$_1$), 166.8 (**C**$_1$*), 144.4 (**C**$_3$*), 130.5 (**C**$_3$), 123.0 (**C**$_2$*), 118.5 (**C**$_2$), 65.0 (**C**$_5$), 64.5 (**C**$_5$*), 39.3 (**C**$_4$*), 32.0, 29.7 (2C) 29.6, 29.4 (3C), 28.8, 28.7, 26.1, 26.0, 22.8, 18.1 (**C**$_4$), 14.2 .

FTIR (thin film) cm^{-1}: 2926 (s), 2856 (s), 1740 (s), 1468 (w), 1259 (m), 1177 (s), 992 (m).

HRMS (DART) (*m/z*): calc'd for $C_{14}H_{27}O_2$ $[M+H]^+$: 227.2006, found: 227.2012.

TLC (20% dichloromethane in hexanes), R*f*: 0.16 ($KMnO_4$).



S2 **S3**

***n*-Decyl-2-(1-hydroxyethyl)but-(3)-enoate S3:**

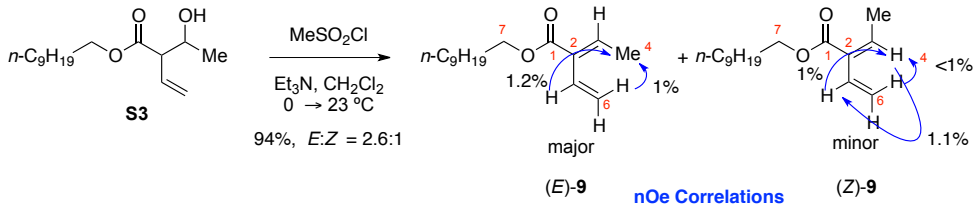
A solution of *n*-butyllithium (1.84 M in hexanes, 17.3 mL, 31.8 mmol, 1.20 equiv) was added via syringe to a solution of *N*,*N*-diisopropylamine (4.81 mL, 34.5 mmol, 1.30 equiv) in tetrahydrofuran (60 mL) at −78 °C, and the resulting mixture was warmed to 0 °C. After 10 min, the mixture was cooled to −78 °C. After 10 min, *N*,*N'*-dimethylpropylene urea (3.85 mL, 31.8 mmol, 1.20 equiv) was added via syringe. After 30 min, an ice-cooled solution of *n*-decyl-*E*-but-(2)-enoate **S2** (6.00 g, 26.5 mmol, 1 equiv) in tetrahydrofuran (60 mL) was added via cannula. The transfer was quantitated with additional tetrahydrofuran (3 × 10 mL). After 1 h, acetaldehyde (1.93 mL, 34.5 mmol, 1.30 equiv) was added via syringe. After 45 min, saturated aqueous ammonium chloride solution (200 mL) was added and the solution allowed to warm to 23 ºC. Saturated aqueous sodium chloride solution (200 mL) and ethyl acetate (200 mL) were sequentially added, and the layers were separated. The aqueous layer was further extracted with ethyl acetate (3 × 250 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (0 → 20% ethyl acetate in hexanes) to afford *n*-decyl 2-(1-hydroxyethyl)but-(3)-enoate **S3** (6.81 g, 95.0%) as a colorless oil. Structural assignments were made using additional information from a gCOSY and gHSQC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, 1.08:1 diastereomeric mixture, * denotes minor diastereomer): δ 5.92 (dd, *J* = 17.1, 9.7 Hz, 1H, C_5**H**), 5.80 (dd, *J* = 17.1, 9.4 Hz, 1H, C_5**H***), 5.31 (d, *J* = 10.1 Hz, 1H, C_6**H**$_a$), 5.25 (d, *J* = 7.1 Hz, 1H, C_6**H**$_b$), 5.21 (app-d, *J* = 10.2 Hz, 2H, C_6**H**$_2$*), 4.15–3.98 (m, 6H, C_3**H**, C_3**H***, C_7**H**$_2$, C_7**H**$_2$*), 3.07–2.95 (m, 2H, C_2**H**, C_2**H***), 2.67 (d, *J* = 3.5 Hz, 1H, O**H**), 2.59 (d, *J* = 6.1 Hz, 1H, O**H***), 1.62 (q, *J* = 7.0 Hz, 4H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***), 1.41–1.21 (m, *J* = 16.9 Hz, 28H, *n*-C_9H_{19}–**H**), 1.19 (d, *J* = 6.9 Hz, 3H, C_4**H**$_3$), 1.18 (d, *J* = 6.9 Hz, 3H, C_4**H**$_3$*), 0.87 (t, *J* = 6.7 Hz, 6H, *n*-C_9H_{19}–**H**).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, 1.08:1 diastereomeric mixture, * denotes minor diastereomer): δ 173.4 (2C, **C**$_1$, **C**$_1$*), 133.0 (**C**$_5$), 132.1 (**C**$_5$*), 120.6 (**C**$_6$), 119.5 (**C**$_6$*), 68.6 (**C**$_3$*), 67.7 (**C**$_3$), 65.2 (2C, **C**$_7$, **C**$_7$*), 58.5 (**C**$_2$*), 57.4 (**C**$_2$), 32.0, 29.6 (2C), 29.4, 29.3 (2C), 28.7, 28.6, 26.0, 22.8, 20.9 (**C**$_4$), 20.2 (**C**$_4$*), 14.2.

FTIR (thin film) cm^{-1}: 3453 (br-m), 2927 (s), 2856 (s), 1735 (s), 1640 (w), 1467 (w), 1246 (m), 1173 (m), 922 (m).

HRMS (DART) (*m/z*):	calc'd for $C_{16}H_{31}O_3$ $[M+H]^+$: 271.2268, found: 271.2267.
TLC (10% ethyl acetate in hexanes), R*f*:	0.19 ($KMnO_4$).



_n_-Decyl (_E_)-2-vinylbut-(2)-enoate 9:

Methanesulfonylchloride (2.93 mL, 37.8 mmol, 1.50 equiv) was added via syringe to a solution of *n*-decyl 2-(1-hydroxyethyl)but-(3)-enoate **S3** (6.81 g, 25.2 mmol, 1 equiv) and triethylamine (10.6 mL, 75.6 mmol, 3.00 equiv) in dichloromethane (200 mL) at 0 °C. The resulting mixture was warmed to 23 °C. After 36 h, saturated aqueous ammonium chloride solution (200 mL) was added, and the layers were separated. The aqueous layer was further extracted with dichloromethane (3 × 200 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (200 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (50% dichloromethane in hexanes) to afford *n*-decyl (*E*)-2-vinylbut-(2)-enoate **9** (5.94 g, 93.5%) as a colorless oil. Structural assignments were made using additional information from a gCOSY, nOe, and gHSQC experiments.

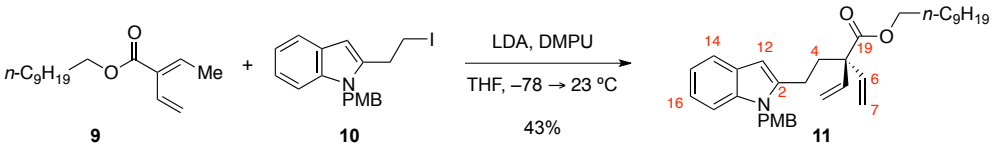
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, 2.6:1 *E*:*Z* mixture, * denotes the *Z* isomer): δ 6.83 (q, *J* = 7.3, 6.9 Hz, 1H, C_3**H**), 6.48 (dd, *J* = 17.7, 11.6 Hz, 1H, C_5**H**), 6.33 (dd, *J* = 17.5, 10.9 Hz, 1H, C_5**H***), 6.04 (q, *J* = 7.2 Hz, 1H, C_3**H***), 5.57 (dd, *J* = 17.7, 1.8 Hz, 1H, C_6**H$_a$**), 5.39 (d, *J* = 11.8 Hz, 1H, C_6**H$_b$**), 5.25 (d, *J* = 17.5 Hz, 1H, C_6**H$_a$***), 5.07 (d, *J* = 10.9 Hz, 1H, C_6**H$_b$***), 4.22 (t, *J* = 6.8 Hz, 2H, C_7**H**$_2$*), 4.15 (t, *J* = 6.7 Hz, 2H, C_7**H**$_2$), 1.91 (d, *J* = 7.3 Hz, 6H, C_4**H**$_3$, C_4**H**$_3$*), 1.80–1.56 (m, 4H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***), 1.45–1.13 (m, 28H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***), 0.94–0.80 (m, 6H, *n*-C_9H_{19}–**H**, *n*-C_9H_{19}–**H***).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, *E*:*Z* mixture, * denotes the *Z* isomer): δ 167.7 (**C**$_1$*), 167.3 (**C**$_1$), 138.5 (**C**$_3$), 134.9 (**C**$_5$*), 134.7 (**C**$_3$*), 134.4 (**C**$_2$*), 131.7 (**C**$_2$), 129.1 (**C**$_5$), 119.5 (**C**$_6$), 114.6 (**C**$_6$*), 64.9 (2C, **C**$_7$, **C**$_7$*), 32.0, 29.7, 29.6 (2C), 29.4 (4C), 28.8 (2C), 26.2, 22.8, 15.7 (**C**$_4$*), 14.8, 14.2 (**C**$_4$).

FTIR (thin film) cm^{-1}: 2927 (s), 2856 (s), 1721 (s), 1636 (w), 1467 (m), 1378 (w), 1264 (s), 1154 (m).

HRMS (DART) (*m/z*): calc'd for $C_{16}H_{29}O_2$ $[M+H]^+$: 253.2162, found: 253.2170.

TLC (40% dichloromethane in hexanes), R*f*: 0.41 (UV, $KMnO_4$).



α,α'-Divinyl quaternary ester 11:

A solution of *n*-butyllithium (2.40 M in hexanes, 4.96 mL, 11.9 mmol, 1.20 equiv) was added via syringe to a solution of *N*,*N*-diisopropylamine (1.80 mL, 12.9 mmol, 1.30 equiv) in tetrahydrofuran (60 mL) at −78 °C, and the resulting mixture was warmed to 0 °C. After 10 min, the mixture was cooled to −78 °C. After 10 min, *N*,*N'*-dimethylpropylene urea (11.9 mL, 99.1 mmol, 10.0 equiv) was added via syringe. After 30 min, an ice-cooled solution of *n*-decyl (*E*)-2-vinylbut-(2)-enoate **9** (2.50 g, 9.91 mmol, 1 equiv) in tetrahydrofuran (30 mL) was added via cannula. The transfer was quantitated with additional tetrahydrofuran (2 × 5 mL). After 30 min, an ice-cooled solution of iodide **10** (4.27 g, 10.9 mmol, 1.10 equiv)[5] in tetrahydrofuran (30 mL) was added via cannula. The transfer was quantitated with additional tetrahydrofuran (2 × 5 mL). After 2 h, the solution allowed to warm to 23 ºC. After 12 h, saturated aqueous ammonium chloride solution (80 mL) was added. Saturated aqueous sodium chloride solution (80 mL) and ethyl acetate (200 mL) were sequentially added, and the layers were separated. The aqueous layer was further extracted with ethyl acetate (3 × 250 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (50% dichloromethane in hexanes) to afford α,α'-divinyl quaternary ester **11** (2.21 g, 43.3%) as a colorless oil. Structural assignments were made using additional information from a gCOSY and gHSQC experiments.

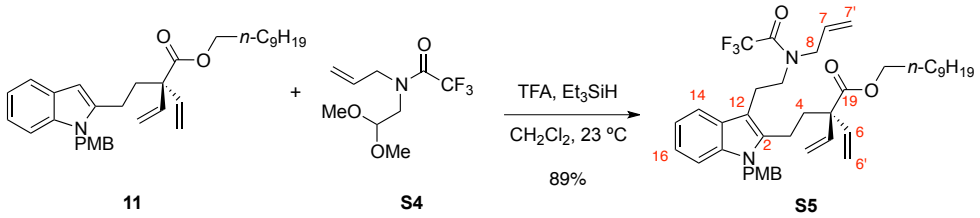
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.57 (dd, *J* = 6.4, 2.0 Hz, 1H, C_{14}**H**), 7.21 (d, *J* = 8.6 Hz, 1H, C_{17}**H**), 7.16–7.01 (m, 2H, C_{15}**H**, C_{16}**H**), 6.89 (d, *J* = 8.8 Hz, 2H, Ar_{PMB}**H**), 6.78 (d, *J* = 8.8 Hz, 2H, Ar_{PMB}**H**), 6.36 (s, 1H, C_{12}**H**), 6.06 (dd, *J* = 17.6, 10.8 Hz, 2H, C_6**H**), 5.30–5.21 (m, 4H, C_7**H**, N_1C**H**$_2$), 5.14 (d, *J* = 18.3 Hz, 2H, C_7**H**), 4.07 (t, *J* = 6.7 Hz, 2H, *n*-$C_9H_{19}C$**H**$_2$), 3.75 (s, 3H, OCH_3), 2.75–2.63 (m, 2H, C_3**H**$_2$), 2.30–2.16 (m, 2H, C_4**H**$_2$), 1.64–1.50 (m, 2H, *n*-C_9H_{19}–**H**), 1.38–1.19 (m, 14H, *n*-C_9H_{19}–**H**), 0.89 (t, *J* = 6.9 Hz, 3H, *n*-C_9H_{19}–**H**).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 173.6 (**C**$_{19}$), 158.9 (Ar_{PMB}), 140.8 (**C**$_2$), 138.5 (**C**$_6$), 137.2 (**C**$_{13}$), 130.0 (N_1CH_2**C**), 128.2 (**C**$_{18}$), 127.3 (Ar_{PMB}), 121.1 (**C**$_{15}$), 120.0 (**C**$_{14}$), 119.6 (**C**$_{16}$), 116.2 (**C**$_7$), 114.2 (Ar_{PMB}), 109.5 (**C**$_{17}$), 99.5 (**C**$_{12}$), 65.5 (*n*-C_9H_{19}**C**), 55.4 (2C, **C**$_5$, O**C**H_3), 46.0

[5] Mewald, M.; Medley, J. W.; Movassaghi, M. *Angew. Chem. Int. Ed.* **2014**, *53*, 11634.

	($N_1\mathbf{C}H_2$), 35.6 ($\mathbf{C}_4$), 32.0, 29.7 (2C), 29.4, 29.3, 28.6, 26.0, 22.8, 22.4 ($\mathbf{C}_3$), 14.3.
FTIR (thin film) cm^{-1}:	2926 (s), 2855 (s), 1729 (s), 1613 (w), 1513 (s), 1463 (s), 1247 (s), 1175 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{34}H_{46}NO_3$ $[M+H]^+$: 516.3472, found: 516.3470

TLC (40% dichloromethane in hexanes), R*f*: 0.20 (UV, CAM, $KMnO_4$).



Trifluoroacetyltryptamine S5:

A solution of trifluoroacetic acid (1.52 mL, 19.9 mmol, 5.00 equiv) and triethylsilane (1.9 mL, 11.9 mmol, 3.00 equiv) in dichloromethane (5 mL) was added via syringe to a solution of α,α'-divinyl quaternary ester **11** (2.05 g, 3.97 mmol, 1 equiv) and trifluoroacetamide **S4**[5] (1.91 g, 7.94 mmol, 2.00 equiv) in dichloromethane (35 mL) at 0 ºC in an ice bath. After 5 min, the ice bath was removed, and the mixture was allowed to warm to 23 °C. After 6 h, a saturated aqueous sodium bicarbonate solution (50 mL) was added to the reaction mixture. Dichloromethane (100 mL) and saturated aqueous sodium chloride solution (50 mL) were added, and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 50 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 20 → 50% dichloromethane in hexanes) to give trifluoroacetyltryptamine **S5** (2.46 g, 89.2%) as a pale yellow oil. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, 1.4:1 mixture of atropisomers, * denotes the minor atropisomer): δ 7.65–7.61 (m, 1H, C_{14}**H**), 7.53–7.46 (m, 1H, C_{14}**H***), 7.24–7.17 (m, 2H, C_{17}**H**, C_{17}**H***), 7.16–7.06 (m, 4H, C_{15}**H**, C_{16}**H**, C_{15}**H***, C_{16}**H***), 6.86 (app-d, J = 8.6 Hz, 4H, Ar_{PMB}**H**, Ar_{PMB}**H***), 6.81–6.72 (m, 4H, Ar_{PMB}**H**, Ar_{PMB}**H***), 6.11–5.97 (m, 4H, C_6**H**, C_6**H***), 5.87–5.76 (m, 1H, C_7**H***), 5.76–5.66 (m, 1H, C_7**H**), 5.34–5.19 (m, 8H, N_1C**H**$_2$, N_1C**H**$_2$*, $C_{7'}$**H**, $C_{7'}$**H***), 5.15 (dd, J = 5.2, 0.8 Hz, 4H, $C_{6'}$**H**, $C_{6'}$**H***), 5.11 (dd, J = 5.1, 0.8 Hz, 4H, $C_{6'}$**H**, $C_{6'}$**H***), 4.19–4.07 (m, 6H, C_8**H**$_2$*, *n*-$C_9H_{19}C$**H**$_2$, *n*-$C_9H_{19}C$**H**$_2$*), 3.87 (d, J = 5.6 Hz, 4H, C_8**H**$_2$,), 3.75 (s, 3H, OC**H**$_3$), 3.75 (s, 3H, OC**H**$_3$*), 3.63–3.57 (m, 4H, C_{10}**H**$_2$, C_{10}**H**$_2$*), 3.08–3.00 (m, 4H, C_{11}**H**$_2$, C_{11}**H**$_2$*), 2.75–2.59 (m, 4H, C_3**H**$_2$, C_3**H**$_2$*), 2.04–1.85 (m, 4H, C_4**H**$_2$, C_4**H**$_2$*), 1.71–1.49 (m, 4H, *n*-C_9H_{19}–**H,** *n*-C_9H_{19}–**H***), 1.40–1.16 (m, 28H, *n*-C_9H_{19}–**H,** *n*-C_9H_{19}–**H***), 0.88 (t, J = 6.8 Hz, 6H, *n*-C_9H_{19}–**H,** *n*-C_9H_{19}–**H***).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 1.4:1 mixture of atropisomers, * denotes the minor atropisomer): δ 173.5 (**C**$_{19}$*), 173.4 (**C**$_{19}$), 159.0 (**C**OCH_3*), 158.9 (**C**OCH_3), 156.8 (q, J = 35.7 Hz,

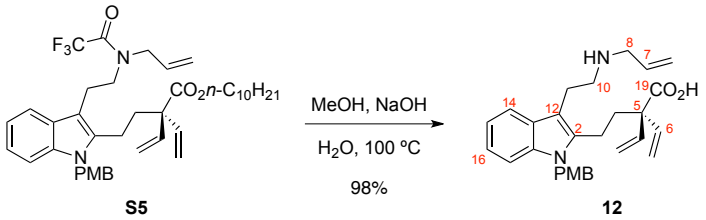
N**C**(O)CF_3), 156.8 (q, *J* = 35.7 Hz, N**C**(O)CF_3*), 138.5 (**C**$_6$), 138.5 (**C**$_6$*), 137.5 (2C, **C**$_2$, **C**$_2$*), 136.8 (**C**$_{13}$*), 136.7 (**C**$_{13}$), 132.3 (**C**$_7$), 131.6 (**C**$_7$*), 130.2 (N_1CH_2**C**), 130.1 (N_1CH_2**C***), 127.9 (**C**$_{18}$), 127.6 (**C**$_{18}$*), 127.2 (2C, Ar_{PMB}, Ar_{PMB}*), 121.6 (**C**$_{15}$*), 121.5 (**C**$_{15}$), 119.7 (**C**$_{16}$*), 119.6 (**C**$_{16}$), 119.2 (**C**$_{7'}$), 118.7 (**C**$_{7'}$*), 118.3 (**C**$_{14}$), 117.8 (**C**$_{14}$*), 116.8 (q, *J* = 288 Hz, **C**F_3*), 116.7 (q, *J* = 288 Hz, **C**F_3), 116.4 (2C, **C**$_{6'}$, **C**$_{6'}$*), 114.2 (Ar_{PMB}*), 114.2 (Ar_{PMB}), 109.9 (**C**$_{17}$*), 109.7 (**C**$_{17}$), 108.2 (**C**$_{12}$), 107.3 (**C**$_{12}$*), 65.7 (*n*-C_9H_{19}**C***), 65.6 (*n*-C_9H_{19}**C**), 55.5 (2C, **C**$_5$, **C**$_5$*), 55.4 (2C, O**C**H_3, O**C**H_3*), 49.6 (**C**$_8$), 47.9 (**C**$_8$*), 47.8 (2C, **C**$_{10}$, **C**$_{10}$*), 46.1 (2C, N_1**C**H_2, N_1**C**H_2*), 37.6 (2C, **C**$_4$, **C**$_4$*), 32.0, 29.7, 29.4, 29.3, 29.3, 28.7, 26.0, 24.4 (**C**$_{11}$*), 22.8, 22.2 (**C**$_{11}$), 20.3 (2C, **C**$_3$, **C**$_3$*), 14.3.

^{19}F NMR (376 MHz, $CDCl_3$, 25 °C, 1.4:1 mixture of atropisomers, * denotes minor atropisomer): δ –68.8 (s, C**F**$_3$*), –69.0 (s, C**F**$_3$).

FTIR (thin film) cm^{-1}: 2928 (s), 2855 (w), 1726 (s), 1692 (s), 1514 (m), 1465 (m), 1248 (m), 1205 (m), 1175 (m), 1144 (m).

HRMS (DART) (*m/z*): calc'd for $C_{41}H_{54}F_3N_2O_4$ $[M+H]^+$: 695.4030, found: 695.4048.

TLC (50% dichloromethane in hexanes), R*f*: 0.16 (UV, CAM, $KMnO_4$).



Allyltryptamine 12:

Sodium hydroxide (1.18 g, 29.5 mmol, 10.0 equiv) was added to a suspension of trifluoroacetyltryptamine **S5** (2.05 g, 2.95 mmol, 1 equiv) in methanol–water (1:1, 60 mL) in a glass pressure vessel at 23 °C. The reaction vessel was sealed, and the mixture was heated to 100 °C. After 40 h, the resulting orange solution was allowed to cool to 23 °C. The mixture was diluted with deionized water and was extracted with diethyl ether (50 mL). The aqueous extract was neutralized (pH 7) with aqueous hydrochloric acid solution (1 N) and was extracted with dichloromethane (4 × 100 mL). The combined dichloromethane extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford allyltryptamine **12** (1.33 g, 98.3%) as a yellow solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.48 (dd, J = 6.1, 2.5 Hz, 1H, $C_{14}\mathbf{H}$), 7.20 (dd, J = 6.5, 2.2 Hz, 1H, $C_{17}\mathbf{H}$), 7.15–7.05 (m, 2H, $C_{15}\mathbf{H}$, $C_{16}\mathbf{H}$), 6.89 (d, J = 8.5 Hz, 2H, $Ar_{PMB}\mathbf{H}$), 6.76 (d, J = 8.5 Hz, 2H, $Ar_{PMB}\mathbf{H}$), 6.21 (dd, J = 17.4, 10.7 Hz, 2H, $C_6\mathbf{H}$), 6.04–5.83 (m, 1H, $C_7\mathbf{H}$), 5.36–5.20 (m, 4H, $C_8CH{=}C\mathbf{H}_2$, $N_1C\mathbf{H}_2$), 5.14 (dd, J = 10.7, 1.4 Hz, 2H, $C_5CH{=}C\mathbf{H}_2$), 5.03 (dd, J = 17.6, 1.4 Hz, 2H, $C_5CH{=}C\mathbf{H}_2$), 3.73 (s, 3H, $OC\mathbf{H}_3$), 3.45 (d, J = 6.5 Hz, 2H, $C_8\mathbf{H}_2$), 3.20 (br-s, 4H, $C_{10}\mathbf{H}_2$, $C_{11}\mathbf{H}_2$), 2.88–2.71 (m, 2H, $C_3\mathbf{H}_2$), 1.93–1.74 (m, 2H, $C_4\mathbf{H}_2$).

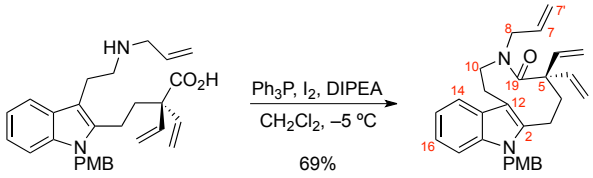
^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 179.4 ($\mathbf{C}_{19}$), 159.0 ($\mathbf{C}OCH_3$), 141.9 ($\mathbf{C}_6$), 139.5 ($\mathbf{C}_2$), 136.5 ($\mathbf{C}_{13}$), 130.1 ($N_1CH_2\mathbf{C}$), 129.3 ($\mathbf{C}_7$), 127.5 (2C, $\mathbf{C}_{18}$, Ar_{PMB}), 122.4 ($C_8CH{=}\mathbf{C}$), 121.3 ($\mathbf{C}_{15}$), 119.6 ($\mathbf{C}_{16}$), 117.9 ($\mathbf{C}_{14}$), 114.3 (Ar_{PMB}), 113.6 ($C_6H{=}\mathbf{C}H_2$), 109.7 ($\mathbf{C}_{17}$), 108.2 ($\mathbf{C}_{12}$), 58.1 ($\mathbf{C}_5$), 55.4 ($O\mathbf{C}H_3$), 50.0 ($\mathbf{C}_8$), 48.2 ($\mathbf{C}_{10}$), 46.5 ($N_1\mathbf{C}H_2$), 38.3 ($\mathbf{C}_4$), 22.0 ($\mathbf{C}_{11}$), 21.4 ($\mathbf{C}_3$).

FTIR (thin film) cm^{-1}: 2928 (m), 2851 (m), 1613 (m), 1560 (w), 1513 (s), 1465 (s), 1357 (m), 1247 (s), 1174 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{29}H_{35}N_2O_3$ $[M+H]^+$: 459.2642, found: 459.2663.

M.p.: 159–160 ºC (CH_2Cl_2).

TLC (10% methanol in dichloromethane), R*f*: 0.13 (UV, CAM, $KMnO_4$).



12 **13**

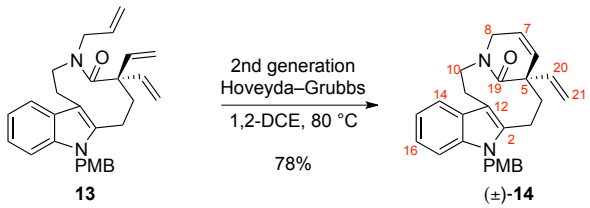
Lactam 13:

A solution of allyltryptamine **12** (1.03 g, 2.25 mmol, 1 equiv) and diisopropylethylamine (2.35 mL, 13.5 mmol, 6.00 equiv) in dichloromethane (60 mL) was added to a solution of triphenylphosphine (2.36 g, 9.00 mmol, 4.00 equiv) and iodine (1.14 g, 4.50 mmol, 2.00 equiv) in dichloromethane (225 mL) at –5 °C via a dropping funnel over a period of 15 h. After the addition was complete, the reaction mixture was allowed to warm to 23 °C. After 1 h, methanol (10 mL) was added. Water (200 mL) was added to the solution, the layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 70 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (200 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 15% ethyl acetate in hexanes) to afford lactam **13** (687 mg, 69.3 %) as a white foam. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, 1.4:1 mixture of atropisomers, * denotes the minor atropisomer): δ 7.58 (d, *J* = 7.5 Hz, 1H, C_{14}**H**), 7.51 (d, *J* = 7.0 Hz, 1H, C_{14}**H***), 7.32–7.23 (m, 1H), 7.22–7.06 (m, 5H), 6.91 (app-d, *J* = 8.8 Hz, 4H, Ar_{PMB}**H**, Ar_{PMB}**H***), 6.83 (app-t, *J* = 10.3 Hz, 4H, Ar_{PMB}**H**, Ar_{PMB}**H***), 6.42 (dd, *J* = 18.0, 9.8 Hz, 2H), 6.07 (t, *J* = 14.8 Hz, 1H), 5.82 (dd, *J* = 17.7, 10.7 Hz, 1H), 5.70 (s, 1H), 5.51–5.07 (m, 12H), 5.05–4.88 (m, 5H), 4.77 (d, *J* = 17.6 Hz, 2H), 4.19 (t, *J* = 17.2 Hz, 4H), 3.78 (s, 6H, OC**H**$_3$, OC**H**$_3$*), 3.53–3.34 (m, 3H), 3.17–2.94 (m, 1H), 2.84 (d, *J* = 14.9 Hz, 4H), 2.63 (dd, *J* = 29.9, 15.2 Hz, 2H), 2.39 (s, 1H), 2.27 (d, *J* = 11.4 Hz, 1H), 2.14 (dd, *J* = 31.6, 14.5 Hz, 1H), 1.91 (app-d, *J* = 14.0 Hz, 1H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 1.4:1 mixture of atropisomers, * denotes the minor atropisomer): δ 174.6 (**C**$_{19}$*), 173.7 (**C**$_{19}$), 158.9, 158.8, 144.2, 141.4, 139.4, 138.7, 136.7, 136.5, 135.5, 133.7, 132.8, 130.0, 129.7, 128.4, 127.5, 127.1, 121.4, 121.2, 119.3, 117.9, 117.4, 117.0, 116.9, 114.9, 114.2, 113.9, 112.0, 111.1, 109.8, 109.4, 108.9, 106.6, 55.7, 55.3 (O**C**H$_3$), 54.5, 52.6, 47.6, 46.3, 46.2, 45.9, 44.1, 36.7, 35.1, 34.7, 33.6,

	31.7, 29.1, 25.3, 22.7, 21.8, 21.2, 20.8, 20.0, 18.8, 18.7, 14.2, 11.5.
FTIR (thin film) cm^{-1}:	3082 (w), 2935 (m), 1623 (s), 1513 (m), 1468 (m), 1247 (m), 1175 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{29}H_{33}N_2O_2$ $[M+H]^+$: 441.2537, found: 441.2531.
M.p.:	42 ºC (CH_2Cl_2).
TLC (25% ethyl acetate in hexanes), R*f*:	0.51 (UV, CAM, $KMnO_4$).



13 (±)-**14**

δ–Lactam (±)-14:

A sample of the 2nd generation Hoveyda–Grubbs catalyst[6] (58.8 mg, 93.9 μmol, 7.00 mol%) was added as a solid to a solution of lactam **13** (591 mg, 1.34 mmol, 1 equiv) in 1,2-dichloroethane (27.0 mL) in a glass pressure vessel at 23 °C. The vessel was sealed, and the mixture was heated to 80 °C. After 18 h, the resulting mixture was allowed to cool to 23 °C, was concentrated under reduced pressure and was subjected to flash column chromatography on silica gel (eluent: 10 → 40% ethyl acetate in hexanes) to afford δ-lactam (±)-**14** (432 mg, 78.1%) as an off-white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.54 (dd, *J* = 8.0, 1.8 Hz, 1H, C_{14}**H**), 7.13–7.02 (m, 3H, C_{15}**H**, C_{16}**H**, C_{17}**H**), 6.85 (d, *J* = 8.7 Hz, 2H, Ar_{PMB}**H**), 6.78 (d, *J* = 8.7 Hz, 2H, Ar_{PMB}**H**), 6.16 (dd, *J* = 17.7, 10.8 Hz, 1H, C_{20}**H**), 5.87 (br-s, 1H, C_6**H**), 5.64 (d, *J* = 9.8 Hz, 1H, C_7**H**), 5.33 (d, *J* = 17.0 Hz, 1H, N_1C**H**$_a$), 5.14 (d, *J* = 17.0 Hz, 1H, N_1C**H**$_b$), 5.11–4.99 (m, 2H, C_{21}**H**$_2$), 4.54 (t, *J* = 12.0 Hz, 1H, C_{10}**H**$_a$), 4.11 (br-s, 1H, C_8**H**$_a$), 3.91 (d, *J* = 18.8 Hz, 1H, C_8**H**$_b$), 3.74 (s, 3H, OCH_3), 3.13 (d, *J* = 13.7 Hz, 1H, C_{11}**H**$_a$), 2.91 (ddd, *J* = 14.4, 10.7, 2.9 Hz, 1H, C_{11}**H**$_b$), 2.86–2.61 (m, 3H, C_3**H**$_2$, C_{10}**H**$_b$), 2.34 (dd, *J* = 12.8, 10.1 Hz, 1H, C_4**H**$_a$), 1.88 (dd, *J* = 13.2, 9.0 Hz, 1H, C_4**H**$_b$).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 171.5 (**C**$_{19}$), 158.8 (**C**OCH_3), 141.9 (**C**$_{20}$), 137.0 (**C**$_2$), 136.6 (**C**$_{13}$), 130.1 (N_1CH_2**C**), 128.6 (**C**$_6$), 128.0 (**C**$_{18}$), 127.2 (Ar_{PMB}), 121.3 (**C**$_{15}$), 121.0 (**C**$_7$), 119.1 (**C**$_{16}$), 117.8 (**C**$_{14}$), 114.2 (Ar_{PMB}), 113.9 (**C**$_{21}$), 110.0 (**C**$_{12}$), 109.7 (**C**$_{17}$), 55.4 (O**C**H_3), 49.1 (**C**$_8$), 47.2 (**C**$_5$), 46.3 (N_1**C**H_2), 46.2 (**C**$_{10}$), 44.0 (**C**$_4$), 22.3 (**C**$_{11}$), 20.4 (**C**$_3$).

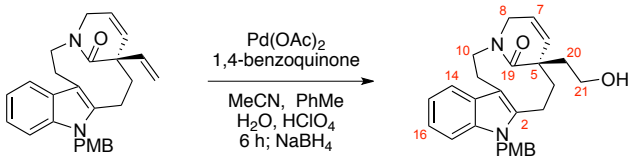
FTIR (thin film) cm^{-1}: 3047 (w), 2920 (m), 1642 (s), 1612 (w), 1513 (s), 1470 (m), 1350 (w), 1247 (s), 1177 (m).

HRMS (DART) (*m/z*): calc'd for $C_{27}H_{29}N_2O_2$ $[M+H]^+$: 413.2224, found: 413.2233.

[6] Garber, S. B; Kingsbury, J. S; Gray B. L; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 8168.

M.p.: 205 ºC (CH_2Cl_2).

TLC (50% ethyl acetate in hexanes), R*f*: 0.48 (UV, CAM, $KMnO_4$).



(±)-**14** (±)-**15**

Alcohol (±)-15:

Palladium acetate (29.7 mg, 132 μmol, 0.200 equiv), 1,4-benzoquinone (85.8 mg, 794 μmol, 1.20 equiv) and perchloric acid (100 μL, 3.00 M, 300 μmol, equiv) were stirred in a solution of acetonitrile (5.0 mL) and water (0.5 mL) at 23 ºC for 30 minutes. δ-Lactam (±)-**14** (273 mg, 662 μmol, 1 equiv) was added as a solid. Toluene (300 μL) was used to rinse any residual solid into the solution and the resulting suspension was stirred for 6 h. Sodium borohydride was then added as a solid (250 mg, 6.62 mmol, 10.0 equiv). After 2 h, saturated aqueous sodium bicarbonate solution (50 mL) was added to the reaction mixture. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (100 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 20 → 100% ethyl acetate in hexanes; 3% methanol in dichloromethane) to give alcohol (±)-**15** (224 mg, 78.5%) as white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

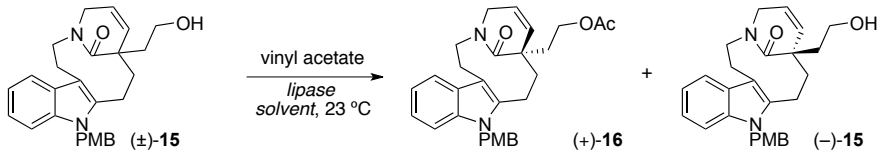
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.53 (dd, *J* = 6.2, 1.6 Hz, 1H, C_{14}**H**), 7.14–7.01 (m, 3H, C_{15}**H**, C_{16}**H**, C_{17}**H**), 6.85 (d, *J* = 8.7 Hz, 2H, Ar_{PMB}**H**), 6.78 (d, *J* = 8.8 Hz, 2H, Ar_{PMB}**H**), 5.86 (br-s, 1H, C_6**H**), 5.43 (d, *J* = 10.1 Hz, 1H, C_7**H**), 5.31 (d, *J* = 17.0 Hz, 1H, N_1C**H**$_a$), 5.13 (d, *J* = 17.1 Hz, 1H, N_1C**H**$_b$), 4.52 (t, *J* = 12.5 Hz, 1H, C_{10}**H**$_a$), 4.20 (br-s, 1H, C_8**H**$_a$) 3.94 (d, *J* = 18.7 Hz, 1H, C_8**H**$_b$), 3.74 (s, 3H, OC**H**$_3$), 3.64–3.45 (m, 2H, C_{21}**H**$_2$), 3.12 (d, *J* = 12.5 Hz, 1H, C_{11}**H**$_a$), 2.97–2.85 (m, 1H, C_{11}**H**$_b$), 2.81–2.69 (m, 2H, C_3**H**$_a$,C_{10}**H**$_b$), 2.62 (dd, *J* = 15.3, 9.6 Hz, 1H, C_3**H**$_b$), 2.41 (br-s, 1H, O**H**), 2.20–2.05 (m, 2H, C_4**H**$_a$,C_{20}**H**$_a$), 1.82 (dd, *J* = 13.1, 8.9 Hz, 1H, C_4**H**$_b$), 1.55–1.43 (m, 1H, C_{20}**H**$_b$).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 173.4 (**C**$_{19}$), 158.8 (**C**OCH_3), 137.0 (**C**$_2$), 136.6 (**C**$_{13}$), 131.0 (**C**$_6$), 130.0 (N_1CH_2**C**), 127.9 (**C**$_{18}$), 127.2 (Ar_{PMB}), 121.5 (**C**$_{15}$), 121.3 (**C**$_7$), 119.3 (**C**$_{16}$), 117.8 (**C**$_{14}$), 114.2 (Ar_{PMB}), 109.8 (2C, **C**$_{12}$, **C**$_{17}$), 59.9 (**C**$_{21}$), 55.4 (OCH_3), 49.4 (**C**$_8$), 46.5 (**C**$_{10}$), 46.3 (N_1CH_2), 44.8 (**C**$_4$), 44.3 (**C**$_5$), 41.1 (**C**$_{20}$), 22.2 (**C**$_{11}$), 20.0 (**C**$_3$).

FTIR (thin film) cm^{-1}:	3390 (s), 2931 (s), 1639 (s), 1586 (m), 1513 (s), 1469 (m), 1247 (w), 1176 (w), 736 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{27}H_{30}N_2NaO_3$ $[M+Na]^+$: 453.2149, found: 453.2158.
M.p.:	161 ºC (hexane).

TLC (3% methanol in dichloromethane), R*f*: 0.35 (UV, CAM, $KMnO_4$).

Table S1. Enzymatic Resolution of Alcohol (±)-15:[a]

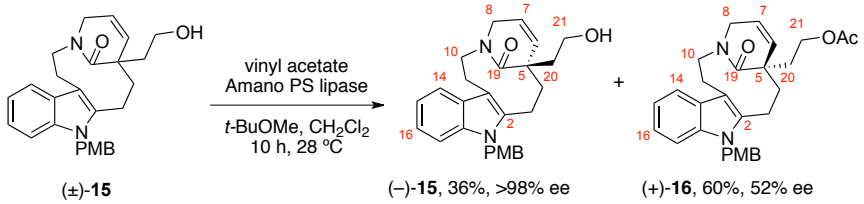


Entry	Lipase	Solvent	Conversion	ee of (+)-**16**	ee of (–)-**15**
1	CAL-B	PhMe	—	—	—
2	CCL	PhMe	<15%	30%	38%
3	CCL	THF	<15%	49%	8%
4	CCL	MeCN	—	—	—
5	CCL	Acetone	—	—	—
6	CCL	PhMe[b]	65%	26%	74%
7	CCL	*t*-BuOMe	55%	42%	60%
8	CCL	Ph_2O	70%	24%	66%
9	Amano PS Lipase	PhMe	30%	64%	30%
10	***Amano PS Lipase***	***t-BuOMe***	***55%***	***50%***	***92%***
11	Porcine Liver Esterase	PhMe	<10%	—	—
12	Porcine Liver Esterase	*t*-BuOMe	<10%	—	—
13	Porcine Pacreatic Lipase	PhMe	<5%	—	—
14	Porcine Pacreatic Lipase	*t*-BuOMe	<15%	—	—

[a]Reagents and conditions: vinyl acetate (2.0 equiv), 23 ºC. Each resolution was monitored for 48 h or until approximately 50% conversion to (+)-**16** (HPLC analysis), whichever occurred first. [b] Triethylamine (1.0 equiv) was utilized as an additive. CAL-B = *Candida antarctica* lipase B; CCL = *Candida rugosa* lipase; Amano PS = lipase from *Burkholderia cepacia* .

Representative Procedure for Table S1, Entry 6:

Vinyl acetate (0.9 µL, 9 µmol, 2 equiv) was added via syringe to a solution of alcohol (±)-**15** (2.0 mg, 4.6 µmol, 1 equiv), triethylamine (1.0 µL, 7.2 µmol, 1.5 equiv) and lipase from *Candida rugosa* (3.3 mg, 1.65 mg/mg of **15**) in toluene (500 µL) in a 3.7-mL glass vial with a plastic screw-cap. The solution was shaken at 23 ºC for 6 hours, at which point the solution was filtered through a silica plug with 1% methanol in dichloromethane as eluent. The reaction progress and the enantiomeric excess of the products were measured by HPLC analysis to be at *ca.* 65% conversion to the ester leading to a mixture of acetate (+)-**16** (26% ee) and recovered alcohol (–)-**15** (74% ee).



(±)-**15** (–)-**15**, 36%, >98% ee (+)-**16**, 60%, 52% ee

Alcohol (–)-15:

Vinyl acetate (38.5 µL, 418 µmol, 1.50 equiv) was added via syringe to a solution of alcohol (±)-**15** (120 mg, 280 µmol, 1 equiv) and Amano PS lipase on diatomite (1.90 g, 15.8 mg/mg of (±)-**15**) in methyl *tert*-butyl ether (58 mL) and dichloromethane (5.8 mL) in an Erlenmeyer flask with rubber septum. The solution was shaken at 23 ºC for 4 h, before vinyl acetate (38.5 µL, 418 µmol, 1.50 equiv) was added via syringe to the solution. The solution was shaken at 23 ºC for 4 more hours, before vinyl acetate (38.5 µL, 418 µmol, 1.50 equiv) was again added via syringe to the solution. After 2 hours, the solution was filtered. The filtrate was rinsed with toluene (10 mL × 2). The solution was concentrated under reduced pressure, and the resulting residue was immediately purified by flash column chromatography on silica gel (eluent: 10 → 50% ethyl acetate in hexanes; 1% methanol in dichloromethane) to give alcohol (–)-**15** (43 mg, 36%, >98% ee) as white solid and acetate (+)-**16** (79 mg, 60%, 52% ee) as a white foam. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments. For full characterization data for alcohol (–)-**15** ($[\alpha]_D^{24} = -34$ (*c* = 0.61, CH_2Cl_2)) see previous procedure in this document.

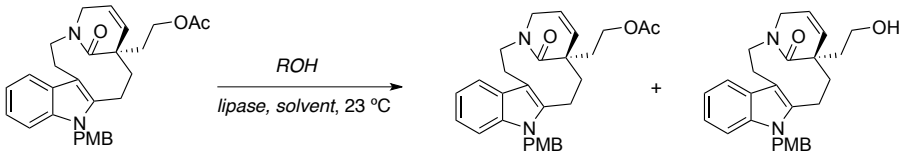
Acetate (+)-16:

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.52 (d, *J* = 6.3 Hz, 1H, C_{14}**H**), 7.07–7.00 (m, 3H, C_{15}**H**, C_{16}**H**, C_{17}**H**), 6.84 (d, *J* = 8.4 Hz, 2H, Ar_{PMB}**H**), 6.78 (d, *J* = 8.7 Hz, 2H, Ar_{PMB}**H**), 5.83 (br-s, 1H, C_6**H**), 5.46 (d, *J* = 10.1 Hz, 1H, C_7**H**), 5.29 (d, *J* = 17.0 Hz, 1H, N_1C**H**$_a$), 5.12 (d, *J* = 17.0 Hz, 1H, N_1C**H**$_b$), 4.52 (t, *J* = 11.8 Hz, 1H, C_{10}**H**$_a$), 4.17–4.03 (m, 1H, C_{21}**H**$_a$), 3.97–3.79 (m, 3H, C_{21}**H**$_b$, C_8**H**$_2$), 3.74 (s, 3H, OC**H**$_3$), 3.11 (d, *J* = 14.6 Hz, 1H, C_{11}**H**$_a$), 2.89 (t, *J* = 12.4 Hz, 1H, C_{11}**H**$_b$), 2.81–2.69 (m, 2H, C_3**H**$_a$, C_{10}**H**$_b$), 2.62 (dd, *J* = 15.7, 9.3 Hz, 1H, C_3**H**$_b$), 2.30 (dt, *J* = 14.5, 7.5 Hz, 1H, C_{20}**H**$_a$), 2.11 (t, *J* = 11.4 Hz, 1H, C_4**H**$_a$), 1.95 (s, 3H, OC(O)C**H**$_3$), 1.90–1.81 (m, 1H, C_4**H**$_b$), 1.46 (dt, *J* = 13.6, 7.0 Hz, 1H, C_{20}**H**$_b$).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 171.4 (**C**(O)CH_3), 171.1 (**C**$_{19}$), 158.8 (**C**OCH_3), 137.0 (**C**$_2$), 136.6 (**C**$_{13}$), 130.2 (**C**$_6$), 130.0 (N_1CH_2**C**), 128.0 (**C**$_{18}$), 127.2 (Ar_{PMB}), 121.3 (**C**$_{15}$), 121.2 (**C**$_7$), 119.2 (**C**$_{16}$), 117.8 (**C**$_{14}$), 114.2 (Ar_{PMB}), 110.0 (**C**$_{12}$), 109.7 (**C**$_{17}$), 61.7 (**C**$_{21}$), 55.4 (O**C**H_3), 49.2 (**C**$_8$), 46.3 (2C, **C**$_{10}$, N_1**C**H_2), 44.5 (**C**$_4$), 44.1

	(**C**$_5$), 36.7 (**C**$_{20}$), 22.2 (**C**$_{11}$), 21.1 (C(O)**C**H$_3$), 20.1 (**C**$_3$).
FTIR (thin film) cm^{-1}:	2918 (m), 1734 (s), 1642 (s), 1469 (s), 1364 (m), 1351 (m), 1248 (s), 1176 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{29}H_{32}N_2NaO_4$ $[M+Na]^+$: 495.2254, found: 495.2243.
$[\alpha]_D^{24}$:	+16 (*c* = 0.59, CH_2Cl_2).
M.p.:	68 ºC (CH_2Cl_2).
TLC (5% ethyl acetate in hexanes), R*f*:	0.46 (UV, CAM).

Table S2. Enzymatic Resolution of Acetate (+)-16:

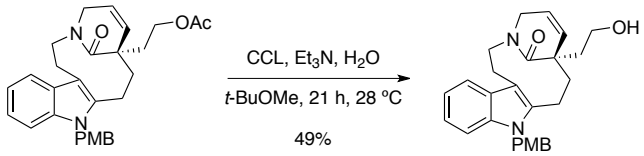


(+)-**16**, 71% ee (+)-**16** (+)-**15**

Entry	Lipase	Solvent	Conversion	ROH (equiv)	ee of (+)-**16**	ee of (+)-**15**	additives
1	Amano PS Lipase	*t*-BuOMe	ND	H_2O (300)	64%	30%	
2	Amano PS Lipase	toluene	ND	H_2O (60)	50%	92%	
3	Amano PS Lipase	*t*-BuOMe	30%	H_2O (1)	44%	93%	
4	Amano PS Lipase	*t*-BuOMe	<10%	MeOH (2)	—	—	
5	Amano PS Lipase	*t*-BuOMe	<10%	MeOH (2)	—	—	Et_3N
6	CCL	*t*-BuOMe	80%	*i*-PrOH (2)	—	79%	
7	CCL	*t*-BuOMe	<20%	MeOH (2)	—	—	Et_3N
8	CCL	*t*-BuOMe	56%	H_2O (15)	—	90%	

Representative Procedure for Table S2, Entry 3:

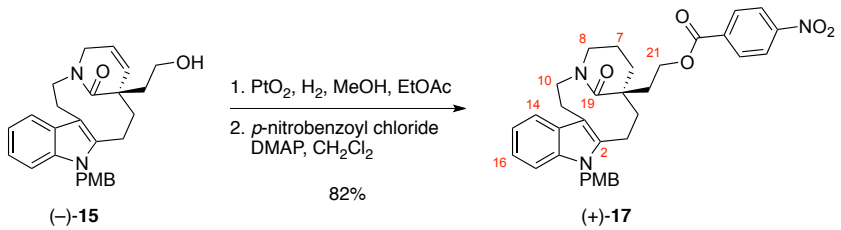
Amano PS lipase (36 mg, 15.8 mg/mg of **16**) was added to a solution of acetate (+)-**16** (2.3 mg, 4.9 μmol, 1 equiv), and water (110 μL, 0.044 M solution in methyl *tert*-butyl ether, 4.9 μmol, 1.0 equiv) in methyl *tert*-butyl ether (400 μL). The solution was shaken at 23 ºC for 24 hours in a 3.7-mL glass vial with a plastic screw-cap. The reaction progress and the enantiomeric excess of the products were measured by HPLC analysis to be at *ca*. 30% conversion to the alcohol leading to a mixture of recovered acetate (+)-**16** (44% ee) and alcohol (+)-**15** (93% ee).



(+)-**16**, 71% ee (+)-**15,** 91% ee

Alcohol (+)-15:

Lipase from *Candida rugosa* (CCL, 340 mg, 3.0 g/mmol of **16**) was added to a solution of acetate (+)-**16** (38 mg, 81 μmol, 1 equiv), triethylamine (11 μL, 81 μmol, 1.0 equiv) and water (22 μL, 1.2 mmol, 15 equiv) in methyl *tert*-butyl ether (40 mL). The solution was shaken at 23 ºC for 21 hours. The solution was filtered. The filtrate was rinsed with toluene (2 × 10 mL). The solution was concentrated under reduced pressure, and the resulting residue was immediately purified by flash column chromatography on silica gel (eluent: 10 → 50% ethyl acetate in hexanes; 1% methanol in dichloromethane) to give alcohol (+)-**15** (17 mg, 49%, 91% ee) as white foam. For full characterization data for alcohol (+)-**15** ($[\alpha]_D^{24}$ = +33 (*c* = 0.58, CH_2Cl_2)) see previous procedure in this document.



(–)-**15** (+)-**17**

Benzoate (+)-17:

Platinum dioxide (15.0 mg, 66.1 μmol, 0.120 equiv) was added as a solid to a solution of alcohol (–)-**15** (229 mg, 533 μmol, 1 equiv) in mixture of methanol (1.0 mL) and ethyl acetate (3.0 mL) at 23 ºC. The reaction mixture was purged with hydrogen gas for 10 min and then stirred under an atmosphere of hydrogen gas (balloon) at 23 ºC. After 16 h, the reaction mixture was opened to air and filtered through a plug of silica gel. The filtrate was concentrated under reduced pressure.

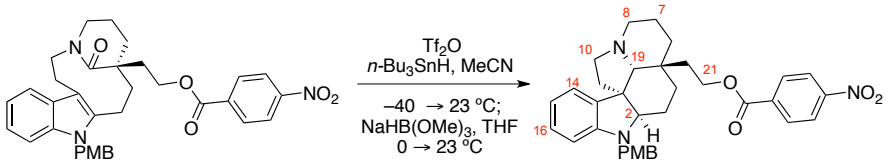
The solid was dissolved in dichloromethane (5.0 mL), and 4-(dimethylamino)-pyridine (195 mg, 1.60 mmol, 3.00 equiv) and *para*-nitrobenzoylchloride (247 mg, 1.33 mmol, 2.50 equiv) were added. After 12 h, saturated aqueous sodium bicarbonate solution (150 mL) was added to the reaction mixture. The layers were separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (200 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 25 → 50% ethyl acetate in hexanes) to give benzoate (+)-**17** (253 mg, 81.8%) as an orange gum. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.30–8.20 (m, 2H, Ar_{NO2}**H**), 8.19–8.11 (m, 2H, Ar_{NO2}**H**), 7.56–7.50 (m, 1H, C_{14}**H**), 7.19–7.06 (m, 3H, C_{15}**H**, C_{16}**H**, C_{17}**H**), 6.90–6.84 (m, 2H, Ar_{PMB}**H**), 6.81–6.75 (m, 2H, Ar_{PMB}**H**), 5.27 (d, J = 6.0 Hz, 2H, N_1C**H**$_2$), 4.51 (ddd, J = 11.1, 7.4, 5.2 Hz, 1H, C_{21}**H**$_a$), 4.46–4.33 (m, 2H, C_{10}**H**$_a$, C_{21}**H**$_b$), 3.74 (s, 3H, OC**H**$_3$), 3.39–3.21 (m, 1H, C_{11}**H**$_a$), 3.00 (t, J = 13.0 Hz, 2H, C_3**H**$_a$, C_8**H**$_a$), 2.95–2.85 (m, 1H, C_{11}**H**$_b$), 2.70 (tdd, J = 12.5, 7.6, 4.3 Hz, 3H, C_3**H**$_b$, C_8**H**$_b$, C_{10}**H**$_b$), 2.37 (dt, J = 14.0, 7.6 Hz, 1H, C_{20}**H**$_a$), 2.13 (ddd, J = 13.5, 6.9, 3.3 Hz, 1H, C_7**H**$_a$), 1.90 (ddd, J = 13.3, 10.6, 2.7 Hz, 1H, C_7**H**$_b$), 1.81 (br-s, 2H, C_4**H**$_a$, C_{20}**H**$_b$), 1.52 (br-s, 3H, C_4**H**$_b$, C_6**H**$_2$).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 174.5 (**C**$_{19}$), 164.7 (**C**(O)Ar_{NO2}), 159.2 (**C**OCH_3), 150.9 (Ar_{NO2}), 136.9 (2C, **C**$_2$, **C**$_{13}$), 136.0 (Ar_{NO2}), 130.9 (Ar_{NO2}), 130.9, 130.1 (Ar_{PMB}), 128.3, 127.4 (Ar_{PMB}), 123.6 (Ar_{NO2}), 121.6 (**C**$_{15/16}$), 119.5 (**C**$_{15/16}$), 117.9 (**C**$_{14}$), 114.5 (Ar_{PMB}), 110.3, 109.8 (**C**$_{17}$), 63.2 (**C**$_{21}$), 55.4 (OCH_3), 50.7 (**C**$_3$), 48.5 (**C**$_{10}$), 46.6

	($N_1\mathbf{C}H_2$), 44.0 ($\mathbf{C}_7$), 38.8 ($\mathbf{C}_{20}$), 32.9 ($\mathbf{C}_4$), 21.0 (3C, $\mathbf{C}_6$, $\mathbf{C}_8$, $\mathbf{C}_{11}$).[7]
FTIR (thin film) cm^{-1}:	3053 (w), 2933 (m), 1723 (s), 1636 (s), 1527 (s), 1468 (m), 1349 (s), 1276 (w), 1104 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{34}H_{36}N_3O_6$ $[M+H]^+$: 582.2599, found: 582.2586.
$[\alpha]_D^{24}$:	+5 (*c* = 0.60, CH_2Cl_2).
TLC (50% ethyl acetate in hexanes), R*f*:	0.31 (UV, CAM).

[7] Due to atropisomerism, not all carbon signals are observed as sharp distinguished peaks.



***N*-Paramethoxylbenzylpentacycle (–)-S6:**

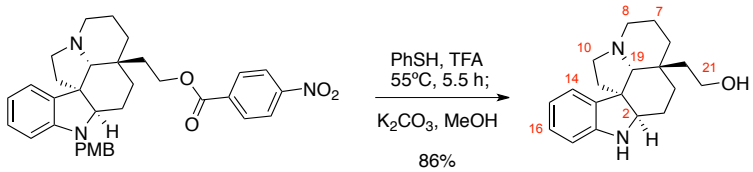
Trifluoromethanesulfonic anhydride (13.5 µL, 80.5 µmol, 1.30 equiv) was added dropwise via syringe to a mixture of benzoate (+)-**17** (36.0 mg, 61.9 µmol, 1 equiv) and tri-*n*-butyltin hydride (32.8 µL, 124 µmol, 2.00 equiv) in acetonitrile (1.5 mL) at –40 °C. After 10 min, the reaction mixture was warmed to 0 °C. After 10 min, the ice bath was removed, and the solution was allowed to warm to 23 °C. After 2 h, the solution was cooled to 0 °C, and an ice-cooled suspension of sodium trimethoxyborohydride (39.6 mg, 0.310 mmol, 5.00 equiv) in THF (1.5 mL) was added via cannula. The reaction mixture was allowed to warm to 23 °C. After 4 h, saturated aqueous solution of sodium bicarbonate (15 mL) was added to the reaction mixture. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0 → 30% ethyl acetate in hexanes with 3% triethylamine) to give *N*-paramethoxylbenzylpentacycle (–)-**S6** (27.1 mg, 77.2%) as yellow film. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 8.26 (d, *J* = 8.9 Hz, 2H, Ar_{NO2}**H**), 8.09 (d, *J* = 8.8 Hz, 2H, Ar_{NO2}**H**), 7.28 (d, *J* = 8.4 Hz, 2H, Ar_{PMB}**H**), 7.11–6.95 (m, 2H, C_{14}**H**, C_{16}**H**), 6.87 (d, *J* = 8.6 Hz, 2H, Ar_{PMB}**H**), 6.63 (t, *J* = 7.4 Hz, 1H, C_{15}**H**), 6.40 (d, *J* = 7.8 Hz, 1H, C_{17}**H**), 4.41 (d, *J* = 14.5 Hz, 1H, N_1CH_a), 4.36–4.23 (m, 2H, $C_{21}H_2$), 4.01 (d, *J* = 14.5 Hz, 1H, N_1CH_b), 3.81 (s, 3H, OCH_3), 3.37 (dd, *J* = 10.9, 5.7 Hz, 1H, C_2**H**), 3.13–3.05 (m, 1H, $C_{10}H_a$), 3.02 (d, *J* = 11.1 Hz, 1H, C_8H_a), 2.39–2.19 (m, 3H, $C_{10}H_b$, $C_{11}H_a$, C_{19}**H**), 2.07–1.89 (m, 3H, C_4H_a, C_8H_b, $C_{20}H_a$), 1.78 (t, *J* = 13.3 Hz, 1H, C_3H_a), 1.69 (d, *J* = 13.3 Hz, 2H, C_6H_a, C_7H_a), 1.61–1.38 (m, 4H, C_3H_b, C_7H_b, $C_{11}H_b$, $C_{20}H_b$), 1.36–1.21 (m, 1H, C_6H_b), 1.11 (d, *J* = 13.9 Hz, 1H, C_4H_b).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 164.8 ($OCAr_{NO2}$), 158.9 ($COCH_3$), 150.6 (Ar_{NO2}), 150.0 (C_{18}), 136.2 (C_{13}), 135.9 (Ar_{NO2}), 130.7 (Ar_{NO2}), 130.4 (N_1CH_2C), 129.1 (Ar_{PMB}), 127.6 (C_{16}), 123.6 (Ar_{NO2}), 122.5 (C_{14}), 117.6 (C_{15}), 114.1 (Ar_{PMB}), 107.0 (C_{17}), 70.5 (C_{19}), 68.5 (C_2), 62.5 (C_{21}), 55.4 (OCH_3), 53.7 (C_8), 52.9 (C_{10}), 52.7

	(**C**$_{12}$), 47.8 (N$_1$**C**H$_2$), 38.7 (**C**$_{11}$), 35.9 (**C**$_{20}$), 35.5 (2C, **C**$_5$, **C**$_6$), 24.4 (**C**$_4$), 22.6 (**C**$_3$), 21.8 (**C**$_7$).
FTIR (thin film) cm^{-1}:	2932 (s), 1723 (m), 1604 (s), 1527 (s), 1511 (m), 1349 (w), 1274 (m), 1103 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{34}H_{38}N_3O_5$ $[M+H]^+$: 568.2806, found: 568.2802
$[\alpha]_D^{24}$:	–44 (*c* = 0.85, $CHCl_3$).

TLC (3% triethylamine and 10% ethyl acetate in hexanes), R*f*: 0.35 (UV, CAM).



(–)-**S6** (+)-limaspermidine (**20**)

(+)-Limaspermidine (20):

Thiophenol (33.4 µL, 328 mmol, 20.0 equiv) was added to a solution of *N*-paramethoxylbenzylpentacycle (–)-**S6** (9.3 mg, 16.4 µmol, 1 equiv) in trifluoroacetic acid (1.00 mL) at 23 ºC. The reaction mixture was heated to 55 ºC. After 5.5 h, the solution was concentrated in vacuo, and potassium carbonate (45.3 mg, 328 µmol, 20 equiv) and methanol (1.0 mL) were added. After 12 h, saturated aqueous ammonium chloride solution (10 mL) was added and the resulting mixture was extracted with dichloromethane (3 × 10 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: gradient, 0 → 50% ethyl acetate, 3% triethylamine in hexanes) to give (+)-limaspermidine (**20**, 4.2 mg, 86%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.08 (d, *J* = 7.7 Hz, 1H, C_{14}**H**), 7.01 (app-td, *J* = 7.6, 1.3 Hz, 1H, C_{16}**H**), 6.73 (app-td, *J* = 7.4, 1.0 Hz, 1H, C_{15}**H**), 6.64 (d, *J* = 7.7 Hz, 1H, C_{17}**H**), 3.63 (td, *J* = 10.0, 5.5 Hz, 1H, C_{21}**H**$_a$), 3.58–3.47 (m, 2H, C_2**H**, C_{21}**H**$_b$), 3.17–3.08 (m, 1H, C_{10}**H**$_a$), 3.05 (d, *J* = 11.1 Hz, 1H, C_8**H**$_a$), 2.37–2.17 (m, 3H, C_{10}**H**$_b$, C_{11}**H**$_a$, C_{19}**H**), 2.16–1.90 (m, 2H, C_8**H**$_b$, C_4**H**$_a$), 1.87–1.58 (m, 5H, N**H**, C_3**H**$_a$, C_6**H**$_a$, C_7**H**$_a$, C_{20}**H**$_a$), 1.58–1.37 (m, 3H, C_3**H**$_b$, C_7**H**$_b$, C_{11}**H**$_b$), 1.37–1.12 (m, 2H, C_6**H**$_b$, C_{20}**H**$_b$), 1.03 (d, *J* = 13.7 Hz, 1H, C_4**H**$_b$), 0.89 (br-s, 1H O**H**).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 149.6 (**C**$_{18}$), 135.4 (**C**$_{13}$), 127.5 (**C**$_{16}$), 122.9 (**C**$_{14}$), 119.3 (**C**$_{15}$), 110.6 (**C**$_{17}$), 70.8 (**C**$_{19}$), 65.5 (**C**$_2$), 58.8 (**C**$_{21}$), 53.9 (**C**$_8$), 53.6 (**C**$_{12}$), 53.0 (**C**$_{10}$), 40.7 (**C**$_{20}$), 38.7 (**C**$_{11}$), 35.6 (2C, **C**$_5$, **C**$_6$), 28.4 (**C**$_3$), 24.5 (**C**$_4$), 21.9 (**C**$_7$).

FTIR (thin film) cm^{-1}: 3305 (s), 2932 (s), 1607 (m), 1492 (m), 1464 (m), 1256 (m), 1044 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{19}H_{27}N_2O$ $[M+H]^+$: 299.2118, found: 299.2111

$[\alpha]_D^{24}$: +13 (*c* = 0.25, $CHCl_3$).

TLC (3% triethylamine and 20% ethyl acetate in hexanes), R*f*: 0.16 (UV, CAM).

Table S3. Comparison of our ^{1}H NMR data for (+)-limaspermidine (20) with literature data ($CDCl_3$):

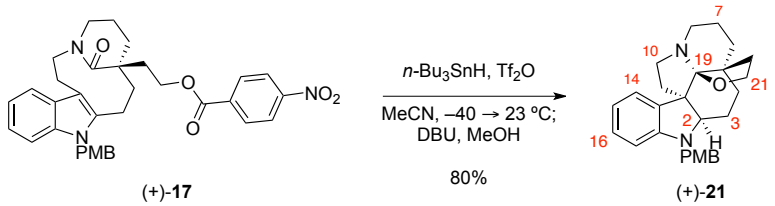
Assignment	Overman's Report[8] (+)-limaspermidine (**20**) ^{1}H NMR, 500 MHz, $CDCl_3$	Fan's Report[9] (+)-limaspermidine (**20**) ^{1}H NMR, 300 MHz, $CDCl_3$	This Work (+)-limaspermidine (**20**) ^{1}H NMR, 400 MHz $CDCl_3$, 25 °C
C2	3.52–3.45 (m, 1H)	3.56–3.43 (m, 1H)	3.58–3.47 (m, 1H)
C3	1.83–1.60 (m, 1H) 1.52–1.45 (m, 1H)	1.73 (m, 1H) 1.58–1.37 (m, 1H)	1.87–1.58 (m, 1H) 1.58–1.37 (m, 1H)
C4	2.04 (dt, *J* =13.8, 3.1 Hz, 1H) 1.16–1.00 (m, 1H)	2.10–1.92 (m, 1H) 1.02 (d, *J* = 13.5 Hz, 1H)	2.16–1.90 (m, 1H) 1.03 (d, *J* = 13.7 Hz, 1H)
C5	–	–	–
C6	1.83–1.60 (m, 1H) 1.33–1.13 (m, 1H)	1.73 (m, 1H) 1.31–1.14 (m, 1H)	1.87–1.58 (m, 1H) 1.37–1.12 (m, 1H)
C7	1.83–1.60 (m, 1H) 1.52–1.45 (m, 1H)	1.73 (m, 1H) 1.58–1.37 (m, 1H)	1.87–1.58 (m, 1H) 1.58–1.37 (m, 1H)
C8	3.04 (bd, *J* = 10.8 Hz, 1H) 1.98 (dt *J* = 11.7, 2.5 Hz, 1H)	3.05 (d, *J* = 10.4 Hz, 1H) 2.10–1.92 (m, 1H)	3.05 (d, *J* = 11.1 Hz, 1H) 2.16–1.90 (m, 1H)
C10	3.11 (bdd, *J* = 10.3, 7.0 Hz, 1H) 2.32–2.20 (m, 1H)	3.17–3.08 (m, 1H) 2.36–2.18 (m, 1H)	3.17–3.08 (m, 1H) 2.37–2.17 (m, 1H)
C11	2.32–2.20 (m, 1H) 1.52–1.45 (m, 1H)	2.36–2.18 (m, 1H) 1.58–1.37 (m, 1H)	2.37–2.17 (m, 1H) 1.58–1.37 (m, 1H)
C12	–	–	–
C13	–	–	–
C14	7.08 (d, *J* = 7.4 Hz, 1H)	7.08 (d, *J* = 7.6 Hz, 1H)	7.08 (d, *J* = 7.7 Hz, 1H)
C15	6.73 (td, *J* = 7.4, 0.8 Hz, 1H))	6.73 (app-td, *J* = 7.3, 1.0 Hz, 1H)	6.73 (app-td, *J* = 7.4, 1.0 Hz, 1H)
C16	7.00 (td, *J* = 7.6, 1.1 Hz, 1H)	7.01 (td, *J* = 7.6, 1.1 Hz, 1H)	7.01 (app-td, *J* = 7.6, 1.3 Hz, 1H)
C17	6.63 (d, *J* = 7.7 Hz, 1H)	6.64 (d, *J* = 7.8 Hz, 1H)	6.64 (d, *J* = 7.7 Hz, 1H)
C18	–	–	–
C19	2.32–2.20 (m, 1H)	2.36–2.18 (m, 1H)	2.37–2.17 (m, 1H)
C20	1.83–1.60 (m, 1H) 1.33–1.13 (m, 1H)	1.73 (m, 1H) 1.31–1.14 (m, 1H)	1.87–1.58 (m, 1H) 1.37–1.12 (m, 1H)
C21	3.61 (td, *J* = 10.4, 5.5 Hz, 1H) 3.52–3.45 (m, 1H)	3.67–3.56 (m, 1H) 3.56–3.43 (m, 1H)	3.63 (td, *J* = 10.0, 5.5 Hz, 1H) 3.58–3.47 (m, 1H)

[8] Overman, L. E.; Robertson, G. M.; Robichaud, A. J. *J. Am. Chem. Soc.* **1991**, *113*, 2598.
[9] Du, J.-Y.; Zeng, C.; Han, X.-J.; Qu, H.; Zhao, X.-H.; An, X.-T.; Fan, C.-A. *J. Am. Chem. Soc.* **2015**, *137*, 4267.

Table S4. Comparison of ^{13}C NMR data of (+)-limaspermidine (20) with literature data ($CDCl_3$):

Assignment	Overman's Report[8,10] (+)-limaspermidine (**20**) ^{13}C NMR, 125 MHz $CDCl_3$	Fan's Report[9,11] (+)-limaspermidine (**20**) ^{13}C NMR, 150 MHz $CDCl_3$, 25 ºC	This Work (+)-limaspermidine (**20**) ^{13}C NMR, 125 MHz $CDCl_3$, 25 ºC	Chemical Shift Difference $\Delta\delta = \delta$ (this work)–δ (Overman Report)	Chemical Shift Difference $\Delta\delta = \delta$ (this work)–δ (Fan Report)
C2	65.3	65.3	65.5	0.2	0.2
C3	28.2	28.2	28.4	0.2	0.2
C4	24.2	24.3	24.5	0.3	0.2
C5	29.7	35.4	35.6	5.7[12]	0.2
C6	35.4	35.5	35.6	0.2	0.1
C7	21.7	21.7	21.9	0.2	0.2
C8	53.7	53.7	53.9	0.2	0.2
C10	52.8	52.8	53.0	0.2	0.2
C11	38.5	38.5	38.7	0.2	0.2
C12	53.4	53.4	53.6	0.2	0.2
C13	135.2	135.2	135.4	0.2	0.2
C14	122.7	122.7	122.9	0.2	0.2
C15	119.3	119.2	119.3	0	0.1
C16	127.3	127.3	127.5	0.2	0.2
C17	110.5	110.5	110.6	0.1	0.1
C18	149.4	149.4	149.6	0.2	0.2
C19	70.7	70.7	70.8	0.1	0.1
C20	40.5	40.5	40.7	0.2	0.2
C21	58.6	58.6	58.8	0.2	0.2

[10] The ^{13}C NMR data was not assigned in this report but the values are in good agreement with our assignments.
[11] The ^{13}C NMR data was not assigned in this report but the values are in excellent agreement with our assignments.
[12] Our assignment is supported by HMBC correlations and is consistent with Fan's report (reference 9).



Hexacycle (+)-21:

Trifluoromethanesulfonic anhydride (73.4 µL, 436 µmol, 1.20 equiv) was added dropwise via syringe to a mixture of benzoate (+)-**17** (215 mg, 364 µmol, 1 equiv) and tri-*n*-butyltin hydride (193 µL, 727 µmol, 2.00 equiv) in acetonitrile (9.0 mL) at –40 °C. After 10 min, the reaction mixture was warmed to 0 °C. After 10 min, the ice bath was removed, and the solution was allowed to warm to 23 °C. After 2 h, methanol (9.00 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (543 µL, 3.64 mmol, 10.0 equiv) were added sequentially. After 13 h, the reaction was concentrated under reduced pressure, dissolved in ethyl acetate (30 mL), and saturated aqueous sodium bicarbonate solution (50 mL) was added to the reaction mixture. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (50 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0 → 30% ethyl acetate in hexanes with 3% triethylamine) to give hexacycle (+)-**21** (121 mg, 79.8%) as white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.42 (dd, *J* = 7.4, 1.3 Hz, 1H, C_{14}**H**), 7.25 (d, *J* = 8.9 Hz, 2H, Ar_{PMB}**H**), 7.02 (app-td, *J* = 7.6, 1.3 Hz, 1H, C_{16}**H**), 6.86 (d, *J* = 8.6 Hz, 2H, Ar_{PMB}**H**), 6.66 (app-td, *J* = 7.4, 1.1 Hz, 1H, C_{15}**H**), 6.37 (d, *J* = 7.8 Hz, 1H, C_{17}**H**), 4.37 (d, *J* = 15.0 Hz, 1H, N_1C**H**$_a$), 4.05 (d, *J* = 15.0 Hz, 1H, N_1C**H**$_b$), 3.98–3.89 (m, 1H, C_{21}**H**$_a$), 3.86 (t, *J* = 8.3 Hz, 1H, C_{21}**H**$_b$), 3.81 (s, 3H, O**CH**$_3$), 3.24 (dd, *J* = 8.0, 4.1 Hz, 1H, C_2**H**), 3.02–2.87 (m, 2H, C_8**H**$_2$), 2.83–2.72 (m, 1H, C_{10}**H**$_a$), 2.62 (d, *J* = 11.1 Hz, 1H, C_{10}**H**$_b$), 2.20 (ddd, *J* = 13.1, 9.0, 6.5 Hz, 1H, C_7**H**$_a$), 2.02–1.88 (m, 2H, C_7**H**$_b$, C_6**H**$_a$), 1.84 (q, *J* = 10.5 Hz, 1H, C_{20}**H**$_a$), 1.74–1.56 (m, 3H, C_{11}**H**$_a$, C_6**H**$_b$, C_4**H**$_a$), 1.58–1.45 (m, 3H, C_3**H**$_2$, C_4**H**$_b$), 1.33 (d, *J* = 11.8 Hz, 1H, C_{11}**H**$_b$), 1.27 (dd, *J* = 12.0, 6.1 Hz, 1H, C_{20}**H**$_b$).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 158.8 (**C**OCH_3), 151.1 (**C**$_{18}$), 135.0 (**C**$_{13}$), 130.9 (N_1CH_2**C**), 128.9 (Ar_{PMB}), 127.4 (**C**$_{16}$), 125.9 (**C**$_{14}$), 117.8 (**C**$_{15}$), 114.0 (Ar_{PMB}), 106.5 (**C**$_{17}$), 102.0 (**C**$_{19}$), 71.2 (**C**$_2$), 64.9 (**C**$_{21}$), 57.8 (**C**$_{12}$), 55.4 (O**C**H_3), 49.2 (**C**$_8$), 48.8 (N_1**C**H_2), 44.1 (**C**$_{10}$), 38.6 (**C**$_7$), 38.2 (**C**$_5$), 36.9 (**C**$_{20}$), 34.6 (**C**$_{11}$), 27.4 (**C**$_4$), 21.6 (2C, **C**$_3$, **C**$_6$).

FTIR (thin film) cm^{-1}:	2934 (s), 2871 (m), 2833 (m), 1600 (m), 1512 (s), 1478 (m), 1461 (w), 1247 (m), 1172 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{27}H_{33}N_2O_2$ $[M+H]^+$: 417.2537, found: 417.2524
$[\alpha]_D^{24}$:	+4 (*c* = 0.41, CH_2Cl_2).
M.p.:	92 ºC (CH_2Cl_2).

TLC (Al_2O_3, 5% ethyl acetate in hexanes), R*f*: 0.54 (UV, CAM).

(+)-Fendleridine (3):

Thiophenol (0.510 mL, 4.99 mmol, 20.0 equiv) was added to a solution of hexacycle (+)-**21** (120.0 mg, 288.1 μmol, 1 equiv) in trifluoroacetic acid (6.00 mL) at 23 ºC. The reaction mixture was heated to 55 ºC. After 5.5 h, the solution was concentrated in vacuo, and triethylamine (1.00 mL) and methanol (10.0 mL) were added via syringe. After 12 h, saturated sodium bicarbonate solution (30 mL) was added and the resulting mixture was extracted with dichloromethane (3 × 30 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: gradient, 0 → 50% ethyl acetate, 3% triethylamine in hexanes) to give (+)-fendleridine (**3**, 71.0 mg, 83.5%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.45 (d, J = 7.5 Hz, 1H, C_{14}**H**), 7.01 (app-t, J = 7.5 Hz, 1H, C_{16}**H**), 6.73 (app-t, J = 7.6 Hz, 1H, C_{15}**H**), 6.60 (d, J = 7.9 Hz, 1H, C_{17}**H**), 4.05–3.91 (m, 2H, C_{21}**H**$_2$), 3.50 (br-s, 1H, N**H**), 3.40 (dd, J = 8.9, 5.1 Hz, 1H, C_2**H**), 3.01 (ddd, J = 9.4, 8.1, 4.3 Hz, 1H, C_{10}**H**$_a$), 2.93 (ddd, J = 10.1, 8.2, 6.2 Hz, 1H, C_{10}**H**$_b$), 2.79 (t, J = 10.8 Hz, 1H, C_8**H**$_a$), 2.65 (d, J = 10.3 Hz, 1H, C_8**H**$_b$), 2.25 (ddd, J = 13.3, 8.7, 5.9 Hz, 1H, C_{11}**H**$_a$), 2.00–1.55 (m, 7H, C_3**H**$_2$, C_4**H**$_a$, C_6**H**$_a$, C_7**H**$_a$, C_{11}**H**$_b$, C_{20}**H**$_a$), 1.52 (dt, J = 11.8, 3.3 Hz, 1H, C_7**H**$_b$), 1.46 (dt, J = 13.6, 4.6 Hz, 1H, C_6**H**$_b$), 1.36 (d, J = 12.6 Hz, 1H, C_4**H**$_b$), 1.25 (ddd, J = 12.0, 5.4, 1.8 Hz, 1H, C_{20}**H**$_b$).

^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 150.3 (**C**$_{18}$), 134.5 (**C**$_{13}$), 127.3 (**C**$_{16}$), 126.1 (**C**$_{14}$), 119.5 (**C**$_{15}$), 110.0 (**C**$_{17}$), 102.1 (**C**$_{19}$), 66.6 (**C**$_2$), 64.9 (**C**$_{21}$), 59.0 (**C**$_{12}$), 49.3 (**C**$_{10}$), 44.1 (**C**$_8$), 39.2 (**C**$_5$), 37.0 (**C**$_{11}$), 35.8 (**C**$_{20}$), 34.1 (**C**$_4$), 27.3 (**C**$_3$), 27.0 (**C**$_6$), 21.5 (**C**$_7$).

FTIR (thin film) cm^{-1}: 3307 (s), 2941 (s), 2874 (m), 2834 (m), 1603 (m), 1468 (m), 1339 (w), 1015 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{19}H_{25}N_2O$ $[M+H]^+$: 297.1961,
found: 297.1963.

$[\alpha]_D^{24}$: +79 (c = 0.40, $CHCl_3$).

M.p.: 187–188 ºC (hexane).[13]

TLC (3% triethylamine and 30% ethyl acetate in hexanes), R*f*: 0.17 (UV, CAM).

[13] Literature value: M.p. = 185–186 ºC, see R. H. Burnell, J. D. Ayer, W. D. Medina, *Can. J. Chem.* **1966**, *44*, 28.

Table S5. Comparison of our ^{1}H NMR data for (+)-fendleridine (3) with literature data ($CDCl_3$):

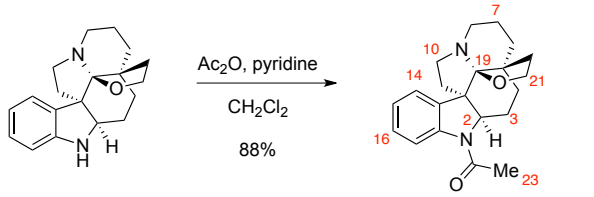
Assignment	Boger's Report[14] (+)-fendleridine (**3**) ^{1}H NMR, $CDCl_3$	This Work (+)-fendleridine (**3**) ^{1}H NMR, 400 MHz $CDCl_3$, 25 ºC
N1	5.90 (br-s, 1H)	3.50 (br-s, 1H)[15]
C2	3.40 (dd, *J* = 9.1, 4.8 Hz, 1H)	3.40 (dd, *J* = 8.9, 5.1 Hz, 1H)
C3	1.92–1.66 (m, 2H)	2.00–1.55 (m, 2H)
C4	1.92–1.66 (m, 1H) 1.35 (d, *J* = 13.1 Hz, 1H)	2.00–1.55 (m, 1H) 1.36 (d, *J* = 12.6 Hz, 1H)
C5	–	–
C6	1.92–1.66 (m, 1H) 1.45 (dt, *J* = 13.6, 4.4 Hz, 1H)	2.00–1.55 (m, 1H) 1.46 (dt, *J* = 13.6, 4.6 Hz, 1H)
C7	1.92–1.66 (m, 1H) 1.52 (dd, *J* = 7.7, 4.6 Hz, 1H)	2.00–1.55 (m, 1H) 1.52 (dt, *J* = 11.8, 3.3 Hz, 1H)
C8	2.79 (td, *J* = 11.5, 2.6 Hz, 1H) 2.65 (d, *J* = 11.4 Hz, 1H)	2.79 (t, *J* = 10.8 Hz, 1H) 2.65 (d, *J* = 10.3 Hz, 1H)
C10	3.01 (td, *J* = 8.7, 4.3 Hz, 1H) 2.92 (dt, *J* = 14.6, 7.3 Hz, 1H)	3.01 (ddd, *J* = 9.4, 8.1, 4.3 Hz, 1H) 2.93 (ddd, *J* = 10.1, 8.2, 6.2 Hz, 1H)
C11	2.25 (ddd, *J* = 15.0, 9.1, 6.3 Hz, 1H) 1.92–1.66 (m, 1H)	2.25 (ddd, *J* = 13.3, 8.7, 5.9 Hz, 1H) 2.00–1.55 (m, 1H)
C12	–	–
C13	–	–
C14	7.46 (d, *J* = 7.8 Hz, 1H)	7.45 (d, *J* = 7.5 Hz, 1H)
C15	6.73 (t, *J* = 7.2 Hz, 1H)	6.73 (app-t, *J* = 7.6 Hz, 1H)
C16	7.01 (t, *J* = 7.8 Hz, 1H)	7.01 (app-t, *J* = 7.5 Hz, 1H)
C17	6.61 (d, *J* = 7.8 Hz, 1H)	6.60 (d, *J* = 7.9 Hz, 1H),
C18	–	–
C19	–	–
C20	1.92–1.66 (m, 1H) 1.25 (d, *J* = 5.4 Hz, 1H)	2.00–1.55 (m, 1H) 1.25 (ddd, *J* = 12.0, 5.4, 1.8 Hz, 1H)
C21	4.01–3.98 (m, 2H)	4.05–3.91 (m, 2H)

[14] Campbell, E. L.; Zuhl, A. M.; Liu, C. M.; Boger, D. L. *J. Am. Chem. Soc.* **2010**, *132*, 3009.
[15] We do not observe any resonance at 5.90 ppm, and believe the resonance at 3.50 ppm present in both our ^{1}H NMR spectrum as well as that in reference 14 corresponds to the N1-H.

Table S6. Comparison of ^{13}C NMR data of (+)-fendleridine (3) with literature data ($CDCl_3$):

Assignment	**Boger's Report**[14,16] (+)-fendleridine (**3**) ^{13}C NMR $CDCl_3$	**This Work** (+)-fendleridine (**3**) ^{13}C NMR, 100 MHz $CDCl_3$, 25 ºC	**Chemical Shift Difference** $\Delta\delta = \delta$ (this work)–δ (Boger Report)
C2	66.3	66.6	0.3
C3	27.0	27.3	0.3
C4	33.9	34.1	0.2
C5	39.1	39.2	0.1
C6	26.8	27.0	0.2
C7	21.3	21.5	0.2
C8	43.9	44.1	0.2
C10	49.1	49.3	0.2
C11	35.6	37.0	1.4
C12	58.8	59.0	0.2
C13	134.4	134.5	0.1
C14	125.9	126.1	0.2
C15	119.3	119.5	0.2
C16	127.1	127.3	0.2
C17	109.9	110.0	0.2
C18	150.0	150.8	0.8
C19	101.9	102.1	0.2
C20	35.7	35.8	0.1
C21	64.8	64.9	0.1

[16] The ^{13}C NMR data was not assigned in this report but the values are in excellent agreement with our assignments.



(+)-Acetylaspidoalbidine (4):

Acetic anhydride (10.5 µL, 113 µmol, 3.00 equiv) and pyridine (14.9 µL, 186 µmol, 5.00 equiv) were added via syringe to (+)-fendleridine (**3**, 11.0 mg, 37.1 µmol, 1 equiv) in dichloromethane (1.00 mL) at 23 ºC. After 6 h, saturated sodium bicarbonate solution (5 mL) was added to the reaction mixture, the resulting mixture was extracted with dichloromethane (3 × 10 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 3% triethylamine and 10% ethyl acetate in hexanes) to give (+)-acetylaspidoalbidine (**4**, 11.1 mg, 88.4%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, 3.8:1 mixture of atropisomers, * denotes minor atropisomer):
δ 8.14 (d, J = 8.0 Hz, 1H, C_{17}**H**), 7.67 (d, J = 7.4 Hz, 1H, C_{17}**H***), 7.60 (d, J = 7.7 Hz, 1H, C_{14}**H**), 7.19 (app-t, J = 7.8 Hz, 1H, C_{16}**H**), 7.05 (app-td, J = 7.4, 1.1 Hz, 1H, C_{15}**H**), 4.41 (br–s, 1H, C_2**H***), 4.17 (t, J = 8.6 Hz, 1H, C_{21}**H**$_a$), 4.09 (dt, J = 11.1, 7.6 Hz, 1H, C_{21}**H**$_b$), 3.86 (dd, J = 10.9, 5.1 Hz, 1H, C_2**H**), 3.02 (td, J = 8.8, 4.2 Hz, 1H, C_{10}**H**$_a$), 2.98–2.86 (m, 1H, C_{10}**H**$_b$), 2.80 (t, J = 9.8 Hz, 1H, C_8**H**$_a$), 2.65 (d, J = 10.9 Hz, 1H, C_8**H**$_b$), 2.39 (s, 3H, C_{23}**H**$_3$*), 2.26 (s, 3H, C_{23}**H**$_3$), 2.10 (ddd, J = 14.4, 9.1, 5.9 Hz, 1H, C_{11}**H**$_a$), 1.99–1.64 (m, 6H, C_3**H**$_2$, C_4**H**$_a$, C_6**H**$_a$, C_7**H**$_a$, C_{11}**H**$_b$, C_{20}**H**$_a$), 1.62–1.46 (m, 1H, C_7**H**$_b$), 1.46–1.30 (m, 2H, C_4**H**$_b$, C_6**H**$_b$), 1.30–1.18 (m, 1H, C_{20}**H**$_b$).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 3.8:1 mixture of atropisomers, * denotes minor atropisomer):
δ 168.2 (**C**$_{22}$), 168.0 (**C**$_{22}$*), 141.2 (**C**$_{18}$), 137.9 (**C**$_{13}$), 131.7*, 129.9*, 127.5 (**C**$_{16}$), 127.1*, 126.1 (**C**$_{17}$*), 124.9 (**C**$_{14}$), 124.8 (**C**$_{15}$), 124.3*, 117.9 (**C**$_{17}$), 115.1*, 102.5 (**C**$_{19}$*), 102.1 (**C**$_{19}$), 68.9 (**C**$_2$), 67.0 (**C**$_2$*), 65.1 (**C**$_{21}$), 65.0 (**C**$_{21}$*), 58.3 (**C**$_{12}$), 57.2 (**C**$_{12}$*), 49.0 (**C**$_{10}$), 48.9 (**C**$_{10}$*), 44.0 (2C, **C**$_8$, **C**$_8$*), 39.8 (**C**$_5$), 39.6 (**C**$_5$*), 37.2 (**C**$_{11}$), 36.9 (**C**$_{11}$*), 35.1 (**C**$_{20}$*), 34.8 (**C**$_{20}$), 33.4 (**C**$_4$*), 33.2 (**C**$_4$), 26.7 (**C**$_6$*), 26.5 (**C**$_6$), 25.5 (**C**$_3$), 24.3 (**C**$_3$*), 23.7 (**C**$_{23}$*), 23.5 (**C**$_{23}$), 21.2 (**C**$_7$).

FTIR (thin film) cm^{-1}:	3086 (m), 2963 (s), 2901 (s), 1734 (w), 1653 (s), 1595 (w), 1473 (m), 1396 (m), 1018 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{21}H_{27}N_2O_2$ $[M+H]^+$: 339.2067, found: 339.2083.
$[\alpha]_D^{24}$:	+39 (*c* = 0.18, $CHCl_3$).[17]
M.p.:	169–171 ºC (dichloromethane).[17]

TLC (3% triethylamine and 15% ethyl acetate in hexanes), R*f*: 0.46 (UV, CAM).

[17] a) Literature isolation value: $[\alpha]_D^{24}$ = +46 ($CHCl_3$). b) Literature isolation value: M.p. = 173–174 ºC, see K.S. Brown, H. Budzikiewicz, C. Djerassi, *Tetrahedron Lett*. **1963**, *4*, 1731. Synthetic value: $[\alpha]_D^{24}$ = +38 (c = 0.2, $CHCl_3$), see Campbell, E. L.; Zuhl, A. M.; Liu, C. M.; Boger, D. L. *J. Am. Chem. Soc*. **2010**, *132*, 3009.

Table S7. Comparison of our ^{1}H NMR data for (+)-acetylaspidoalbidine (4) with literature data ($CDCl_3$):

Assignment	Zeches-Hanrot's Isolation Report[18] (+)-acetylaspidoalbidine (**4**) ^{1}H NMR, 300 MHz, $CDCl_3$	Boger's Report[14] (+)-acetylaspidoalbidine (**4**) ^{1}H NMR, $CDCl_3$	This Work (+)-acetylaspidoalbidine (**4**) ^{1}H NMR, 400 MHz $CDCl_3$, 25 ºC
C2	3.85 (dd, *J* = 10.6, 5.8 Hz, 1H)	3.86 (dd, *J* =10.9, 5.1 Hz, 1H)	3.86 (dd, *J* = 10.9, 5.1 Hz, 1H)
C3	2.1–1.6	2.1–1.6	1.99–1.64 (m, 2H)
C4	2.1–1.6 1.45 (dt, *J* = 13.7, 3.5 Hz, 1H)	1.99–1.66 (m, 1H) 1.43 (dt, *J* =13.9, 3.3 Hz, 1H)	1.99–1.64 (m, 1H) 1.46–1.30 (m, 1H)
C5	–	–	–
C6	2.1–1.6 (m, 1H) 1.35 (br-d, *J* = 8.0 Hz, 1H)	2.96 (d, *J* = 4.0 Hz, 1H) 1.38 (br d, *J* = 11.4 Hz, 1H)	1.99–1.64 (m, 1H) 1.46–1.30 (m, 1H)
C7	1.55 (m, 1H)	1.55 (dd, *J* = 12.1 Hz, 1H)	1.99–1.64 (m, 1H) 1.62–1.46 (m, 1H)
C8	2.8 (td, *J* = 8.5, 4.3 Hz, 1H) 2.6 (m, 1H)	2.79 (t, *J* = 9.6 Hz, 1H) 2.65 (d, J = 10.8 Hz, 1H)	2.80 (t, *J* = 9.8 Hz, 1H) 2.65 (d, *J* = 10.9 Hz, 1H)
C10	3.0 (td, *J* = 8.5, 4.3 Hz, 1H) 2.9 (m, 1H)	3.02 (td, *J* = 8.7, 4.2 Hz, 1H) 2.92 (dd, *J* = 15.4, 9.1 Hz, 1H)	3.02 (td, *J* = 8.8, 4.2 Hz, 1H) 2.98–2.86 (m, 1H)
C11	2.1–1.6 (m, 1H)	2.13–2.06 (m, 1H)	2.10 (ddd, *J* = 14.4, 9.1, 5.9 Hz, 1H) 1.99–1.64 (m, 1H)
C12	–	–	–
C13	–	–	–
C14	8.1 (dd, *J* = 7.7, 1.3 Hz, 1H)	8.14 (d, *J* = 8.0 Hz, 1H)	7.60 (d, *J* = 7.7 Hz, 1H)[19]
C15	7.1 (td, *J* = 7.7 Hz, 1H)	7.05 (t, *J* = 7.5 Hz, 1H)	7.05 (app-td, *J* = 7.4, 1.1 Hz, 1H)
C16	7.2 (td, *J* = 7.7, 1.3 Hz, 1H)	7.19 (t, *J* = 7.7 Hz, 1H)	7.19 (app-t, *J* = 7.8 Hz, 1H)
C17	7.6 (dd, *J* = 7.7, 1.3 Hz, 1H)	7.59 (d, J = 7.6 Hz, 1H)	8.14 (d, *J* = 8.0 Hz, 1H)[19]
C18	–	–	–
C19	–	–	–
C20	2.1–1.6 (m, 2H)	1.99–1.66 (m, 2H)	1.99–1.64 (m, 1H) 1.30–1.18 (m, 1H)
C21	4.15 (t, *J* = 10.8 Hz, 1H) 4.05 (ddd, *J* = 10.8, 8.2, 6.0 Hz, 1H)	4.16 (t, *J* = 8.5 Hz, 1H) 4.08 (dd, *J* = 8.5 Hz, 1H)	4.17 (t, *J* = 8.6 Hz, 1H) 4.09 (dt, *J* = 11.1, 7.6 Hz, 1H)
C22	–	–	–
C23	2.3 (s, 3H)	2.25 (s, 3H)	2.26 (s, 3H)

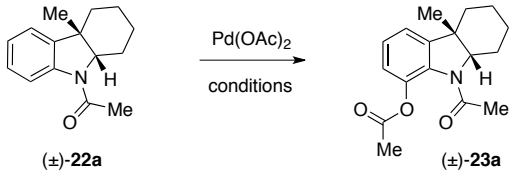
[18] Mitaine, A. C.; Mesbah, K.; Richard, B.; Petermann, C.; Arrazola, S.; Moretti, C.; Zeches-Hanrot, M.; Le Men Olivier, L. *Planta Med*. **1996**, *62*, 458.
[19] Our assignment of these resonances is supported by key gCOSY, gHSQC and gHMBC correlations.

Table S8. Comparison of ^{13}C NMR data of (+)-acetylaspidoalbidine (4) with literature data ($CDCl_3$):

Assignment	Boger's Report[14,20] (+)-acetylaspidoalbidine (**4**) ^{13}C NMR, 150 MHz $CDCl_3$	This Work (+)-acetylaspidoalbidine (**4**) ^{13}C NMR, 125 MHz $CDCl_3$, 25 ºC	Chemical Shift Difference $\Delta\delta = \delta$ (this work)–δ (Boger Report)
C2	68.8	68.9	0.1
C3	25.3	25.5	0.2
C4	33.0	33.2	0.2
C5	39.6	39.8	0.2
C6	26.4	26.5	0.1
C7	21.0	21.2	0.2
C8	43.9	44.0	0.1
C10	48.9	49.0	0.1
C11	37.1	37.2	0.1
C12	58.2	58.3	0.1
C13	137.8	137.9	0.1
C14	124.8	124.9	0.1
C15	124.7	124.8	0.1
C16	127.3	127.5	0.2
C17	117.8	117.9	0.1
C18	141.1	141.2	0.1
C19	102.0	102.1	0.1
C20	34.6	34.8	0.2
C21	65.0	65.1	0.1
C22	168.1	168.2	0.1
C23	23.4	23.5	0.1

[20] The ^{13}C NMR data was not assigned in reference 14; we have tabulated the published values for comparison and the values are in excellent agreement with our data and assignments.

Table S9. Development of the Directed C17-Oxidation of (±)-22a:[a]



(±)-**22a** (±)-**23a**

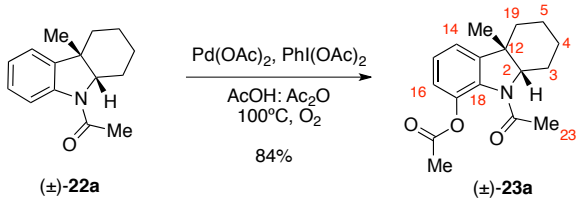
Entry	$Pd(OAc)_2$	Oxidant	Oxidant Equivalents	Time	Temperature	Solvent	Additive	Yield of **23a**
1	20 mol%	$PhI(OAc)_2$	2 equiv	24 h	70 ºC	HFIP, Ac_2O	—	36%
2	20 mol%	$PhI(OAc)_2$	2 equiv	24 h	100 ºC	AcOH, Ac_2O	—	23%
3	20 mol%	$K_2S_2O_8$	2 equiv	24 h	70 ºC	TFA, TFAA	—	—
4	20 mol%	$K_2S_2O_8$	2 equiv	48 h	100 ºC	AcOH, DCE	—	<5%
5	20 mol%	$PhI(OAc)_2$	4 equiv	24 h	70 ºC	HFIP, Ac_2O	—	38%
6	100 mol%	$PhI(OAc)_2$	2 equiv	24 h	55 ºC	HFIP, Ac_2O	—	61%
7	20 mol%	$PhI(OAc)_2$	2 equiv	24 h	100 ºC	AcOH, Ac_2O	—	23%
8	100 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	AcOH, Ac_2O[a]	—	87%
9	***15 mol%***	***$PhI(OAc)_2$***	***2.5 equiv***	***9 h***	***100 ºC***	***AcOH, Ac_2O[a]***	—	***84%***
10	5 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	AcOH, Ac_2O[a]	—	67%
11	—	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	AcOH, Ac_2O[a]	—	NR
12	20 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	DMSO, AcOH, Ac_2O[a]	—	NR
13	20 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	90 ºC	DCE, AcOH, Ac_2O[a]	—	86%
14	20 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	AcOH, Ac_2O[a]	*N*-acetyl glycine	61%
15	20 mol%	$PhI(OAc)_2$	2.5 equiv	12 h	100 ºC	AcOH, Ac_2O[a]	*p*-TsOH	67%
16	20 mol%	$PhI(OAc)_2$	2.5 equiv	13 h	100 ºC	AcOH[a]	—	74%

[a] These oxidation reactions were conducted under an atmosphere of dioxygen.

Representative Procedure for Table S9, Entry 14:

Diacetoxyiodobenzene (50.8 mg, 158 μmol, 2.50 equiv) and palladium acetate (2.1 mg, 9.5 μmol, 0.15 equiv) were added to acetamide[21] (±)-**22a** (21.0 mg, 91.5 μmol, 1 equiv), *N*-acetyl glycine (3.3 mg, 28 μmol, 0.45 equiv), and acetic anhydride (125 μL) in acetic acid (1.25 mL) at 23 ºC. The reaction was sparged with dioxygen for 10 minutes, sealed with a Teflon wrapped glass stopper, and heated to 100 ºC. After 12 h, the reaction mixture was cooled to 23 ºC and diluted in ethyl acetate (5 mL). A saturated aqueous sodium carbonate solution (10 mL) was slowly introduced to neutralized the acid. The resulting mixture was extracted with ethyl acetate (3 × 10 mL) and the combined organic extracts were further washed with saturated aqueous sodium chloride solution (10 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: gradient, 20 → 50% ethyl acetate in hexanes) to give C17-acetoxylated acetamide (±)-**23a** (11 mg, 61%) as a white solid.

[21] Jiao, L.-Y.; Oestreich, M., *Chem.Euro. J.* **2013**, *19*, 10845.

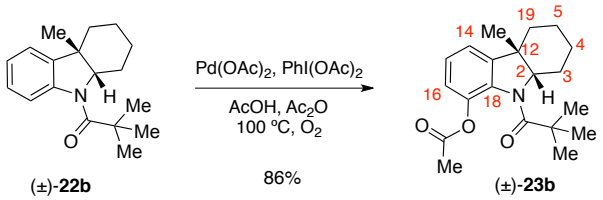


(±)-**22a** (±)-**23a**

C17-Acetoxylated Acetamide (±)-23a:

Diacetoxyiodobenzene (73.7 mg, 229 μmol, 2.50 equiv) and palladium acetate (3.0 mg, 14 μmol, 0.15 equiv) were added to acetamide[21] (±)-**22a** (21.0 mg, 91.5 μmol, 1 equiv) and acetic anhydride (200 μL) in an acetic acid (2.00 mL) at 23 ºC. The reaction was sparged with dioxygen for 10 minutes, sealed with a Teflon wrapped glass stopper, and heated to 100 ºC. After 9 h, the reaction mixture was cooled to 23 ºC and diluted in ethyl acetate (5 mL). Saturated sodium aqueous carbonate solution (10 mL) was carefully added. The resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (10 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: gradient, 20 → 50% ethyl acetate in hexanes) to give C17-acetoxylated acetamide (±)-**23a** (22.0 mg, 83.7%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C):	δ 7.12 (app-t, *J* = 7.7 Hz, 1H, C_{15}**H**), 6.97 (dd, *J* = 7.4, 1.2 Hz, 1H, C_{14}**H**), 6.94 (dd, *J* = 8.1, 1.2 Hz, 1H, C_{16}**H**), 3.95 (s, 1H, C_2**H**), 2.27 (s, 3H, OC(O)C**H**$_3$), 2.29–2.23 (m, 1H, C_{19}**H**$_a$), 2.21 (s, 3H, C_{23}**H**$_3$), 2.08–1.99 (m, 1H, C_3**H**$_a$), 1.64–1.45 (m, 3H, C_{19}**H**$_b$, C_5**H**$_2$), 1.37–1.17 (m, 2H, C_3**H**$_b$, C_4**H**$_a$), 1.15 (s, 3H, C_{11}**H**$_3$), 1.13–0.96 (m, 1H, C_4**H**$_b$).
^{13}C NMR (100 MHz, $CDCl_3$, 25 °C):	δ 167.9 (2C, **C**$_{22}$, O**C**(O)CH$_3$), 143.6 (**C**$_{13}$), 140.9 (**C**$_{17}$), 132.5 (**C**$_{18}$), 125.9 (**C**$_{15}$), 122.4 (**C**$_{16}$), 119.1 (**C**$_{14}$), 70.4 (**C**$_2$), 44.7 (**C**$_{12}$), 32.9 (**C**$_{19}$), 30.2 (**C**$_{11}$), 28.5 (**C**$_3$), 23.1 (**C**$_{23}$), 22.8 (**C**$_5$), 22.0 (**C**$_4$), 21.1 (OC(O)**C**H$_3$).
FTIR (thin film) cm^{-1}:	2929 (m), 2856 (w), 1763 (s), 1666 (s), 1475 (w), 1458 (s), 1394 (s), 1212 (s), 1181 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{17}H_{22}NO_3$ $[M+H]^+$: 288.1594, found: 288.1586.
M.p.:	89–90 ºC (dichloromethane).
TLC (25% ethyl acetate in hexanes), R*f*:	0.19 (UV, CAM, $KMnO_4$).



C17-Acetoxylated Pivalamide (±)-23b:

Diacetoxyiodobenzene (59.3 mg, 184 μmol, 2.50 equiv) and palladium acetate (2.5 mg, 11 μmol, 0.15 equiv) were added to pivalamide[22] (±)-**22b** (20.0 mg, 73.7 μmol, 1 equiv) and acetic anhydride (0.150 mL) in an acetic acid (1.50 mL) at 23 ºC. The reaction was sparged with dioxygen for 10 minutes, sealed with a Teflon wrapped glass stopper, and heated to 100 ºC. After 3.5 h, the reaction mixture was cooled to 23 ºC and diluted in ethyl acetate (5 mL). Saturated sodium aqueous carbonate solution (10 mL) was carefully added. The resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (10 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 20% ethyl acetate in hexanes) to give C17-acetoxylated pivalamide (±)-**23b** (21.0 mg, 86.4%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.13 (dd, J = 8.3, 7.2 Hz, 1H, C_{15}**H**), 7.00–6.92 (m, 2H, C_{14}**H**, C_{16}**H**), 4.11 (dd, J = 10.4, 5.8 Hz, 1H, C_2**H**), 2.33–2.25 (m, 1H, C_{19}**H**$_a$), 2.22 (s, 3H, OC(O)C**H**$_3$), 2.19–2.07 (m, 1H, C_3**H**$_a$), 1.68–1.44 (m, 3H, C_{19}**H**$_b$, C_5**H**$_a$, C_4**H**$_a$), 1.36 (s, 9H, C(C**H**$_3$)$_3$), 1.31–1.24 (m, 1H, C_3**H**$_b$), 1.24–1.05 (m, 2H, C_5**H**$_b$, C_4**H**$_b$), 1.12 (s, 3H, C_{11}**H**$_3$).

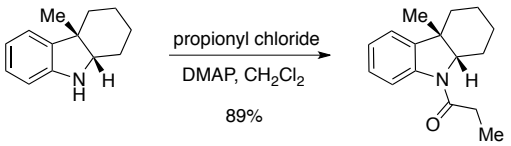
^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ 177.0 (**C**$_{22}$), 168.0 (O**C**(O)CH$_3$), 143.3 (**C**$_{13}$), 142.6 (**C**$_{17}$), 135.0 (**C**$_{18}$), 125.8 (**C**$_{15}$), 122.0 (**C**$_{16}$), 118.6 (**C**$_{14}$), 69.5 (**C**$_2$), 46.8 (**C**$_{12}$), 40.4 (**C**$_{23}$), 33.1 (**C**$_{19}$), 29.7 (**C**$_{11}$), 29.0 (OC(O)**C**H$_3$), 28.7 (**C**$_3$), 23.7 (**C**$_{4/5}$), 22.1 (**C**$_{4/5}$), 21.1 (**C**$_{19}$).

FTIR (thin film) cm^{-1}: 2929 (m), 2860 (w), 1765 (s), 1652 (s), 1606 (w), 1448 (m), 1358 (m), 1207 (s), 1170 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{20}H_{28}NO_3$ $[M+H]^+$: 330.2064, found: 330.2054.

[22] Shin, Y.; Sharma, S.; Mishra, N. K.; Han, S.; Park, J.; Oh, H.; Ha, J.; Yoo, H.; Jung, Y. H.; Kim, I. S. *Advanced Synthesis & Catalysis* **2015**, *357*, 594.

M.p.:	63 ºC (dichloromethane).
TLC (20% ethyl acetate in hexanes), R*f*:	0.28 (UV).



(±)-**S7** (±)-**22c**

Propionamide (±)-22c:

Propionyl chloride (12.0 μL, 138 μmol, 1.50 equiv) was added via syringe to indoline[23] (±)-**S7** (17.2 mg, 91.9 μmol, 1 equiv) and 4-(dimethylamino)-pyridine (22.4 mg, 184 μmol, 2.00 equiv) in dichloromethane (1.00 mL) at 23 ºC. After 12 h, saturated aqueous ammonium chloride solution (10 mL) was added. The resulting mixture was extracted with dichloromethane (3 × 10 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10% ethyl acetate in hexanes) to give propionamide (±)-**22c** (19.8 mg, 88.5%) as a light tan solid.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, 25:1 mixture of atropisomers): δ 8.14 (br-s, 1H), 7.21 (app-td, *J* = 7.6, 1.6 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.05 (app-td, *J* = 7.3, 1.1 Hz, 1H), 3.86 (s, 1H), 2.59 (dd, *J* = 15.4, 7.8 Hz, 1H), 2.47 (br-s, 1H), 2.28 (d, *J* = 14.1 Hz, 1H), 2.04 (br-s, 1H), 1.68–1.50 (m, 3H), 1.26 (t, *J* = 7.4 Hz, 3H), 1.22–1.15 (m, 3H), 1.12 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 25:1 mixture of atropisomers): δ 172.0, 141.0, 138.6, 127.6, 127.6, 123.9, 122.6, 121.5, 118.7, 115.1, 67.7, 43.9, 35.2, 32.6, 31.2, 29.4, 28.4, 26.4, 23.0, 22.1, 21.3, 9.6, 9.1.

FTIR (thin film) cm^{-1}: 2929 (m), 2856 (w), 1763 (s), 1666 (s), 1607 (w), 1475 (s), 1394 (s), 1269 (m), 1181 (s).

HRMS (ESI) (*m/z*): calc'd for $C_{16}H_{22}NO$ $[M+H]^+$: 244.1696, found: 244.1685.

M.p.: 86–87 ºC (dichloromethane).

TLC (12.5% ethyl acetate in hexanes), R*f*: 0.29 (UV).

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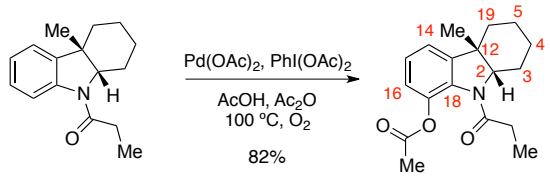
[23] a) Millson, M. F.; Robinson, R. *J. Chem. Soc.* **1955**, 3362. b) Scott, K. R.; Alt, C. J.; Kemp, M.; Hayes, E.; Telang, V. G., *J. Pharm. Sci.* **1984,** *73*, 1531.

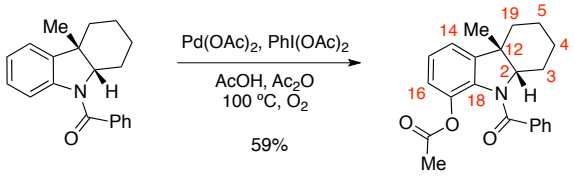


(±)-**22c** (±)-**23c**

C17-Acetoxylated Propionamide (±)-23c:

Diacetoxyiodobenzene (62.9 mg, 195 μmol, 2.50 equiv) and palladium acetate (2.6 mg, 12 μmol, 0.15 equiv) were added to propionamide (±)-**22c** (19.0 mg, 78.1 μmol, 1 equiv) and acetic anhydride (170 μL) in an acetic acid (1.70 mL) at 23 ºC. The reaction was sparged with dioxygen for 10 minutes, sealed with a Teflon wrapped glass stopper, and heated to 100 ºC. After 7 h, the reaction mixture was cooled to 23 ºC and diluted in ethyl acetate (5 mL). Saturated aqueous sodium carbonate solution (10 mL) was carefully added. The resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (10 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 30% ethyl acetate in hexanes) to give C17-acetoxylated propionamide (±)-**23c** (19.3 mg, 82.0%) as a white solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C):	δ 7.12 (dd, *J* = 8.1, 7.4 Hz, 1H, C_{15}**H**), 6.97 (dd, *J* = 7.5, 1.2 Hz, 1H, C_{14}**H**), 6.94 (dd, *J* = 8.1, 1.2 Hz, 1H, C_{16}**H**), 3.93 (s, 1H, C_2**H**), 2.46 (ddt, *J* = 21.9, 15.3, 7.7 Hz, 2H, C**H**$_2$CH$_3$), 2.35–2.25 (m, 1H, C_{19}**H**$_a$), 2.27 (s, 3H, OC(O)C**H**$_3$), 2.10–1.98 (m, 1H, C_3**H**$_a$), 1.70–1.47 (m, 4H, C_{19}**H**$_b$, C_{15}**H**$_2$, C_4**H**$_a$), 1.40–1.25 (m, 1H, C_3**H**$_b$), 1.22 (t, *J* = 7.5 Hz, 3H, CH$_2$C**H**$_3$), 1.20–1.06 (m, 1H, C_4**H**$_b$), 1.14 (s, 3H, C_{11}**H**$_3$).
^{13}C NMR (100 MHz, $CDCl_3$, 25 °C):	171.0 (O**C**(O)CH$_3$), 167.9 (**C**$_{22}$), 143.4 (**C**$_{13}$), 141.0 (**C**$_{17}$), 132.6 (**C**$_{18}$), 125.8 (**C**$_{15}$), 122.3 (**C**$_{16}$), 119.0 (**C**$_{14}$), 69.7 (**C**$_2$), 44.8 (**C**$_{12}$), 33.0 (**C**$_{19}$), 30.2 (**C**$_{11}$), 28.7 (**C**$_3$), 28.2 (**C**H$_2$CH$_3$), 23.2 (**C**$_5$), 22.0 (**C**$_4$), 21.1 (O**C**(O)CH$_3$), 10.2 (CH$_2$**C**H$_3$).
FTIR (thin film) cm^{-1}:	2930 (m), 2857 (w), 1764 (s), 1662 (s), 1607 (w), 1475 (m), 1366 (m), 1209 (s), 1178 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{18}H_{24}NO_3$ $[M+H]^+$: 302.1751, found: 302.1746.
M.p.:	72–73 ºC (hexane).
TLC (33% ethyl acetate in hexanes), R*f*:	0.33 (UV, CAM).



(±)-**22d** (±)-**23d**

C17-Acetoxylated Benzamide (±)-23d:

Diacetoxyiodobenzene (138 mg, 429 μmol, 2.50 equiv) and palladium acetate (5.7 mg, 26 μmol, 0.15 equiv) were added to benzamide[24] (±)-**22d** (50.0 mg, 172 μmol, 1 equiv) and acetic anhydride (400 μL) in an acetic acid (4.00 mL) at 23 ºC. The reaction was sparged with dioxygen for 10 minutes, sealed with a Teflon wrapped glass stopper, and heated to 100 ºC. After 8 h, the reaction mixture was cooled to 23 ºC and diluted in ethyl acetate (10 mL). Saturated aqueous sodium carbonate solution (10 mL) was carefully added. The resulting mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were further extracted with saturated aqueous sodium chloride solution (10 mL), dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10% ethyl acetate in hexanes) to give C17-acetoxylated benzamide (±)-**23d** (35.2 mg, 58.7%) as a colorless amorphous solid. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, 6.8:1 mixture of atropisomers, * denotes minor isomer): δ 7.59 (d, *J* = 7.0 Hz, 2H), 7.54–7.39 (m, 4H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 8.1 Hz, 1H*), 7.02 (dd, *J* = 7.4, 1.0 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 2.3 Hz, 1H*), 4.10 (br-s, 1H*), 3.82 (br-s, 1H), 2.30 (d, *J* = 14.6 Hz, 4H), 2.25 (s, 3H*), 2.16 (d, *J* = 13.2 Hz, 1H), 2.10 (s, 3H), 1.63–1.45 (m, 5H), 1.39 (t, *J* = 12.2 Hz, 1H), 1.25 (d, *J* = 4.7 Hz, 2H), 1.16 (s, 3H), 1.08 (d, *J* = 12.6 Hz, 3H).

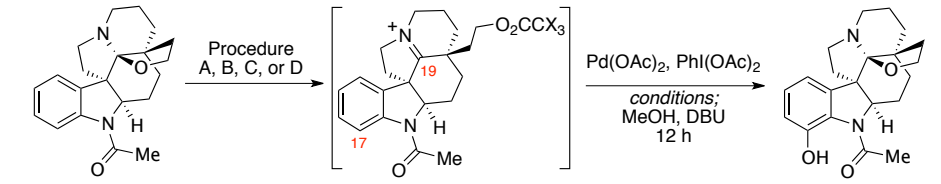
^{13}C NMR (125 MHz, $CDCl_3$, 25 °C, 6.8:1 mixture of atropisomers): δ 169.4, 168.1, 143.9, 137.0, 132.9, 130.8, 128.7, 128.7, 127.2, 126.2, 122.2, 119.2, 71.7, 45.6, 33.0, 32.7, 30.6, 29.6, 28.9, 23.4, 22.9, 22.1, 22.0, 21.3, 21.0.

FTIR (thin film) cm^{-1}: 2929 (m), 2856 (m), 1764 (w), 1645 (s), 1476 (s), 1448 (s), 1369 (m), 1182 (s).

[24] Kim, M.; Mishra, N. K.; Park, J.; Han, S.; Shin, Y.; Sharma, S.; Lee, Y.; Lee, E.-K.; Kwak, J. H.; Kim, I. S. *Chem. Commun.* **2014**, *50*, 14249.

HRMS (ESI) (*m/z*):	calc'd for $C_{22}H_{24}NO_3$ $[M+H]^+$: 350.1751, found: 350.1746.
TLC (30% ethyl acetate in hexanes), R*f*:	0.44 (UV, CAM).

Table S10. Development of the Directed C17-Oxidation (+)-Acetylaspidoalbidine (4):[a]



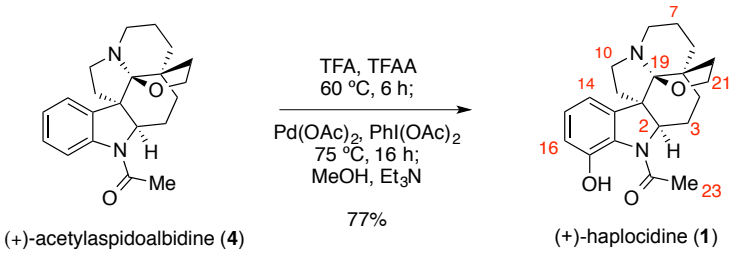
(+)-acetylaspidoalbidine (**4**) **26** (+)-haplocidine (**1**)

Entry	Procedure A, B, C, or D	$Pd(OAc)_2$	$PhI(OAc)_2$	Time	Temperature	Solvent	Conversion of **4** to **1**[b]
1	A	200 mol%	10 equiv	24 h	55 ºC	HFIP, Ac_2O	0%
2	A	1000 mol%	4 equiv	24 h	75 ºC	HFIP, Ac_2O	0%
3	B	200 mol%	10 equiv	24 h	75 ºC	HFIP, Ac_2O	0%
4	B	15 mol%	2.5 equiv	14 h	100 ºC	AcOH, Ac_2O	0%
5	B	200 mol%	2.5 equiv	14 h	100 ºC	AcOH, Ac_2O	25%
6	B	500 mol%	4 equiv	18 h	100 ºC	AcOH, Ac_2O	18%
7	B	200 mol%	2.5 equiv	22 h	110 ºC	AcOH, Ac_2O	0%
8[c]	B	100 mol%	2.5 equiv	12 h	100ºC	AcOH, Ac_2O	9%
9	B	100 mol%	2.5 equiv	42 h	95 ºC	1,2–DCE, AcOH, Ac_2O	5%
10	C	500 mol%	4 equiv	18 h	100 ºC	AcOH, Ac_2O	75%
11	C	500 mol%	4 equiv	18 h	100 ºC	TFA, TFAA	100% (58%)
12	C	100 mol%	4 equiv	16 h	100 ºC	TFA, TFAA	100% (70%)
13[d]	***D***	***20 mol%***	***4 equiv***	***16 h***	***100 ºC***	***TFA, TFAA***	***100% (77%)***
14[d,e]	D	20 mol%	4 equiv	16 h	100 ºC	TFA, TFAA	100%

[a] Reaction conditions: A) (+)-Acetylaspidoalbidine (**4**, 1 equiv) was exposed to the oxidation conditions without derivatization. B) (+)-Acetylaspidoalbidine (**4**, 1 equiv) was exposed to a mixture of acetic acid and acetic anhydride (v/v, 10:1, X=H) at 100 ºC. After 6 h, the volatiles were removed by concentration from toluene under reduced pressure. C) (+)-Acetylaspidoalbidine (**4**, 1 equiv) was exposed to a mixture of trifluoroacetic acid and trifluoroacetic anhydride (v/v, 10:1, X=F) at 60 ºC. After 6 h, the volatiles were removed by concentration from toluene under reduced pressure. D) (+)-Acetylaspidoalbidine (**4**, 1 equiv) was exposed to a mixture of trifluoroacetic acid and trifluoroacetic anhydride (v/v, 10:1, X=F) at 60 ºC. After 4 h, the reaction media was exposed to the oxidation conditions. [b] Isolated yields shown in parentheses. [c] Conducted under an atmosphere of dioxygen. [d] Triethylamine used in place of DBU. [e] $Pd(O_2CCF_3)_2$ and $PhI(O_2CCF_3)_2$ used in place of acetate variants.

General procedure for the C17-hydroxylation:

Following procedures A, B, or C, the substrate was dissolved in the indicated *solvent* mixture, the palladium catalyst and the oxidant were added, the reaction mixture was sealed, and heated to the indicated *temperature*. After the indicated time, the reaction mixture was cooled to 23 ºC, the volatiles were removed by concentration from toluene under reduced pressure, the residue was dissolved in methanol, and DBU (10 equiv) was introduced to promote methanolysis. After 12 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel.



(+)-Haplocidine (1):

(+)-Acetylaspidoalbidine (**4**, 6.1 mg, 18 μmol, 1 equiv) was dissolved in trifluoroacetic anhydride (50 μL) and trifluoroacetic acid (500 μL). The reaction was sealed and heated to 60 ºC. After 4 h, the reaction mixture was cooled to 23 ºC. Palladium acetate (0.8 mg, 3.6 μmol, 0.20 equiv) and diacetoxyiodobenzene (23.2 μL, 72.0 μmol, 4.00 equiv) were added. The reaction vessel was sealed and heated to 75 ºC. After 16 h, the reaction was concentrated under reduced pressure and subsequently dissolved in methanol (1 mL) and triethylamine (0.200 mL). After 12 h, the reaction was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 3% triethylamine and 10% ethyl acetate in hexanes) to give (+)-haplocidine (**1**, 4.9 mg, 77%) as a white film. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 10.65 (s, 1H, $C_{17}O\mathbf{H}$), 7.15 (d, J = 7.5 Hz, 1H, $C_{14}\mathbf{H}$), 7.08 (app-t, J = 7.7 Hz, 1H, $C_{15}\mathbf{H}$), 6.82 (d, J = 8.2 Hz, 1H, $C_{16}\mathbf{H}$), 4.16 (t, J = 8.5 Hz, 1H, $C_{21}\mathbf{H}_a$), 4.13–4.03 (m, 1H, $C_{21}\mathbf{H}_b$), 3.86 (dd, J = 11.1, 5.5 Hz, 1H, $C_2\mathbf{H}$), 3.01 (td, J = 8.5, 4.1 Hz, 1H, $C_{10}\mathbf{H}_a$), 2.97–2.86 (m, 1H, $C_{10}\mathbf{H}_b$), 2.78 (t, J = 12.1 Hz, 1H, $C_8\mathbf{H}_a$), 2.63 (d, J = 15.4 Hz, 1H, $C_8\mathbf{H}_b$), 2.32 (s, 3H, $C_{23}\mathbf{H}_3$), 2.04 (ddd, J = 14.5, 9.6, 6.1 Hz, 1H, $C_{11}\mathbf{H}_a$), 1.99–1.79 (m, 5H, $C_3\mathbf{H}_2$, $C_6\mathbf{H}_a$, $C_{11}\mathbf{H}_b$, $C_{20}\mathbf{H}_a$), 1.79–1.70 (m, 2H, $C_4\mathbf{H}_a$, $C_7\mathbf{H}_a$), 1.55 (d, J = 13.9 Hz, 1H, $C_7\mathbf{H}_b$), 1.45 (d, J = 14.3 Hz, 1H, $C_6\mathbf{H}_b$), 1.37 (d, J = 7.1 Hz, 1H, $C_4\mathbf{H}_b$), 1.24 (dd, J = 12.5, 5.5 Hz, 1H, $C_{20}\mathbf{H}_b$).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 168.9 ($\mathbf{C}_{22}$), 147.0 ($\mathbf{C}_{17}$), 140.7 ($\mathbf{C}_{13}$), 128.4 ($\mathbf{C}_{15}$), 127.4 ($\mathbf{C}_{18}$), 117.8 ($\mathbf{C}_{16}$), 115.6 ($\mathbf{C}_{14}$), 101.8 ($\mathbf{C}_{19}$), 70.3 ($\mathbf{C}_2$), 65.3 ($\mathbf{C}_{21}$), 58.3 ($\mathbf{C}_{12}$), 49.0 ($\mathbf{C}_{10}$), 44.1 ($\mathbf{C}_8$), 39.9 ($\mathbf{C}_5$), 36.5 ($\mathbf{C}_{11}$), 34.6 ($\mathbf{C}_{20}$), 33.0 ($\mathbf{C}_4$), 26.4 ($\mathbf{C}_6$), 24.9 ($\mathbf{C}_3$), 23.1 ($\mathbf{C}_{23}$), 21.1 ($\mathbf{C}_7$).

FTIR (thin film) cm^{-1}: 2933 (br-s), 2858 (m), 1706 (w), 1628 (s), 1600 (m), 1470 (m), 1380 (m), 1260 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{21}H_{27}N_2O_3$ $[M+H]^+$: 355.2016, found: 355.2006.

$[\alpha]_D^{24}$: +207 (c = 0.32, $CHCl_3$).[25]

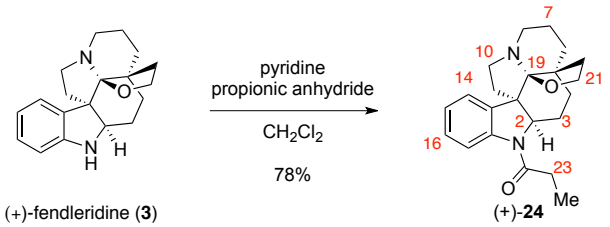
TLC (3% triethylamine and 15% ethyl acetate in hexanes), R*f*: 0.46 (UV, CAM).

[25] Literature value: $[\alpha]_D^{24}$ =+214 ±7 (c = 0.354, $CHCl_3$), see N. J. Dastoor, A. A. Gorman, H. Schmid, *Helv*. *Chim*. *Acta*, **1967**, *50*, 213.

Table S11. Comparison of our ^{1}H NMR data for (+)-haplocidine (1) with literature data ($CDCl_3$):

Assignment	Djerassi's Isolation Report[26] (+)-haplocidine (**1**) ^{1}H NMR $CDCl_3$	This Work (+)-haplocidine (**1**) ^{1}H NMR, 500 MHz $CDCl_3$, 25 ºC	This Work (+)-acetylaspidoalbidine (**4**) ^{1}H NMR, 400 MHz $CDCl_3$, 25 ºC
C2	not reported	3.86 (dd, *J* = 11.1, 5.5 Hz, 1H)	3.86 (dd, *J* = 10.9, 5.1 Hz, 1H)
C3	not reported	1.99–1.79 (m, 2H)	1.99–1.64 (m, 2H)
C4	not reported	1.79–1.70 (m, 1H) 1.37 (d, *J* = 7.1 Hz, 1H)	1.99–1.64 (m, 1H) 1.46–1.30 (m, 1H)
C6	not reported	1.99–1.79 (m, 1H) 1.45 (d, *J* = 14.3 Hz, 1H)	1.99–1.64 (m, 1H) 1.46–1.30 (m, 1H)
C7	not reported	1.79–1.70 (m, 1H) 1.55 (d, *J* = 13.9 Hz, 1H)	1.99–1.64 (m, 1H) 1.62–1.46 (m, 1H)
C8	not reported	2.78 (t, *J* = 12.1 Hz, 1H) 2.63 (d, *J* = 15.4 Hz, 1H)	2.80 (t, *J* = 9.8 Hz, 1H) 2.65 (d, *J* = 10.9 Hz, 1H)
C10	not reported	3.01 (td, *J* = 8.5, 4.1 Hz, 1H) 2.97–2.86 (m, 1H)	3.02 (td, *J* = 8.8, 4.2 Hz, 1H) 2.98–2.86 (m, 1H)
C11	not reported	2.04 (ddd, *J* = 14.5, 9.6, 6.1 Hz, 1H) 1.99–1.79 (m, 1H)	2.10 (ddd, *J* = 14.4, 9.1, 5.9 Hz, 1H) 1.99–1.64 (m, 1H)
C14	not reported	7.15 (d, *J* = 7.5 Hz, 1H)	7.60 (d, *J* = 7.7 Hz, 1H)FO
C15	not reported	7.08 (app-t, *J* = 7.7 Hz, 1H)	7.05 (app-td, *J* = 7.4, 1.1 Hz, 1H)
C16	not reported	6.82 (d, *J* = 8.2 Hz, 1H)	7.19 (app-t, *J* = 7.8 Hz, 1H)
C17	not reported	–	8.14 (d, *J* = 8.0 Hz, 1H)
C20	not reported	1.99–1.79 (m, 1H) 1.24 (dd, *J* = 12.5, 5.5 Hz, 1H)	1.99–1.64 (m, 1H) 1.30–1.18 (m, 1H)
C21	4.30–3.55 (m, 2H)	4.16 (t, *J* = 8.5 Hz, 1H) 4.13–4.03 (m, 1H)	4.17 (t, *J* = 8.6 Hz, 1H) 4.09 (dt, *J* = 11.1, 7.6 Hz, 1H)
C22	–	–	–
C23	2.3 (s, 3H)	2.32 (s, 3H)	2.26 (s, 3H)
OH	10.70 (s, 1H)	10.65 (s, 1H)	

[26] Brown, K. S.; Budzikiewicz, H.; Djerassi, C. *Tetrahedron Lett*. **1963**, *4*, 1731. Signals that deviate from closely related alkaloids are specifically reported. We provide full assignment of the resonances for (+)-haplocidine (**1**) along with direct comparison with (+)-acetylaspidoalbidine (**4**, Table S11) and our complete assignment of (+)-haplocine (**2**, Table S12).



(+)-Propionylaspidoalbidine (24):

Propionic anhydride (10.7 µL, 84.0 µmol, 3.00 equiv) and pyridine (11.3 µL, 140 µmol, 5.00 equiv) were added via syringe to (+)-fendleridine (**3**, 8.3 mg, 28.0 µmol, 1 equiv) in dichloromethane (1.00 mL) at 23 ºC. After 8 h, saturated sodium bicarbonate solution (5 mL) was added to the reaction mixture, the resulting mixture was extracted with dichloromethane (10 mL × 3), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 3% triethylamine and 10% ethyl acetate in hexanes) to give (+)-propionylaspidoalbidine (**24**, 7.7 mg, 78%) as a colorless film. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, 5.5:1 mixture of atropisomers, * denotes minor atropisomer):
δ 8.16 (d, *J* = 8.0 Hz, 1H, C_{17}**H**), 7.66 (br-s, 1H, C_{17}**H***), 7.59 (d, *J* = 7.6 Hz, 1H, C_{14}**H**), 7.19 (app-t, *J* = 7.7 Hz, 1H, C_{16}**H**), 7.04 (app-td, *J* = 7.6, 1.1 Hz, 1H, C_{15}**H**), 4.43 (br–s, 1H, C_2**H***), 4.17 (t, *J* = 8.6 Hz, 1H, C_{21}**H**$_a$), 4.13–4.05 (m, 1H, C_{21}**H**$_b$), 3.90 (dd, *J* = 10.9, 5.1 Hz, 1H, C_2**H**), 3.01 (ddd, *J* = 9.3, 8.3, 4.3 Hz, 1H, C_{10}**H**$_a$), 2.91 (ddd, *J* = 10.3, 8.4, 6.0 Hz, 1H, C_{10}**H**$_b$), 2.83–2.75 (m, 1H, C_8**H**$_a$), 2.64 (d, *J* = 11.1 Hz, 1H, C_8**H**$_b$), 2.55 (dq, *J* = 15.1, 7.5 Hz, 1H, C_{23}**H**$_a$), 2.48–2.32 (m, 3H, C_{23}**H**$_b$, C_{23}**H**$_2$*), 2.07 (ddd, *J* = 13.4, 9.3, 6.0 Hz, 1H, C_{11}**H**$_a$), 2.01–1.88 (m, 1H, C_{20}**H**$_a$), 1.88–1.62 (m, 5H, C_3**H**$_2$, C_6**H**$_a$, C_7**H**$_a$, C_{11}**H**$_b$), 1.54 (d, *J* = 11.5 Hz, 1H, C_7**H**$_b$), 1.46–1.33 (m, 2H, C_4**H**$_b$, C_6**H**$_b$), 1.25 (app-t, *J* = 7.4 Hz, 4H, C_{20}**H**$_b$, C_{24}**H**$_3$), 1.15 (t, *J* = 7.6 Hz, 3H, C_{24}**H**$_3$*).

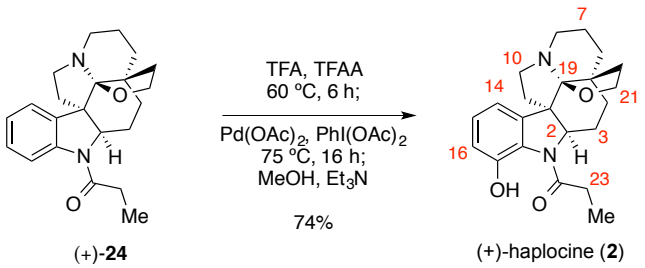
^{13}C NMR (125 MHz, $CDCl_3$, 25 °C):
δ 171.7 (**C**$_{22}$), 141.4 (**C**$_{18}$), 137.9 (**C**$_{13}$), 127.5 (**C**$_{16}$), 124.8 (2C, **C**$_{14}$, **C**$_{15}$), 117.9 (**C**$_{17}$), 102.2 (**C**$_{19}$), 67.9 (**C**$_2$), 65.1 (**C**$_{21}$), 58.4 (**C**$_{12}$), 49.0 (**C**$_{10}$), 44.1 (**C**$_8$), 39.8 (**C**$_5$), 37.1 (**C**$_{11}$), 34.8 (**C**$_{20}$), 33.2 (**C**$_4$), 28.5 (**C**$_{23}$), 26.5 (**C**$_6$), 25.6 (**C**$_3$), 21.2 (**C**$_7$), 9.6 (**C**$_{24}$).

FTIR (thin film) cm^{-1}:
2935 (m), 2873 (m), 1660 (s), 1595 (w), 1474 (m), 1459 (m), 1399 (m), 1282 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{22}H_{29}N_2O_2$ $[M+H]^+$: 353.2224, found: 353.2206.

$[\alpha]_D^{24}$: +34 (*c* = 0.30, $CHCl_3$).

TLC (3% triethylamine and 15% ethyl acetate in hexanes), R*f*: 0.36 (UV, CAM).



(+)-Haplocine (2):

(+)-Propionylaspidoalbidine (**24**, 7.7 mg, 22 μmol, 1 equiv) was dissolved in trifluoroacetic anhydride (50 μL) and trifluoroacetic acid (500 μL). The reaction was sealed and heated to 60 ºC. After 4 h, the reaction mixture was cooled to 23 ºC. Palladium acetate (0.98 mg, 4.4 μmol, 0.20 equiv) and diacetoxyiodobenzene (28.3 mg, 88.0 μmol, 4.00 equiv) were added. The reaction vessel was sealed and heated to 75 ºC. After 16 h, the reaction was concentrated under reduced pressure and subsequently dissolved in methanol (1 mL) and triethylamine (0.200 mL). After 12 h, the reaction was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 3% triethylamine and 10% ethyl acetate in hexanes) to give (+)-haplocine (**2**, 5.9 mg, 74%) as a pale yellow film. Structural assignments were made using additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 10.68 (s, 1H, $C_{17}O\mathbf{H}$), 7.15 (dd, J = 7.6, 1.2 Hz, 1H, $C_{14}\mathbf{H}$), 7.07 (app-t, J = 7.8 Hz, 1H, $C_{15}\mathbf{H}$), 6.83 (dd, J = 8.0, 1.2 Hz, 1H, $C_{16}\mathbf{H}$), 4.17 (t, J = 8.5 Hz, 1H, $C_{21}\mathbf{H}_a$), 4.13–4.03 (m, 1H, $C_{21}\mathbf{H}_b$), 3.91 (dd, J = 10.9, 5.5 Hz, 1H, $C_2\mathbf{H}$), 3.00 (td, J = 8.8, 4.2 Hz, 1H, $C_{10}\mathbf{H}_a$), 2.92 (ddd, J = 10.2, 8.3, 6.0 Hz, 1H, $C_{10}\mathbf{H}_b$), 2.83–2.73 (m, 1H, $C_8\mathbf{H}_a$), 2.67–2.56 (m, 2H, $C_8\mathbf{H}_b$, $C_{23}\mathbf{H}_a$), 2.55–2.46 (m, 1H, $C_{23}\mathbf{H}_b$), 2.02 (ddd, J = 13.2, 8.8, 5.7 Hz, 1H, $C_{11}\mathbf{H}_a$), 1.98–1.68 (m, 7H, $C_3\mathbf{H}_2$, $C_4\mathbf{H}_a$, $C_6\mathbf{H}_a$, $C_7\mathbf{H}_a$, $C_{11}\mathbf{H}_b$, $C_{20}\mathbf{H}_a$), 1.60–1.52 (m, 1H, $C_7\mathbf{H}_b$), 1.44 (dt, J = 13.8, 3.6 Hz, 1H, $C_6\mathbf{H}_b$), 1.37 (t, J = 11.2 Hz, 1H, $C_4\mathbf{H}_b$), 1.27 (t, J = 7.4 Hz, 3H, $C_{24}\mathbf{H}_3$), 1.24 (dd, J = 11.8, 5.9 Hz, 1H, $C_{20}\mathbf{H}_b$).

^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ 172.3 ($\mathbf{C}_{22}$), 147.0 ($\mathbf{C}_{17}$), 140.7 ($\mathbf{C}_{13}$), 128.2 ($\mathbf{C}_{15}$), 127.6 ($\mathbf{C}_{18}$), 117.8 ($\mathbf{C}_{16}$), 115.6 ($\mathbf{C}_{14}$), 101.8 ($\mathbf{C}_{19}$), 69.1 ($\mathbf{C}_2$), 65.3 ($\mathbf{C}_{21}$), 58.3 ($\mathbf{C}_{12}$), 48.9 ($\mathbf{C}_{10}$), 44.0 ($\mathbf{C}_8$), 39.9 ($\mathbf{C}_5$), 36.3 ($\mathbf{C}_{11}$), 34.6 ($\mathbf{C}_{20}$), 33.0 ($\mathbf{C}_4$), 28.4 ($\mathbf{C}_{23}$), 26.4 ($\mathbf{C}_6$), 25.1 ($\mathbf{C}_3$), 21.1 ($\mathbf{C}_7$), 9.9 ($\mathbf{C}_{24}$).

FTIR (thin film) cm^{-1}: 2937 (br-s), 2869 (m), 2830 (w), 1627 (s), 1599 (s), 1469 (m), 1437 (m), 1376 (m), 1259 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{22}H_{29}N_2O_3$ $[M+H]^+$: 369.2173, found: 369.2182.

$[\alpha]_D^{24}$: +180 (*c* = 0.23, $CHCl_3$).[27]

TLC (3% triethylamine and 15% ethyl acetate in hexanes), R*f*: 0.34 (UV, CAM).

[27] Literature value: $[\alpha]_D^{24}$ = +193 ($CHCl_3$), see M. P. Cava, S. K. Talpatra, K. Nomura, J. A Wisback, B. Douglas, E. C. Shoop, *Chem. Ind.* **1963**, 1242.

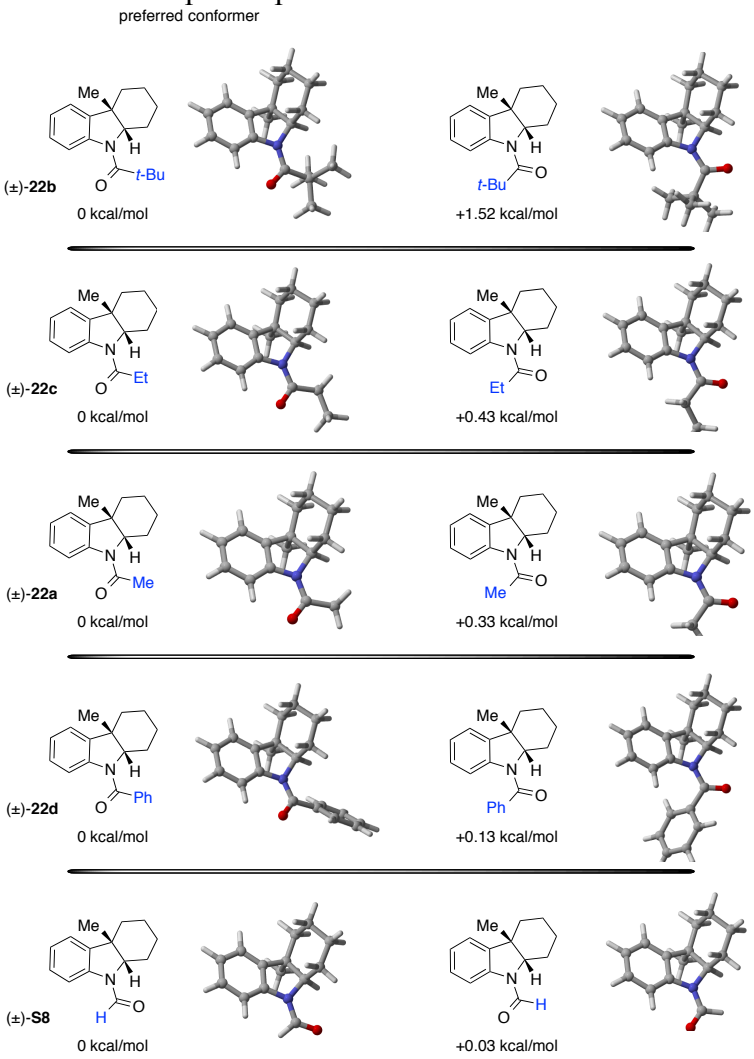
Table S12. Comparison of our ^{1}H NMR data for (+)-haplocine (2) with literature data ($CDCl_3$):

Assignment	**Cava's Isolation Report**[27] (+)-haplocine (**2**) ^{1}H NMR $CDCl_3$	**This Work** (+)-haplocine (**2**)[28] ^{1}H NMR, 500 MHz $CDCl_3$, 25 ºC	**This Work** (+)-haplocidine (**1**)[28] ^{1}H NMR, 500 MHz $CDCl_3$, 25 ºC
C2	not reported	3.91 (dd, *J* = 10.9, 5.5 Hz, 1H)	3.86 (dd, *J* = 11.1, 5.5 Hz, 1H)
C3	not reported	1.98–1.68 (m, 2H)	1.99–1.79 (m, 2H)
C4	not reported	1.98–1.68 (m, 1H) 1.37 (t, *J* = 11.2 Hz, 1H)	1.79–1.70 (m, 1H) 1.37 (d, *J* = 7.1 Hz, 1H)
C5	–	–	–
C6	not reported	1.98–1.68 (m, 1H) 1.44 (dt, *J* = 13.8, 3.6 Hz, 1H)	1.99–1.79 (m, 1H) 1.45 (d, *J* = 14.3 Hz, 1H)
C7	not reported	1.98–1.68 (m, 1H) 1.60–1.52 (m, 1H)	1.79–1.70 (m, 1H) 1.55 (d, J = 13.9 Hz, 1H)
C8	not reported	2.83–2.73 (m, 1H) 2.67–2.56 (m, 1H)	2.78 (t, *J* = 12.1 Hz, 1H) 2.63 (d, *J* = 15.4 Hz, 1H)
C10	not reported	3.00 (td, *J* = 8.8, 4.2 Hz, 1H) 2.92 (ddd, *J* = 10.2, 8.3, 6.0 Hz, 1H)	3.01 (td, *J* = 8.5, 4.1 Hz, 1H) 2.97–2.86 (m, 1H)
C11	not reported	2.02 (ddd, *J* = 13.2, 8.8, 5.7 Hz, 1H) 1.98–1.68 (m, 1H)	2.04 (ddd, *J* = 14.5, 9.6, 6.1 Hz, 1H) 1.99–1.79 (m, 1H)
C12	–	–	–
C13	–	–	–
C14	not reported	7.15 (dd, *J* = 7.6, 1.2 Hz, 1H)	7.15 (d, *J* = 7.5 Hz, 1H)
C15	not reported	7.07 (app-t, *J* = 7.8 Hz, 1H)	7.08 (app-t, *J* = 7.7 Hz, 1H)
C16	not reported	6.83 (dd, *J* = 8.0, 1.2 Hz, 1H)	6.82 (d, *J* = 8.2 Hz, 1H)
C17	–	–	–
C18	–	–	–
C19	–	–	–
C20	not reported	1.98–1.68 (m, 1H) 1.24 (dd, *J* = 11.8, 5.9 Hz, 1H)	1.99–1.79 (m, 1H) 1.24 (dd, *J* = 12.5, 5.5 Hz, 1H)
C21	not reported	4.17 (t, *J* = 8.5 Hz, 1H) 4.13–4.03 (m, 1H)	4.16 (t, *J* = 8.5 Hz, 1H) 4.13–4.03 (m, 1H)
C22	–	–	–
C23	2.52 (m, 2H)	2.67–2.56 (m, 1H) 2.55–2.46 (m, 1H)	2.32 (s, 3H)
C24	1.23 (t, *J* = 7.5 Hz, 3H)	1.27 (t, *J* = 7.4 Hz, 3H)	–
OH	10.80	10.68 (s, 1H)	10.65 (s, 1H)

[28] From Cava's isolation report: "The NMR spectrum of haplocidine differs significantly from that of haplocine only in that the signals characteristic of the N-propionyl group are replaced by a sharp singlet at 2.43, attributable to an N-acetyl group. The relationship between haplocine and haplocidine is confirmed by the interconversion of the two alkaloids."

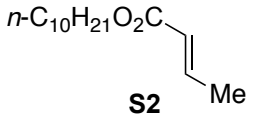
Calculations Related to Amides (±)-22a–d:

The conformation distribution and equilibrium geometries (gas phase) in the ground state of indoline amides were optimized with Merck Molecular Force Field (MMFF)[29] followed by density functional theory at B3LYP level with 6-31G(d) as basis set (Spartan ′14, Version 1.1.1, by Wavefunction, Inc.).[30] The 3D representations of the molecular structures were generated from CYLview.[31] The formamide **S8** was found to deformylate under the *ortho*-acetoxylation conditions. All other amides explored prefer the *s*-cis conformation.

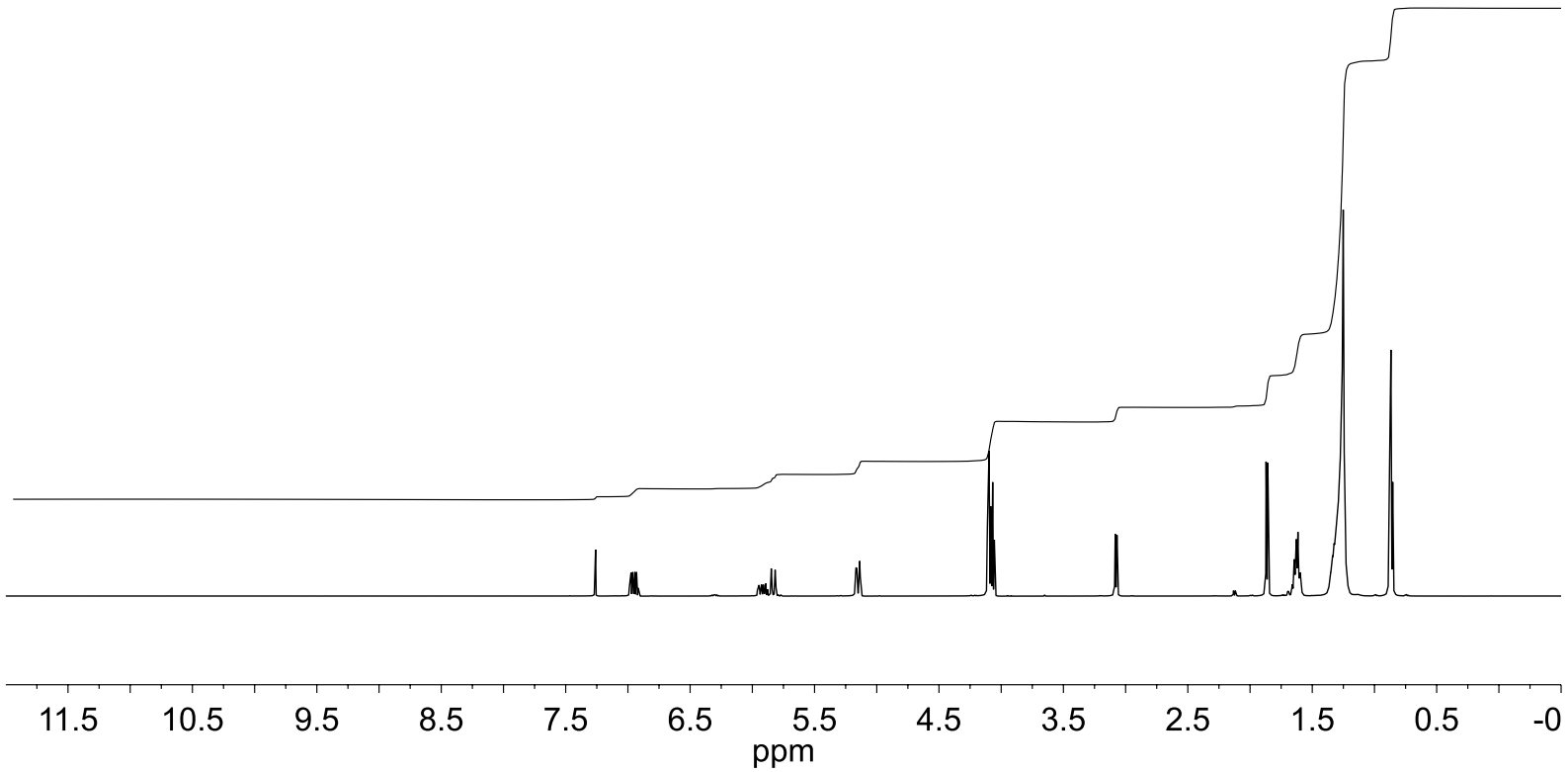


[29] Halgren, T. A. *J. Comput. Chem.* **1996**, *17*, 490.
[30] Spartan'14 Wavefunction, Inc. Irvine, CA. Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan have been documented in: Shao, Y.; Molnar, L. F.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; DiStasio Jr., R. A.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B.D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W. Z.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock III, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172.
[31] CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (http://www.cylview.org).

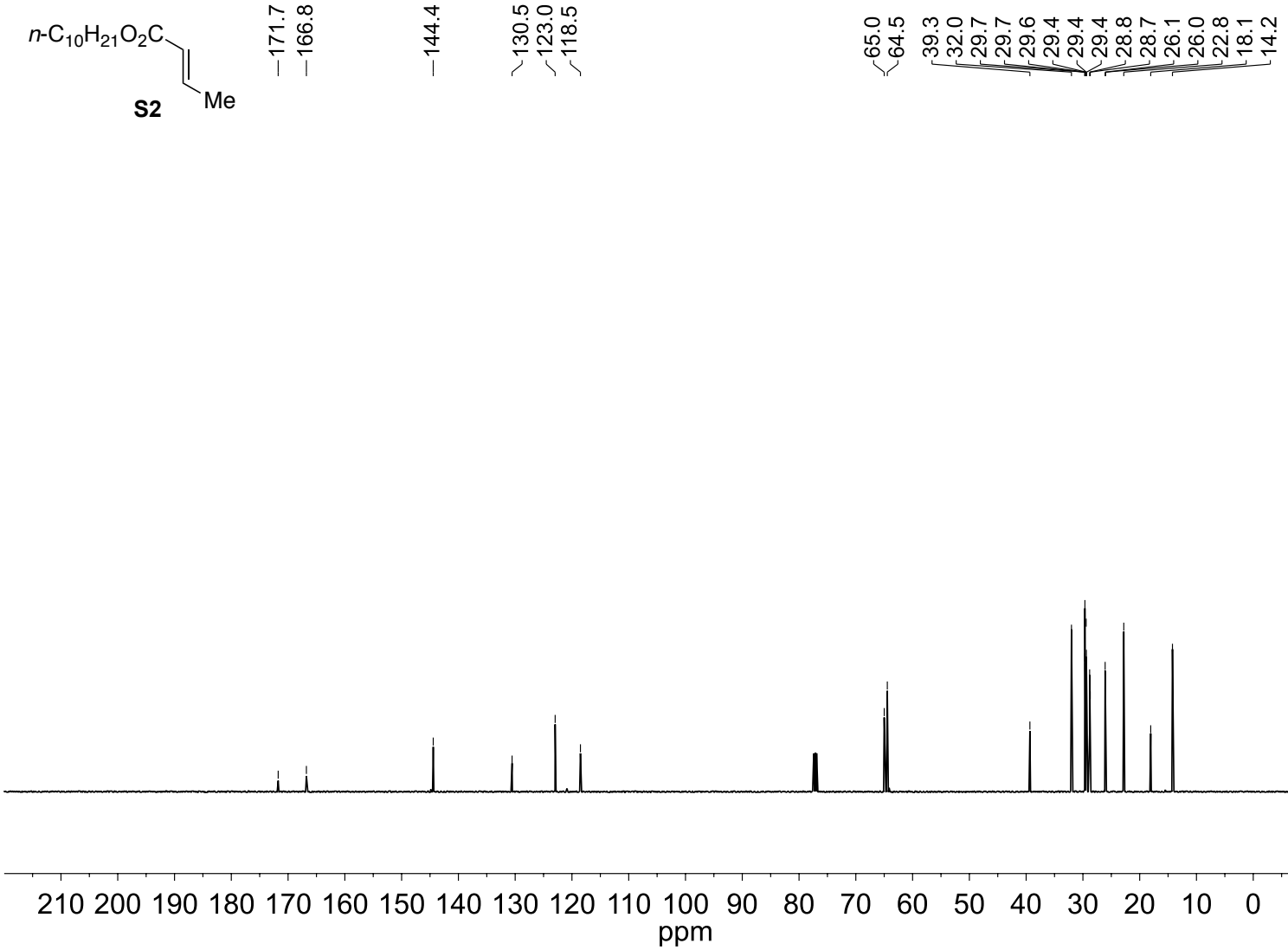
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



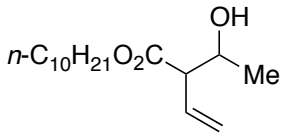
S2



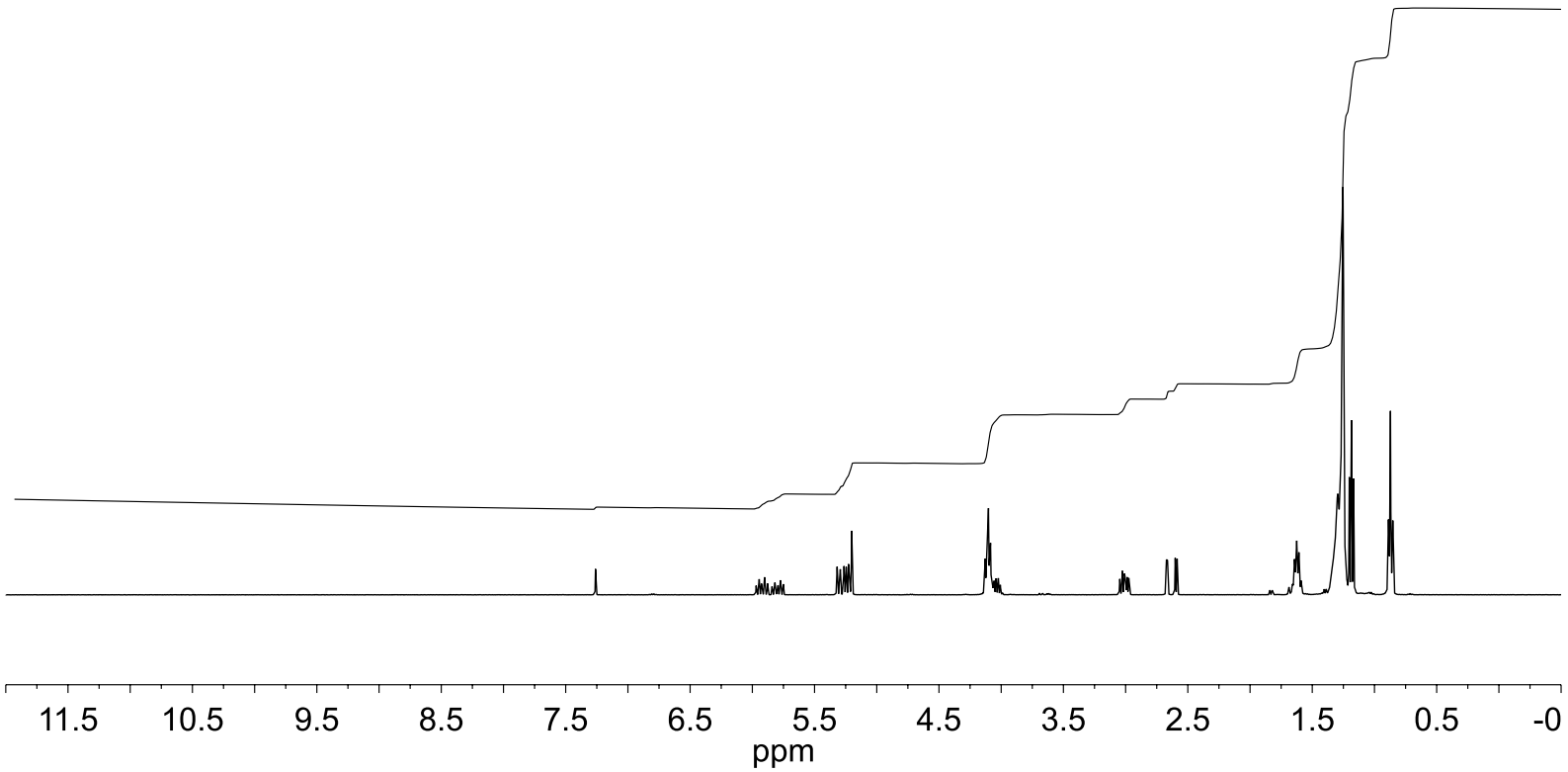
^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C



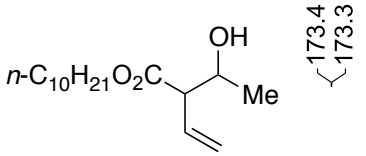
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



S3

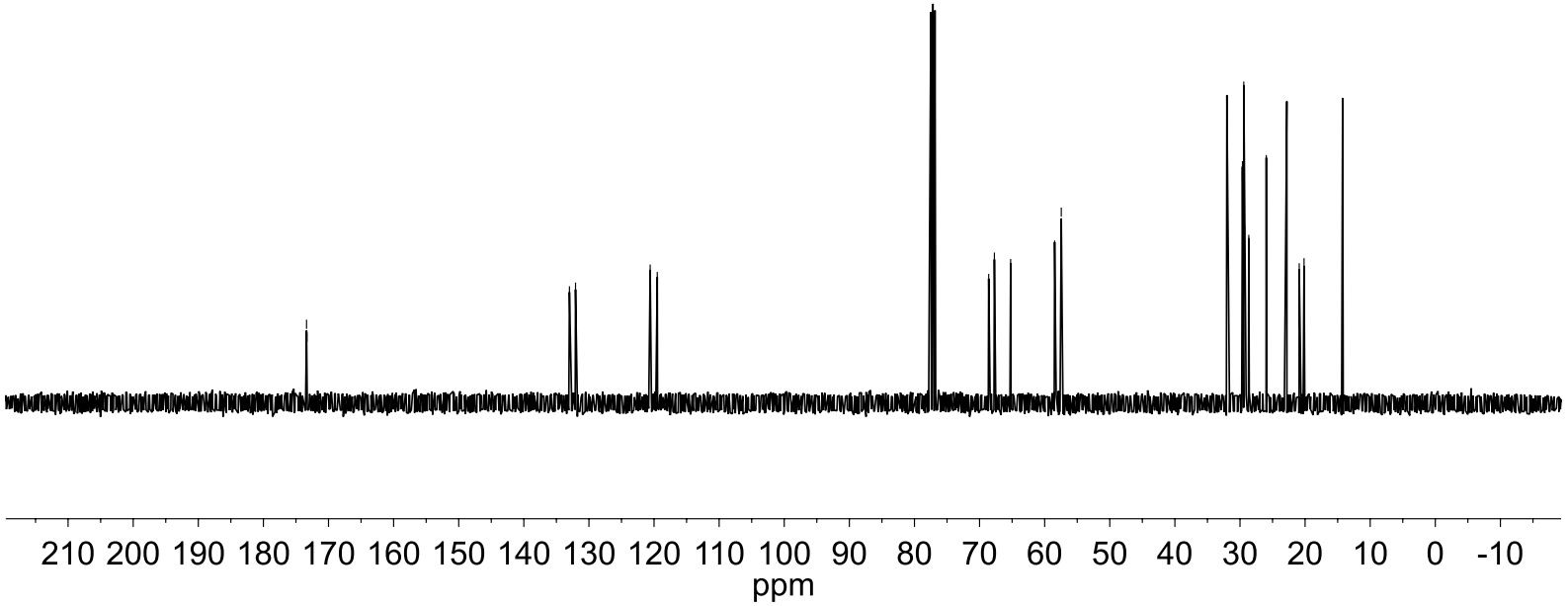


^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

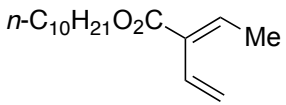


S3

173.4
173.3
133.0
132.1
120.6
119.5
68.6
67.7
65.3
65.2
58.5
57.4
32.0
29.6
29.6
29.4
29.3
29.3
28.7
28.6
26.0
22.8
20.9
20.2
14.2

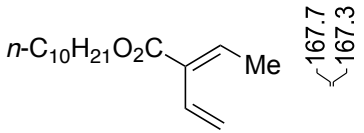


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



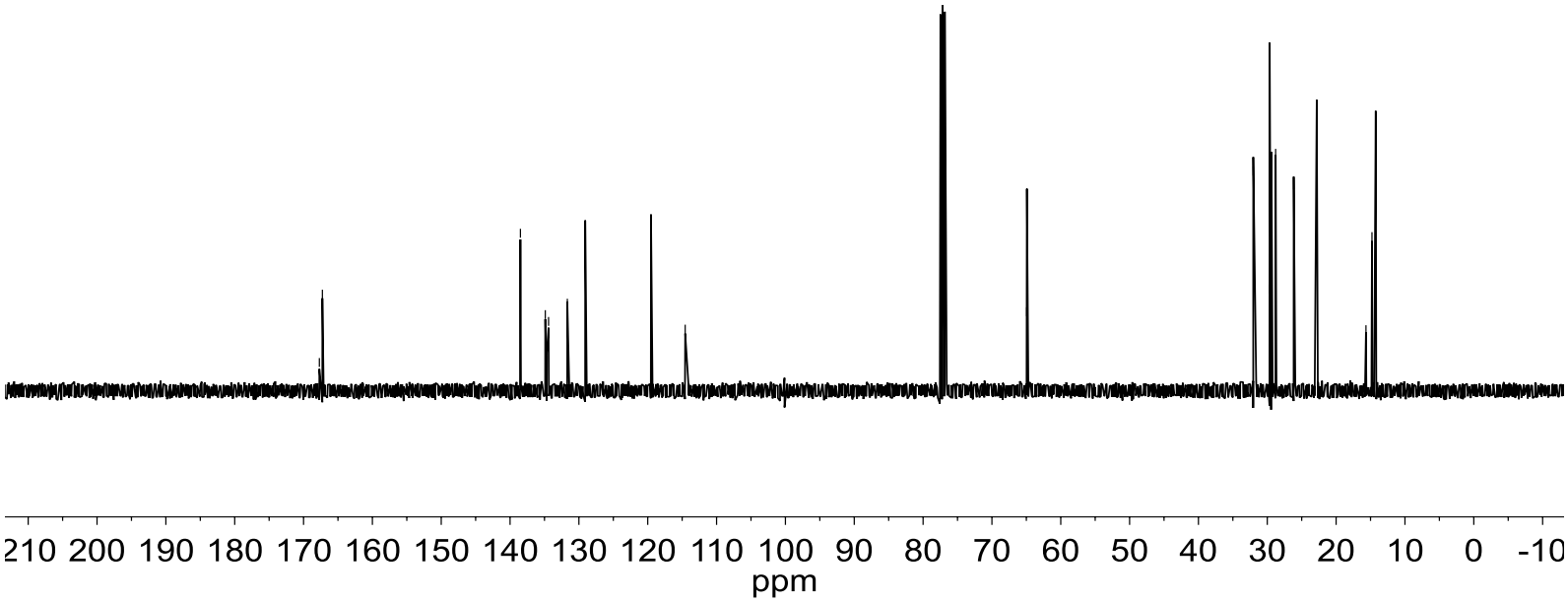
9 (*E*:*Z*, 2.6:1)

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

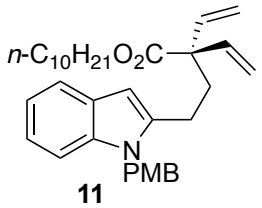


9 (*E*:*Z*, 2.6:1)

167.7
167.3
138.5
134.9
134.7
134.4
131.7
129.1
119.5
114.6
64.9
64.9
32.0
29.7
29.6
29.6
29.4
29.4
29.4
29.4
28.8
28.8
26.2
22.8
15.7
14.8
14.2

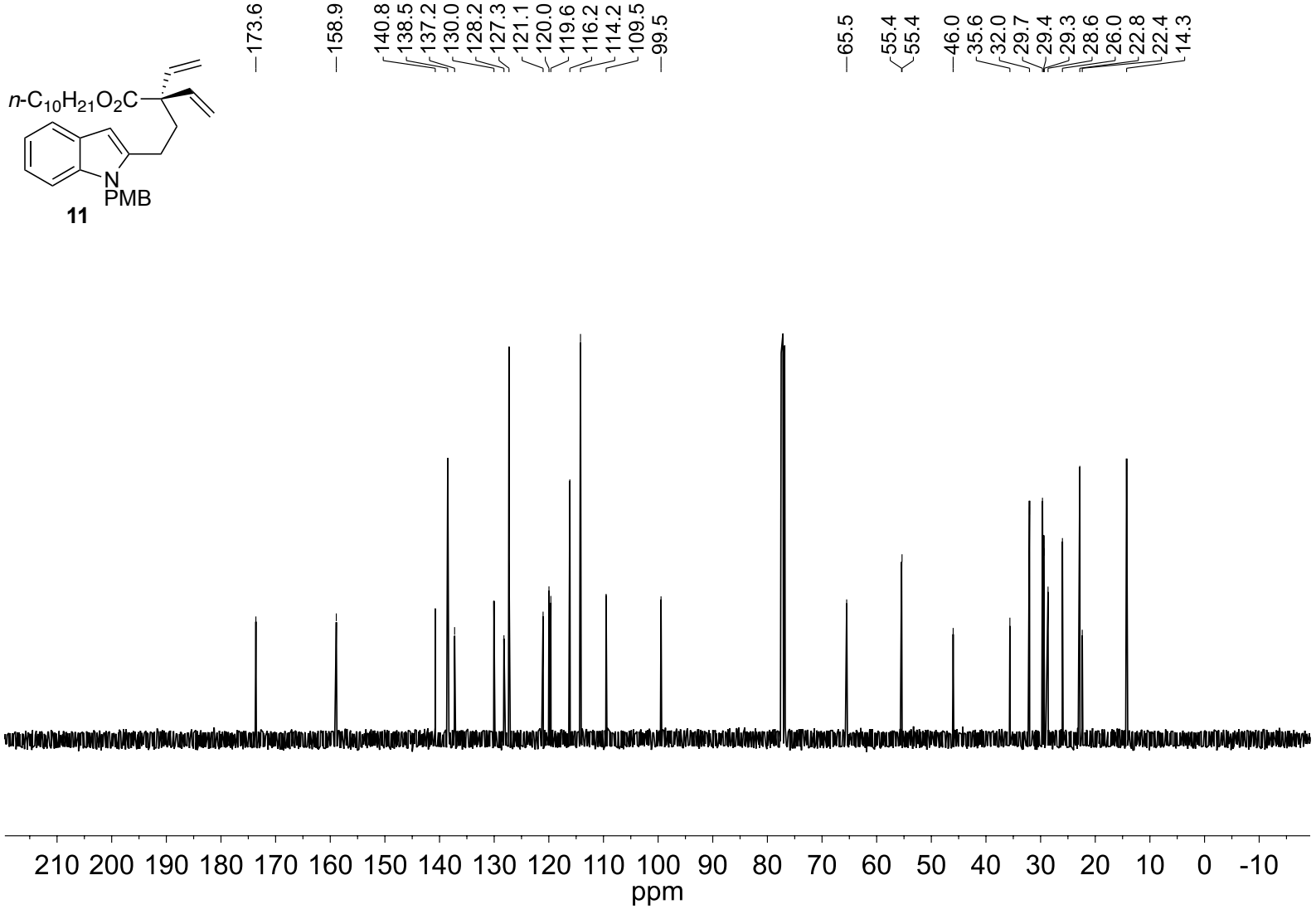


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

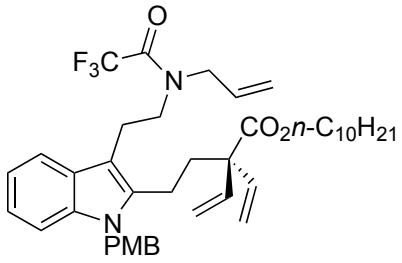


11

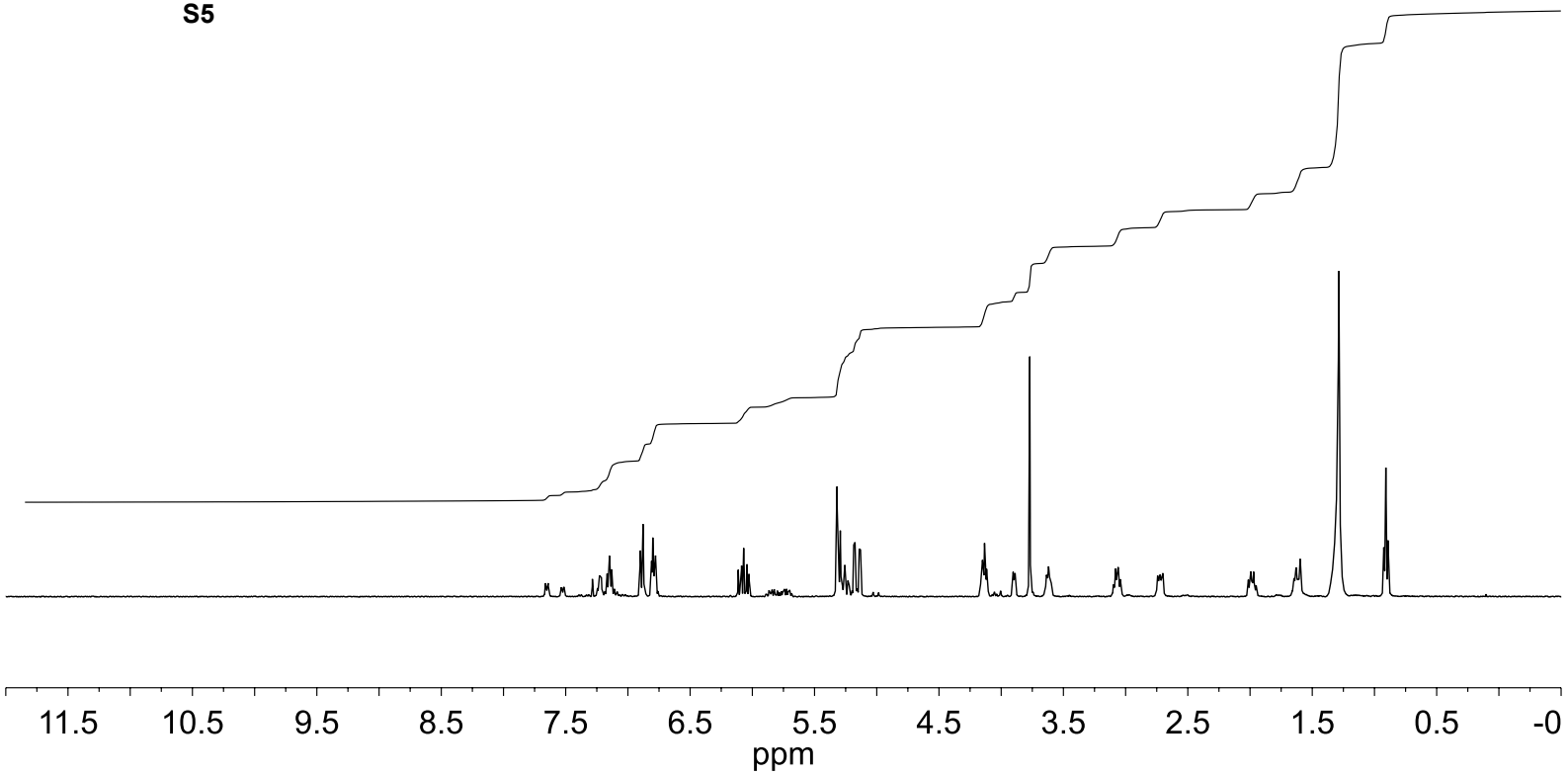
^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C



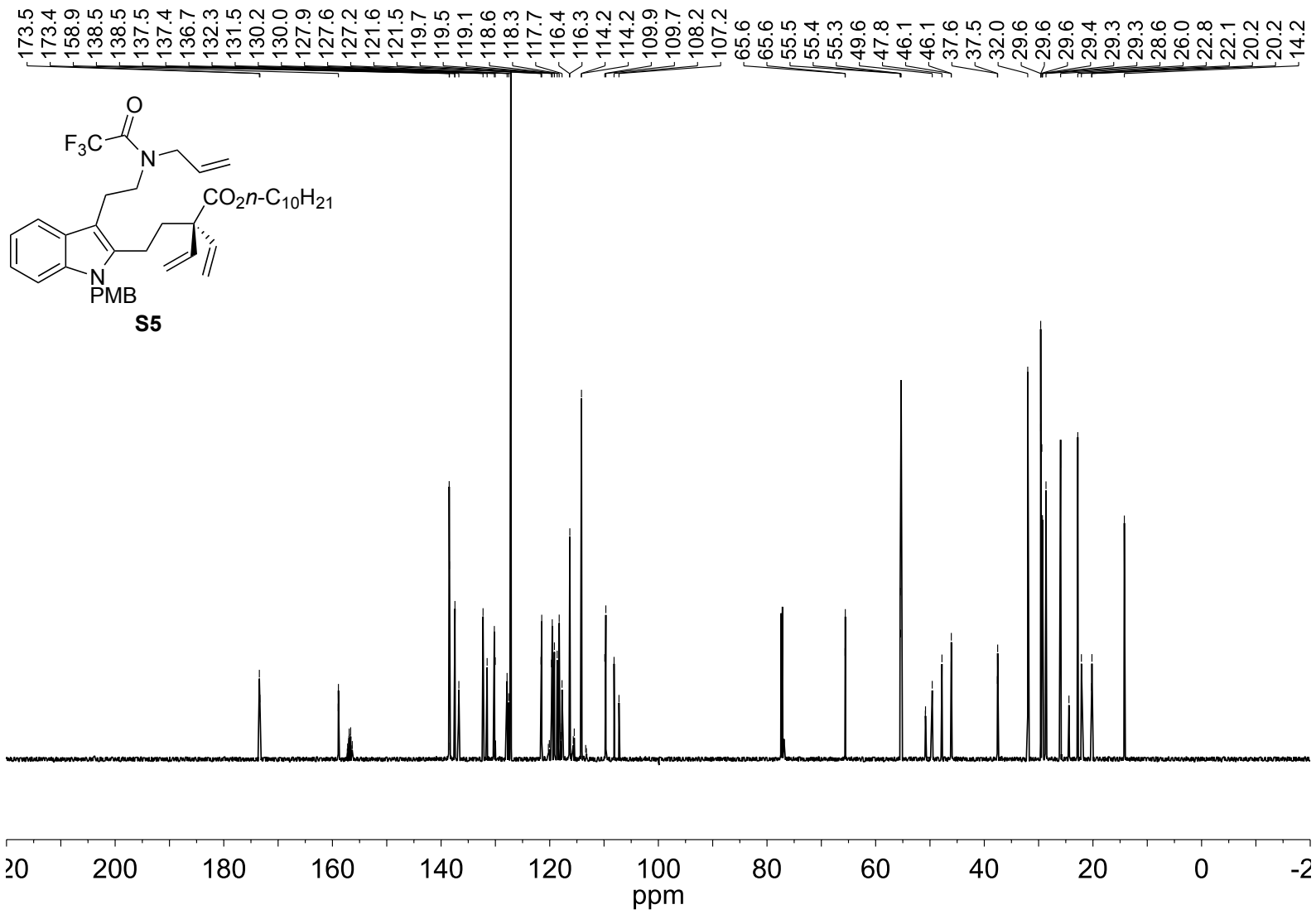
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



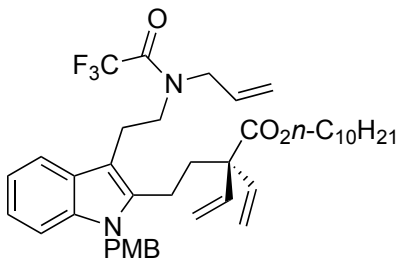
S5



^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

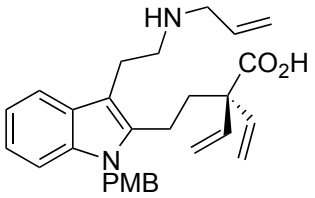


^{19}F NMR, 376 MHz, $CDCl_3$, 25 °C

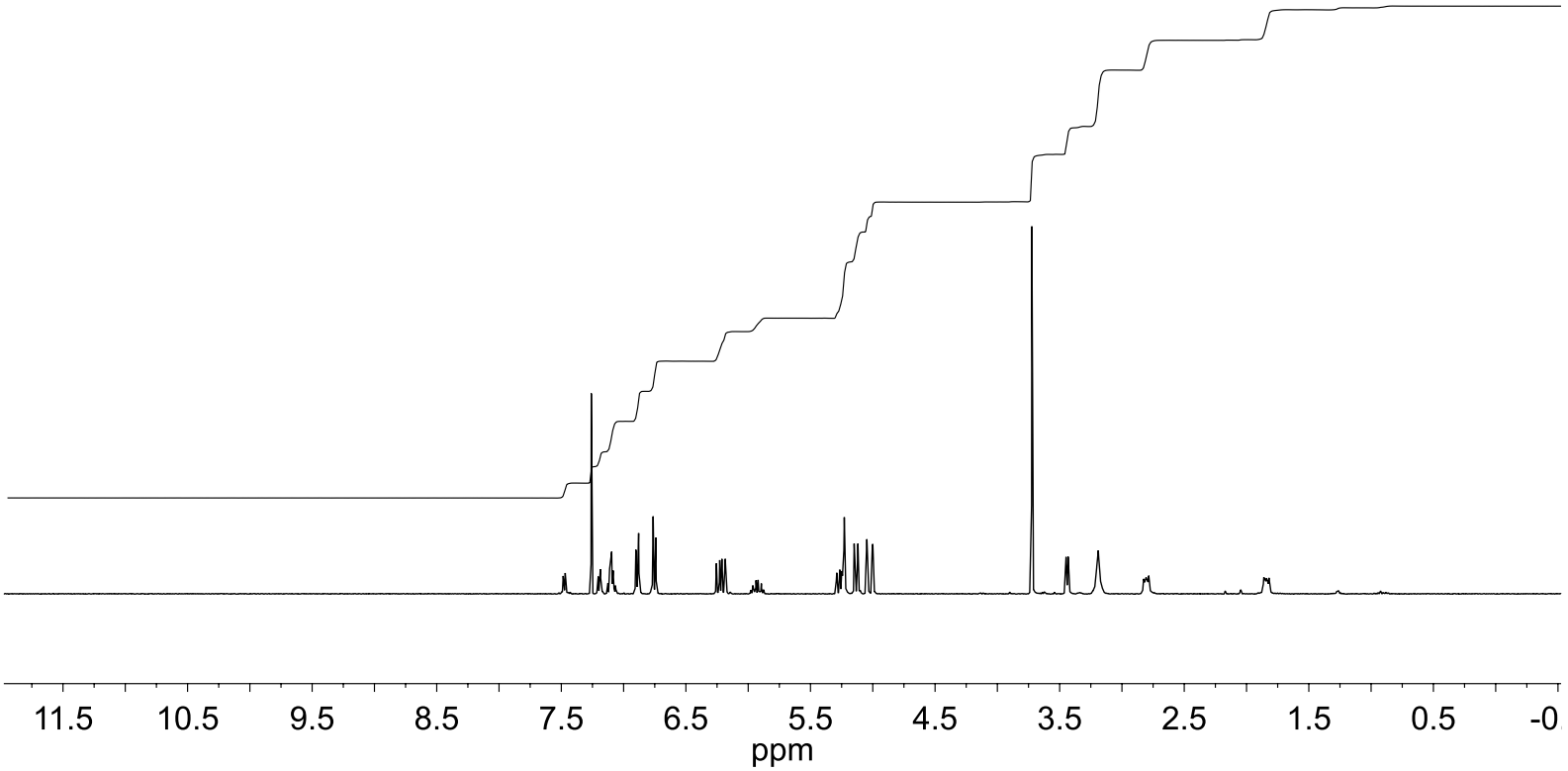


S5

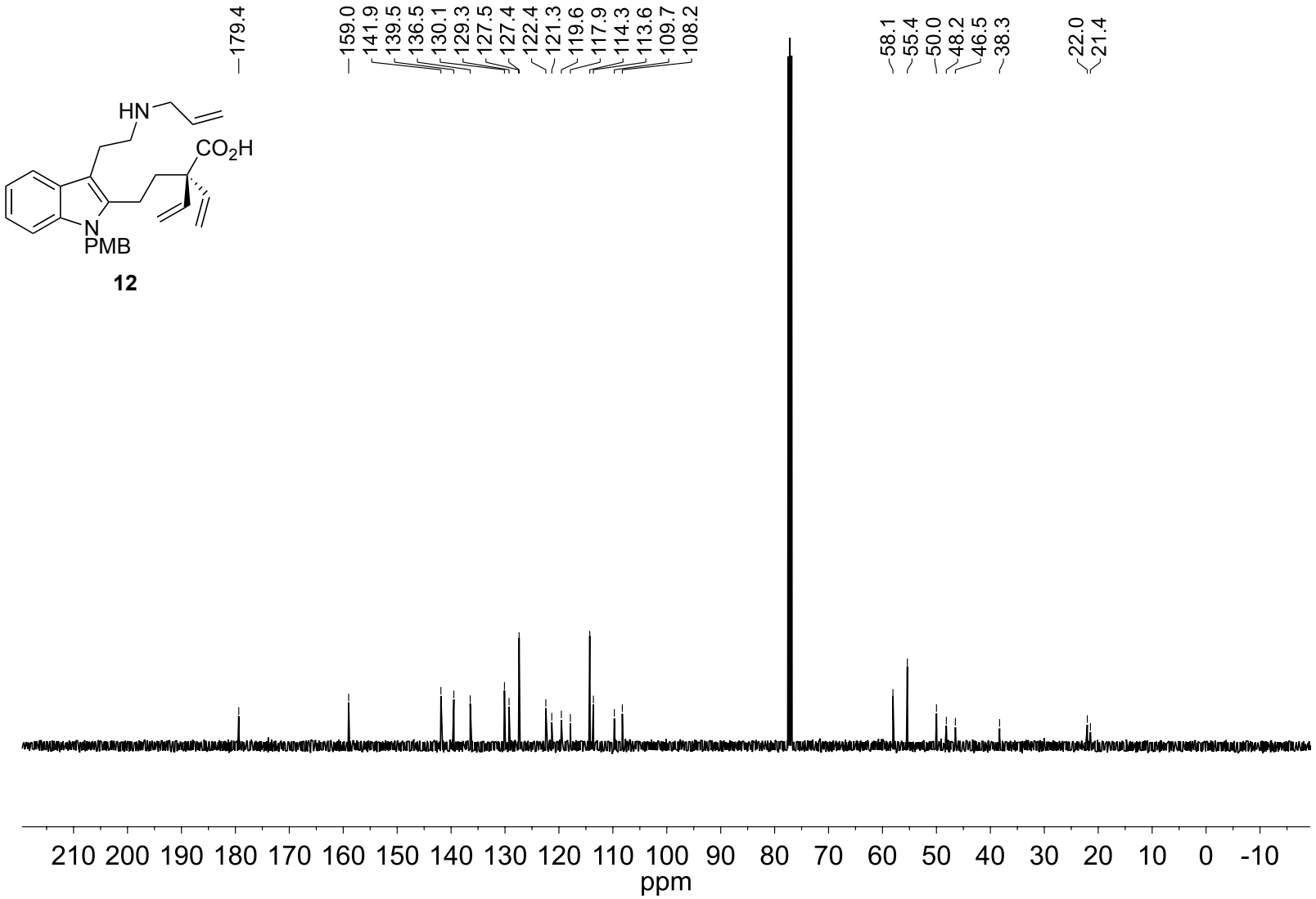
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



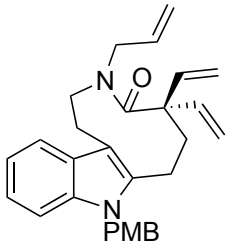
12



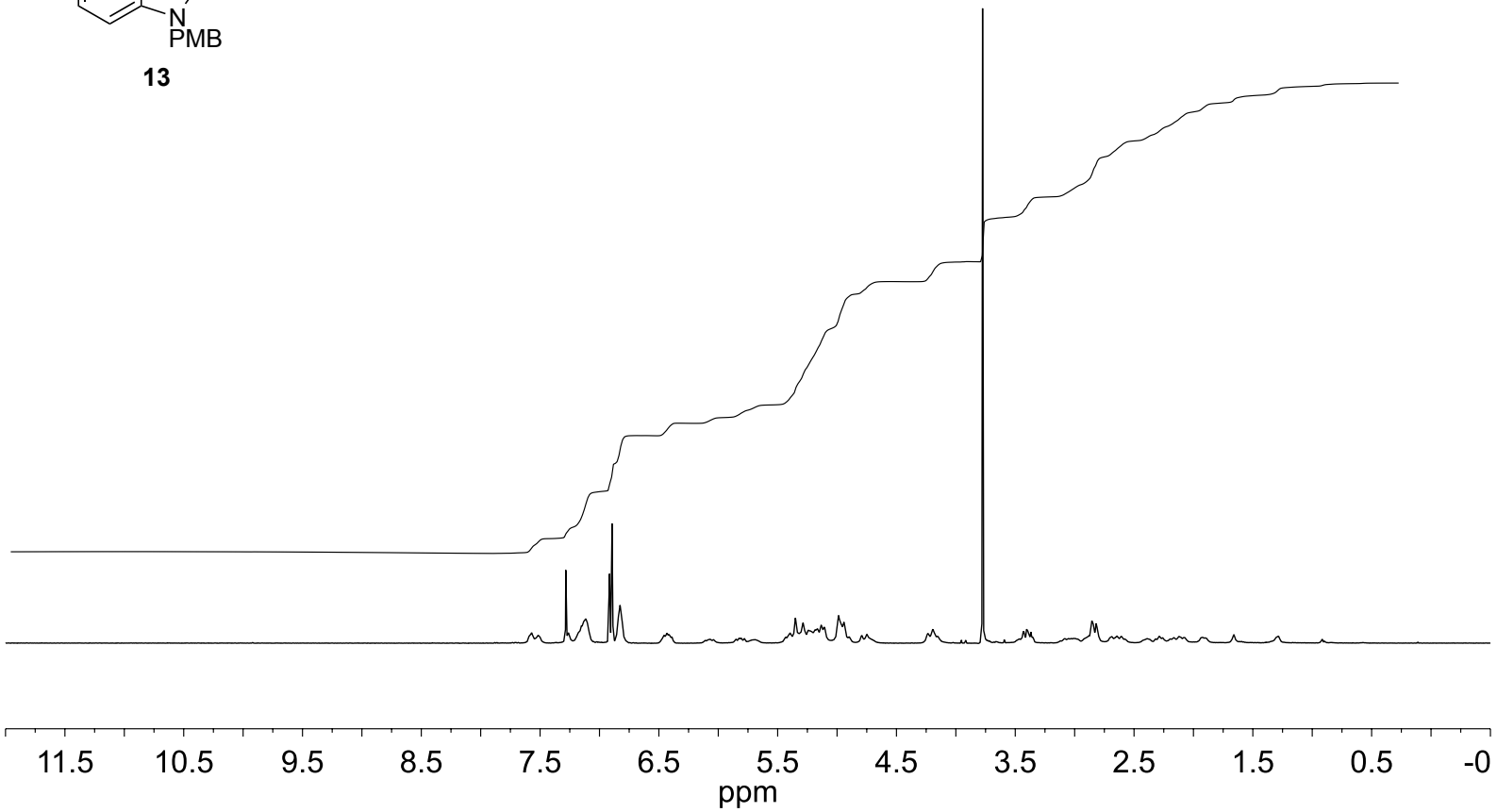
^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C



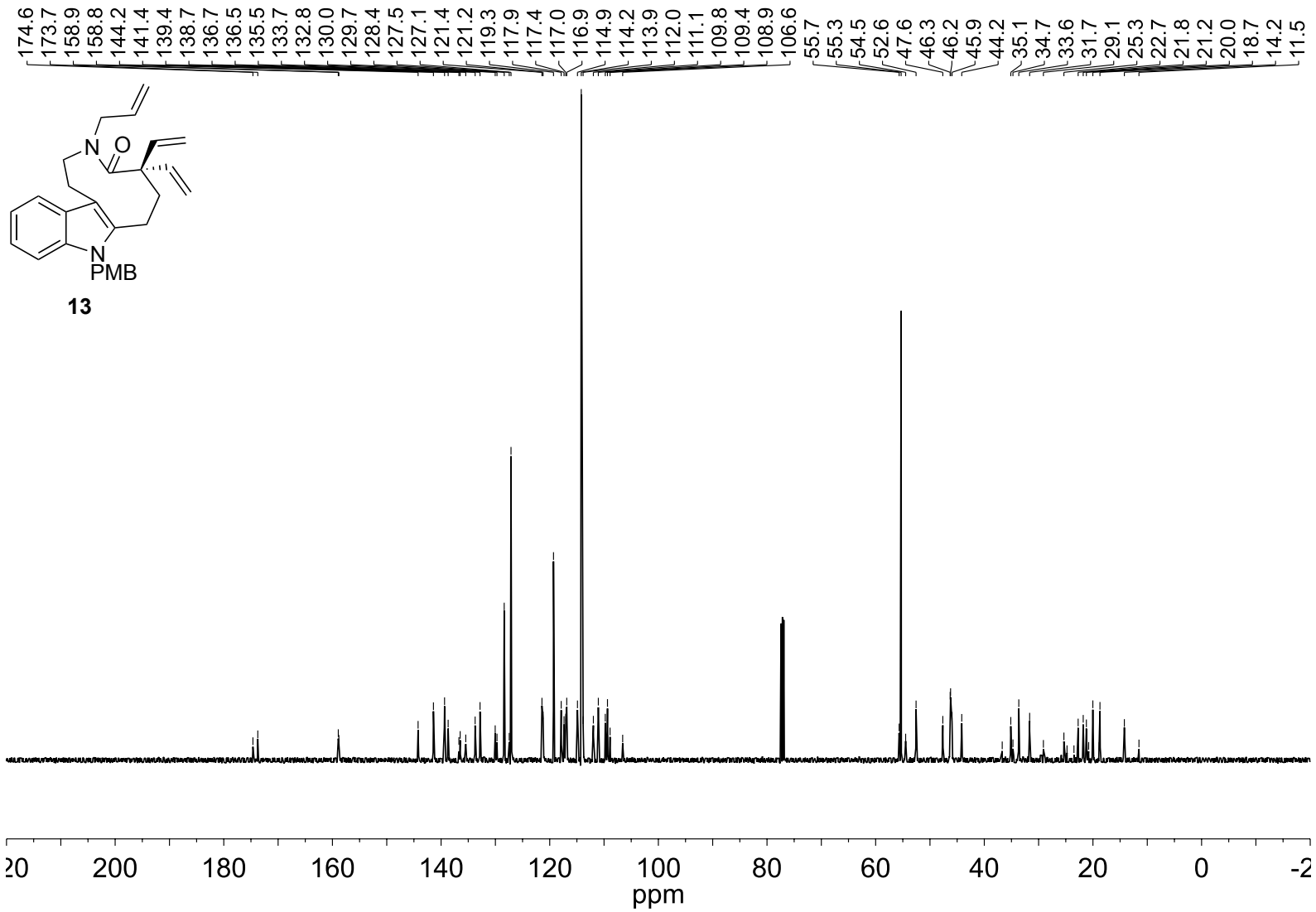
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



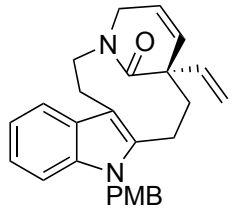
13



^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

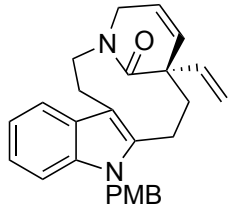


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



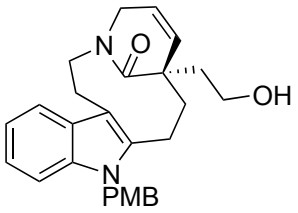
(±)-**14**

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

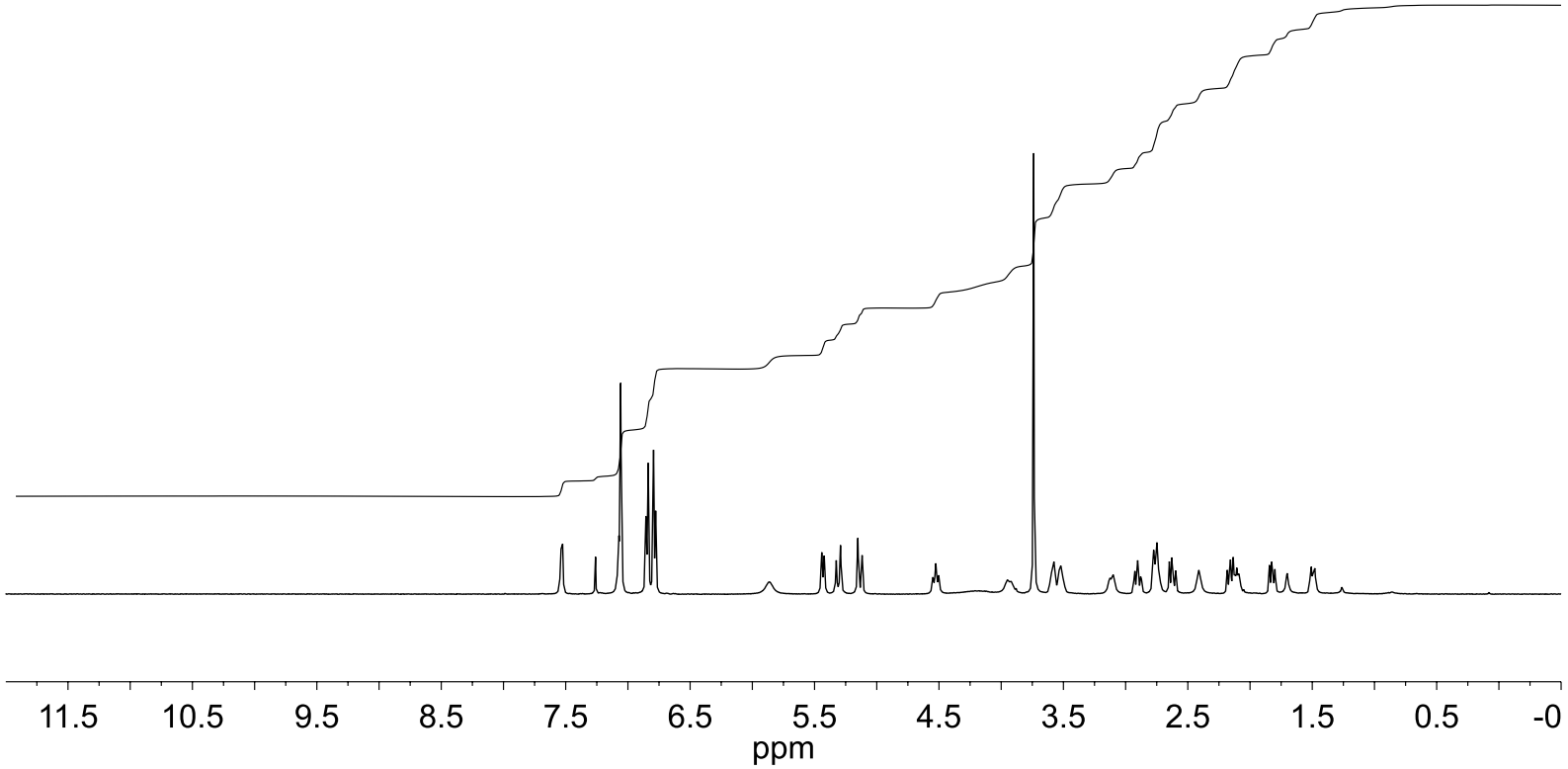


(±)-**14**

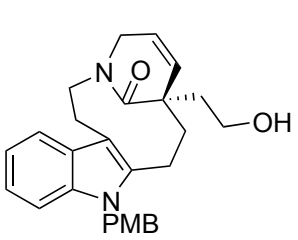
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



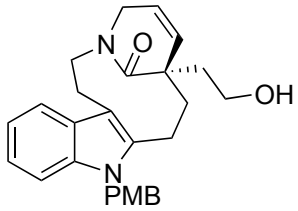
(±)-**15**



^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C



(±)-**15**



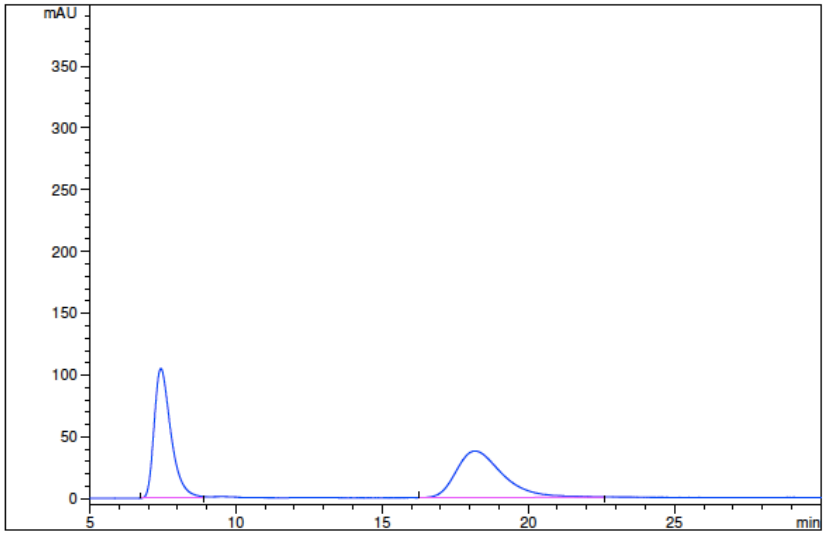
(±)-**15**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

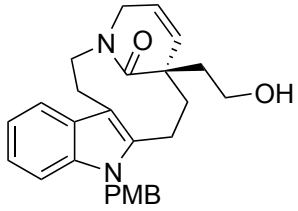
40% Isopropanol/ 60% Hexanes

1.0 mL/min

230 nm



#	Meas. Ret. Time	Area %
1	7.428	50.303
2	18.169	49.697



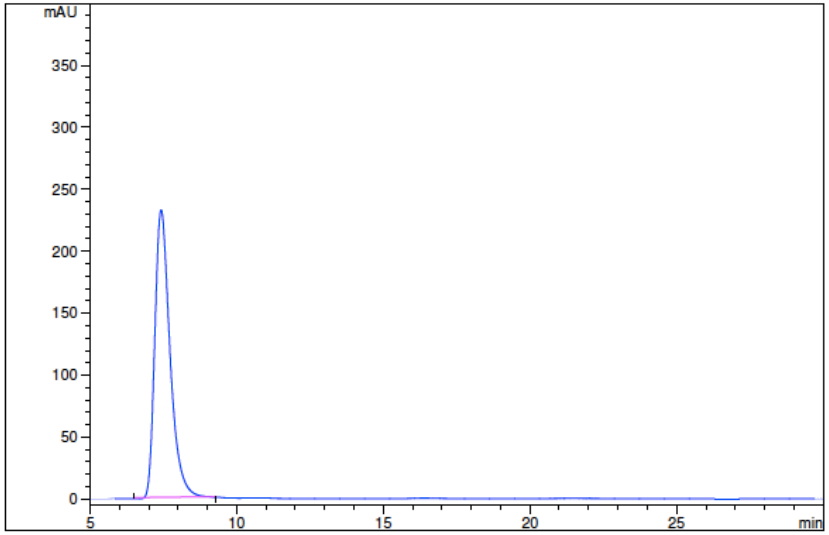
(–)-**15**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

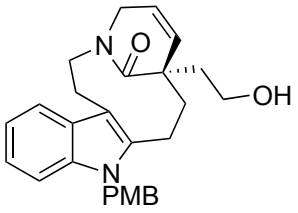
40% Isopropanol/ 60% Hexanes

1.0 mL/min

230 nm



#	Meas. Ret. Time	Area %
1	7.422	100.000



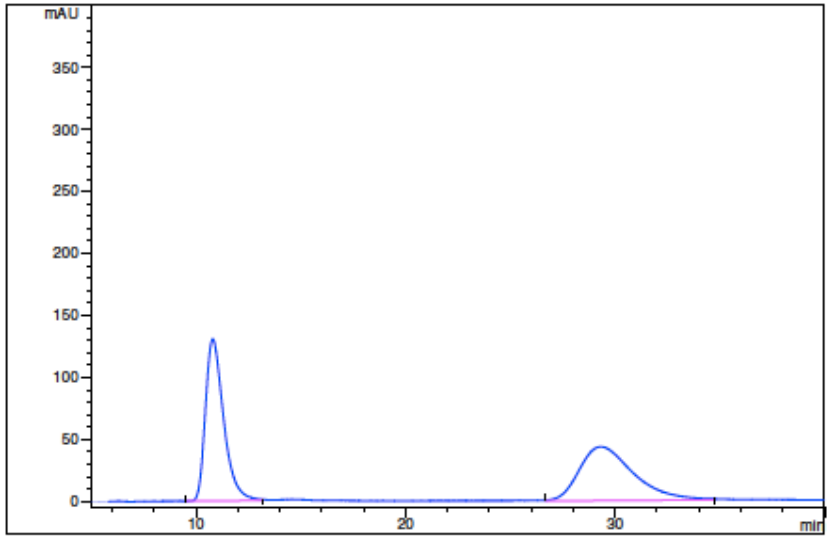
(±)-**15**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

25% Isopropanol/ 75% Hexanes

1.0 mL/min

230 nm



#	Meas. Ret. Time	Area %
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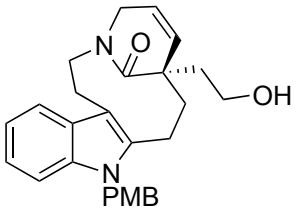
2	29.327	49.818



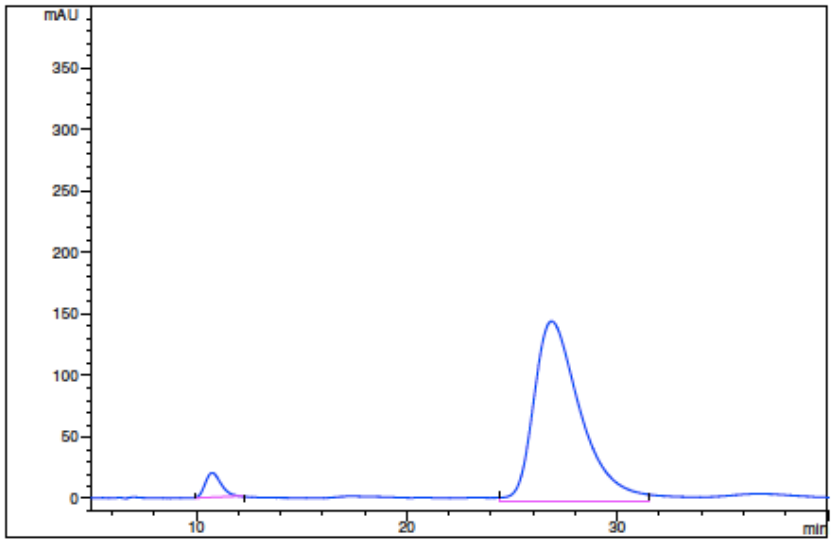
(+)-**15**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

25% Isopropanol/ 75% Hexanes

1.0 mL/min

230 nm



#	Meas. Ret. Time	Area %
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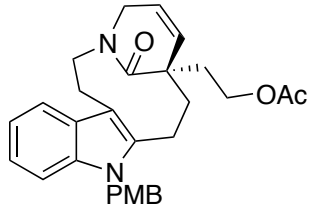
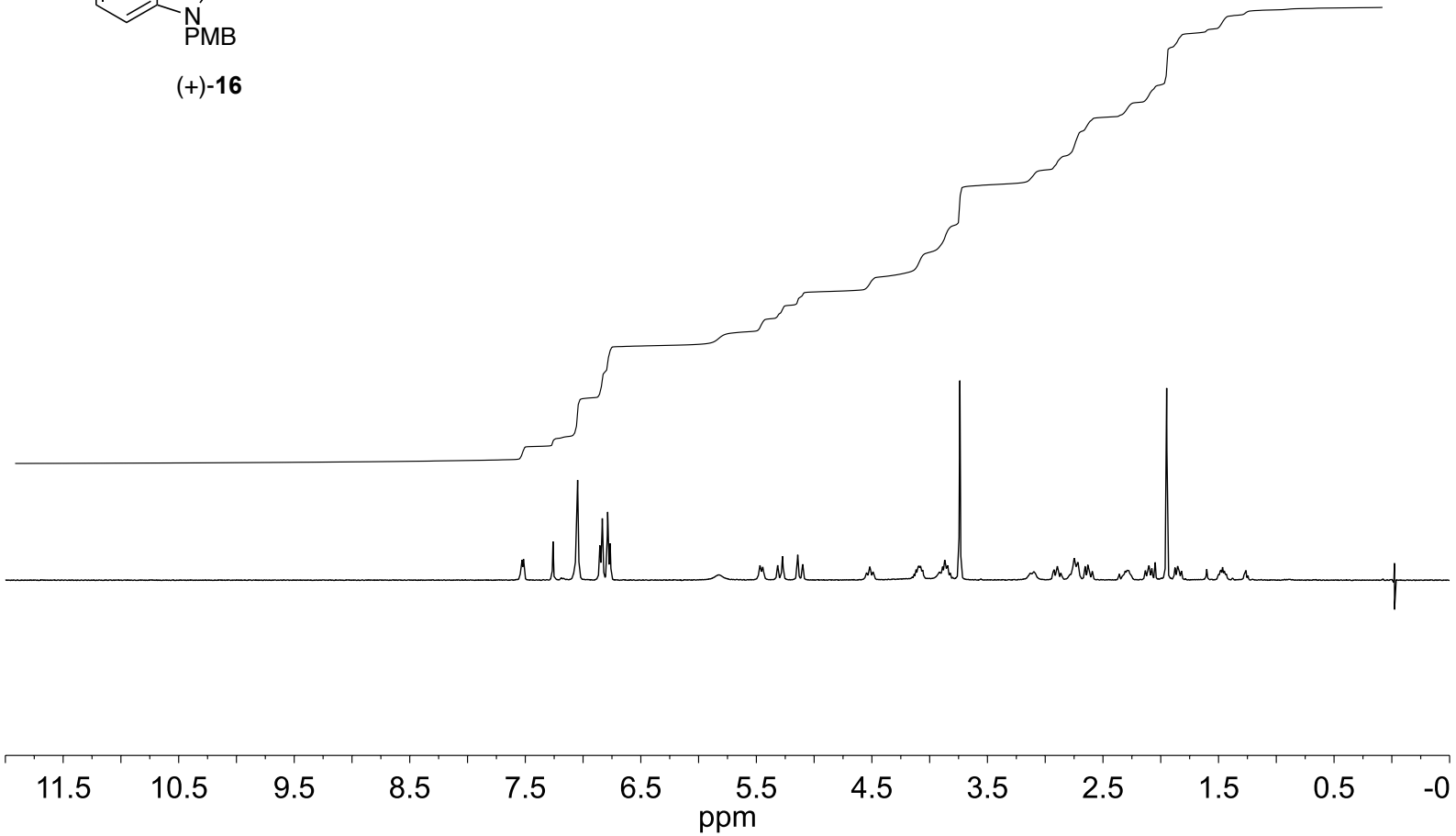
2	26.871	95.542

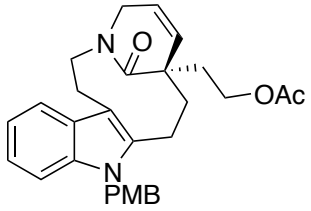
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



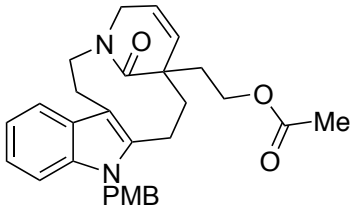
(+)-**16**



^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C



(+)-**16**



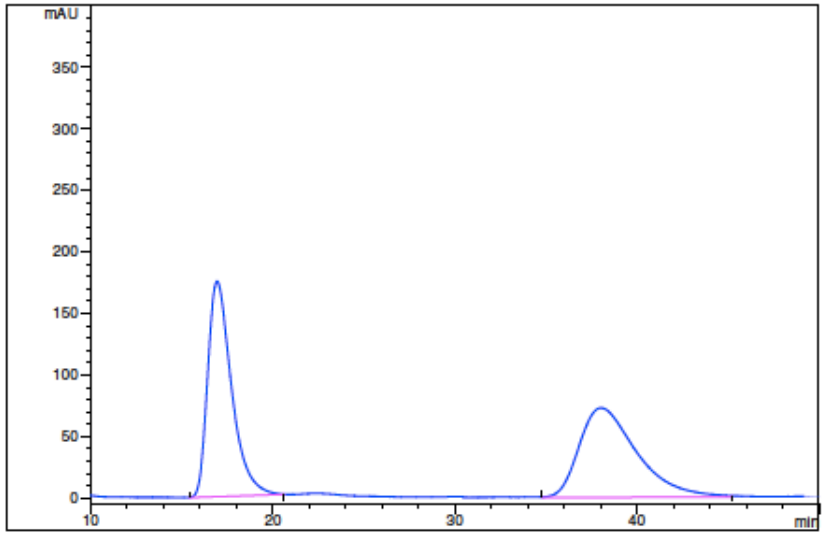
(±)-**16**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

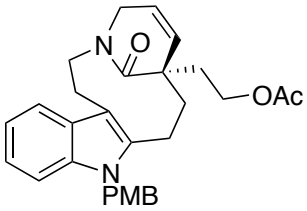
25% Isopropanol/ 75% Hexanes

1.0 mL/min

230 nm



#	Meas. Ret. Time	Area %
1	16.931	49.960
2	38.071	50.040



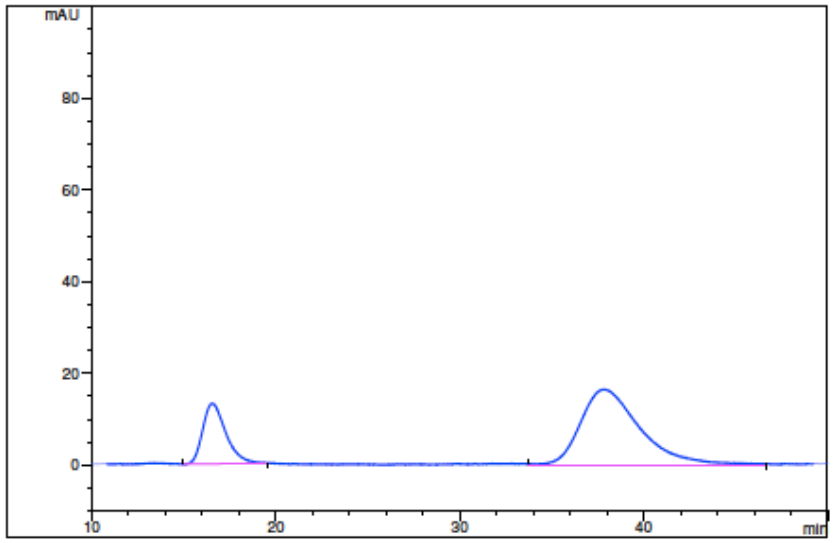
(+)-**16**

HPLC Conditions:
Chiralcel OD-H, column #ODH0CE-KF021

25% Isopropanol/ 75% Hexanes

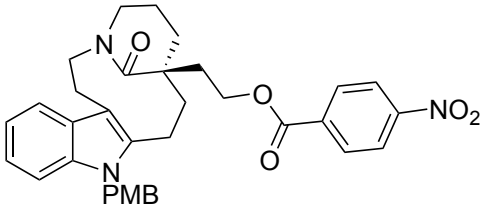
1.0 mL/min

230 nm

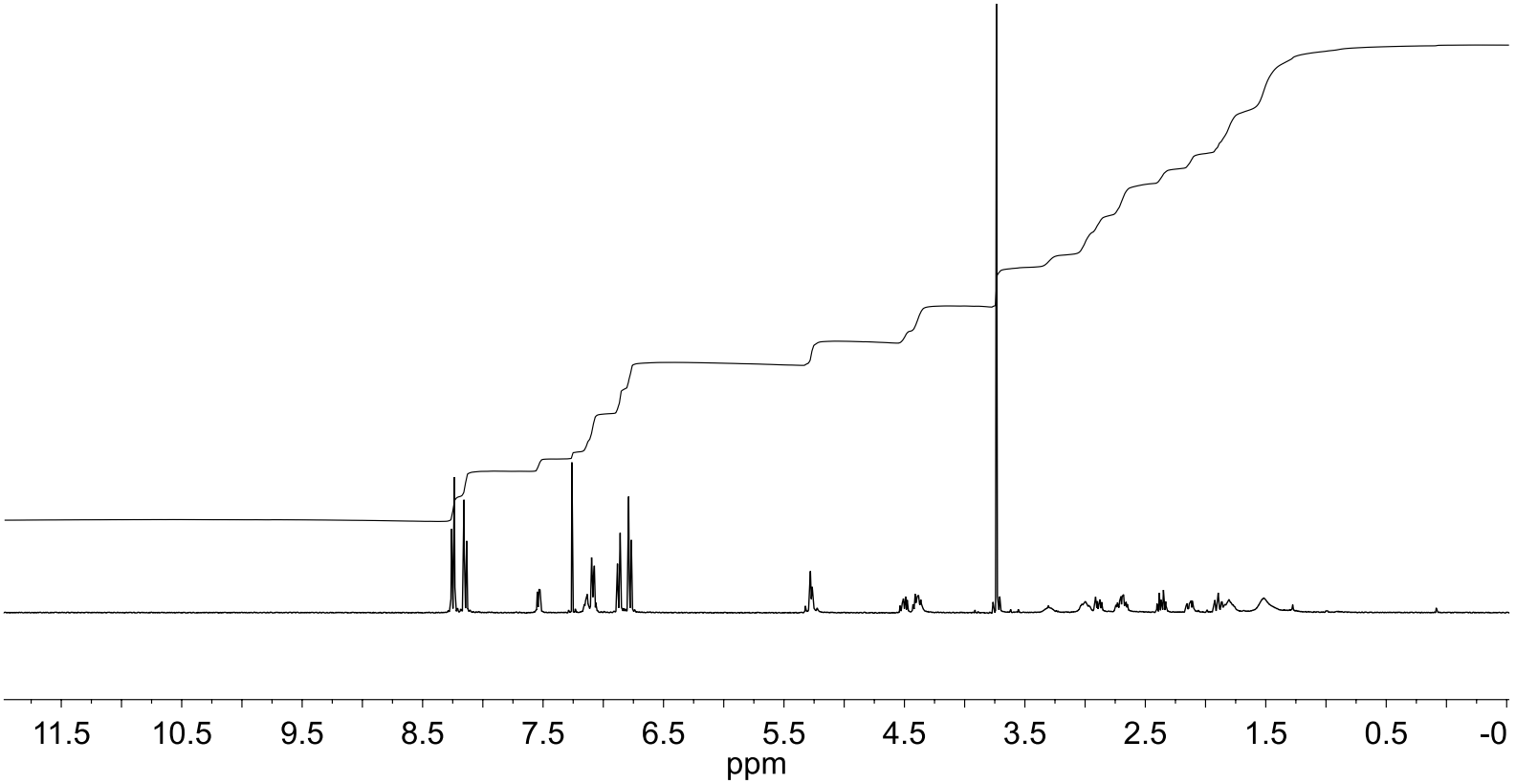


#	Meas. Ret. Time	Area %
1	16.565	23.718
2	37.906	76.282

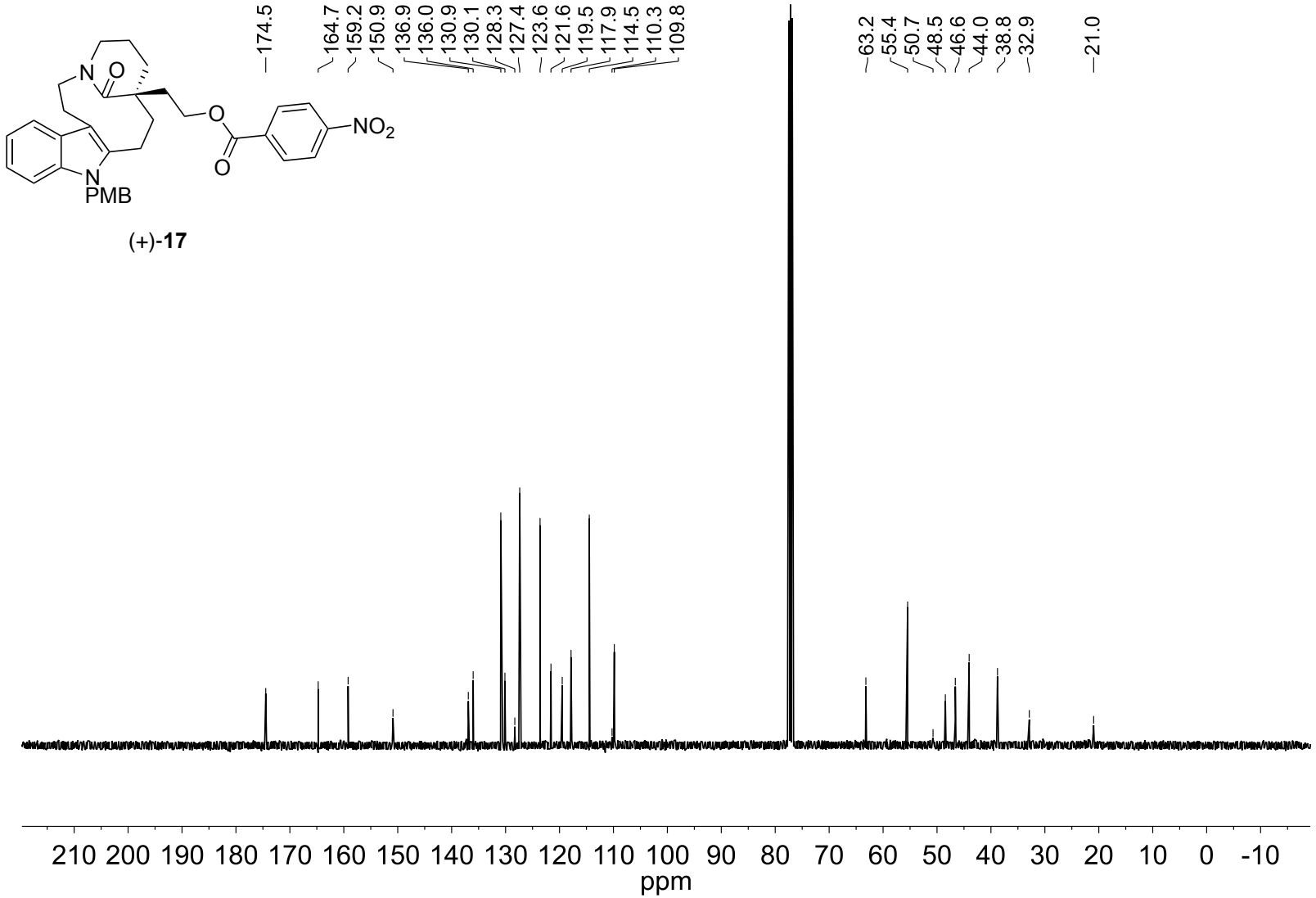
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



(+)-**17**

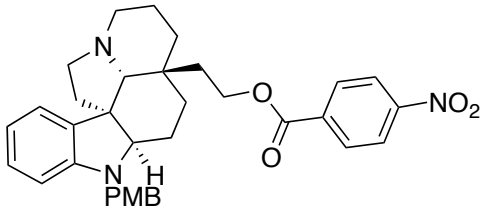


^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

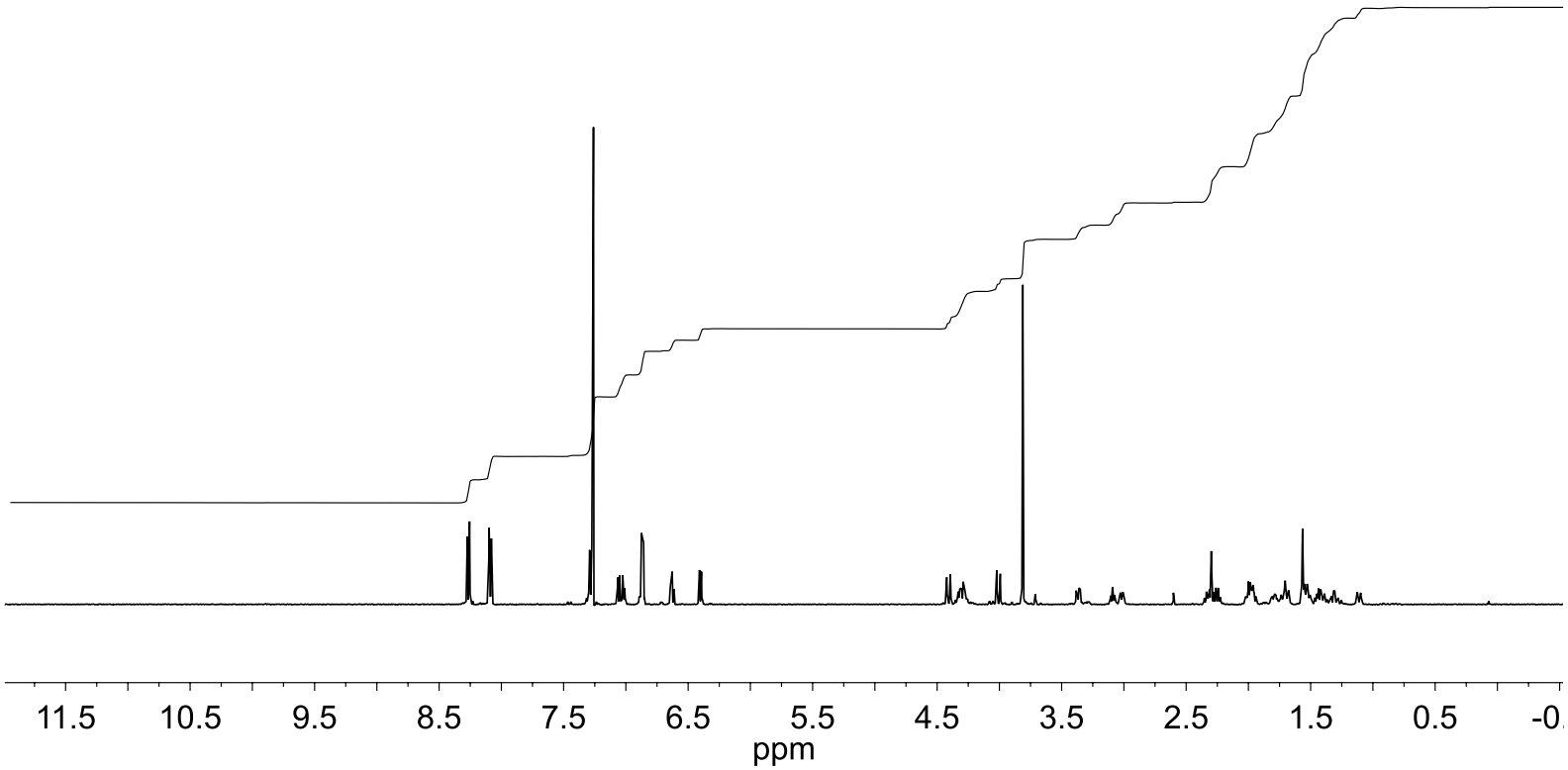


(+)-**17**

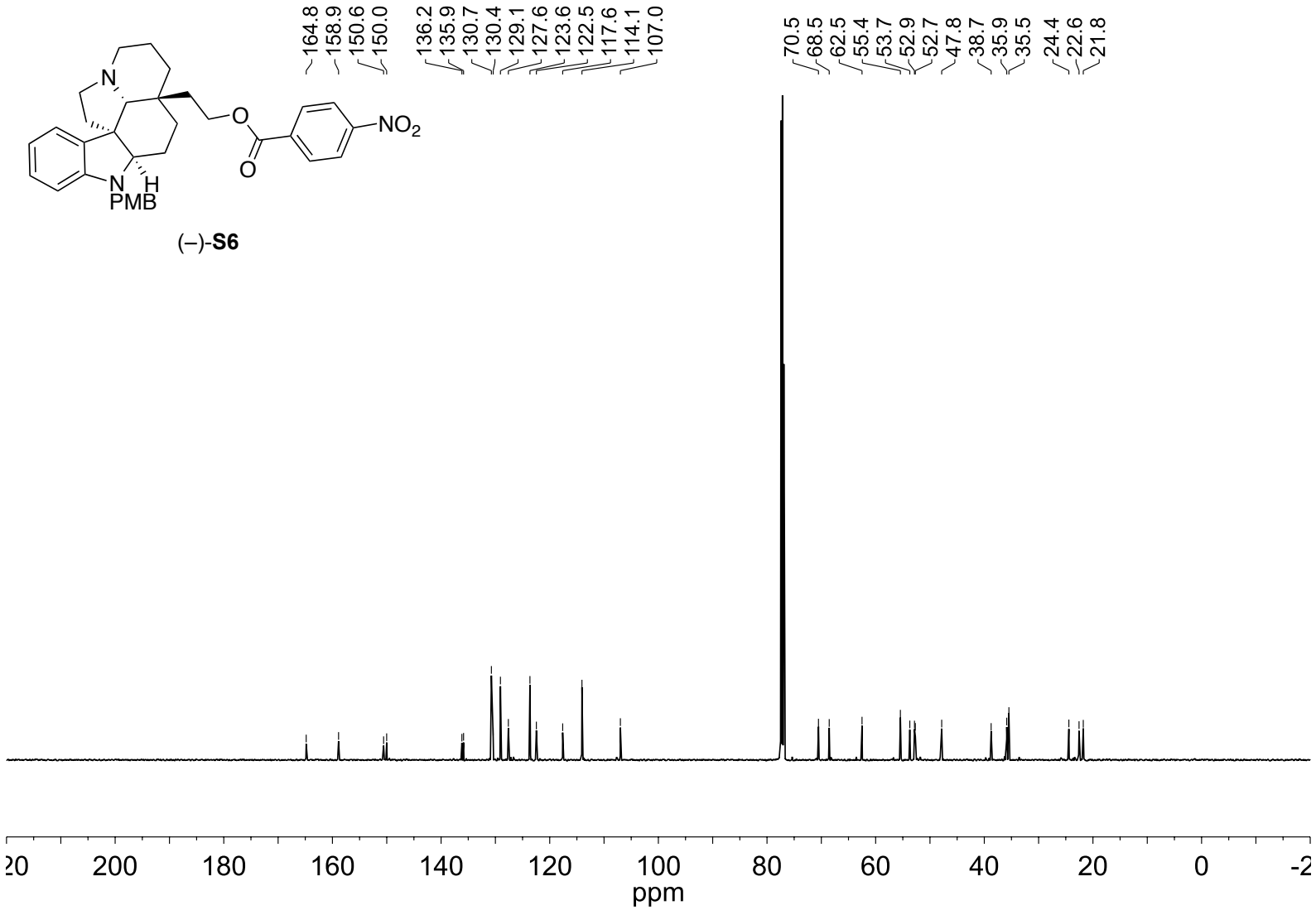
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



(–)-**S6**

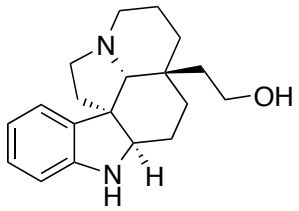


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

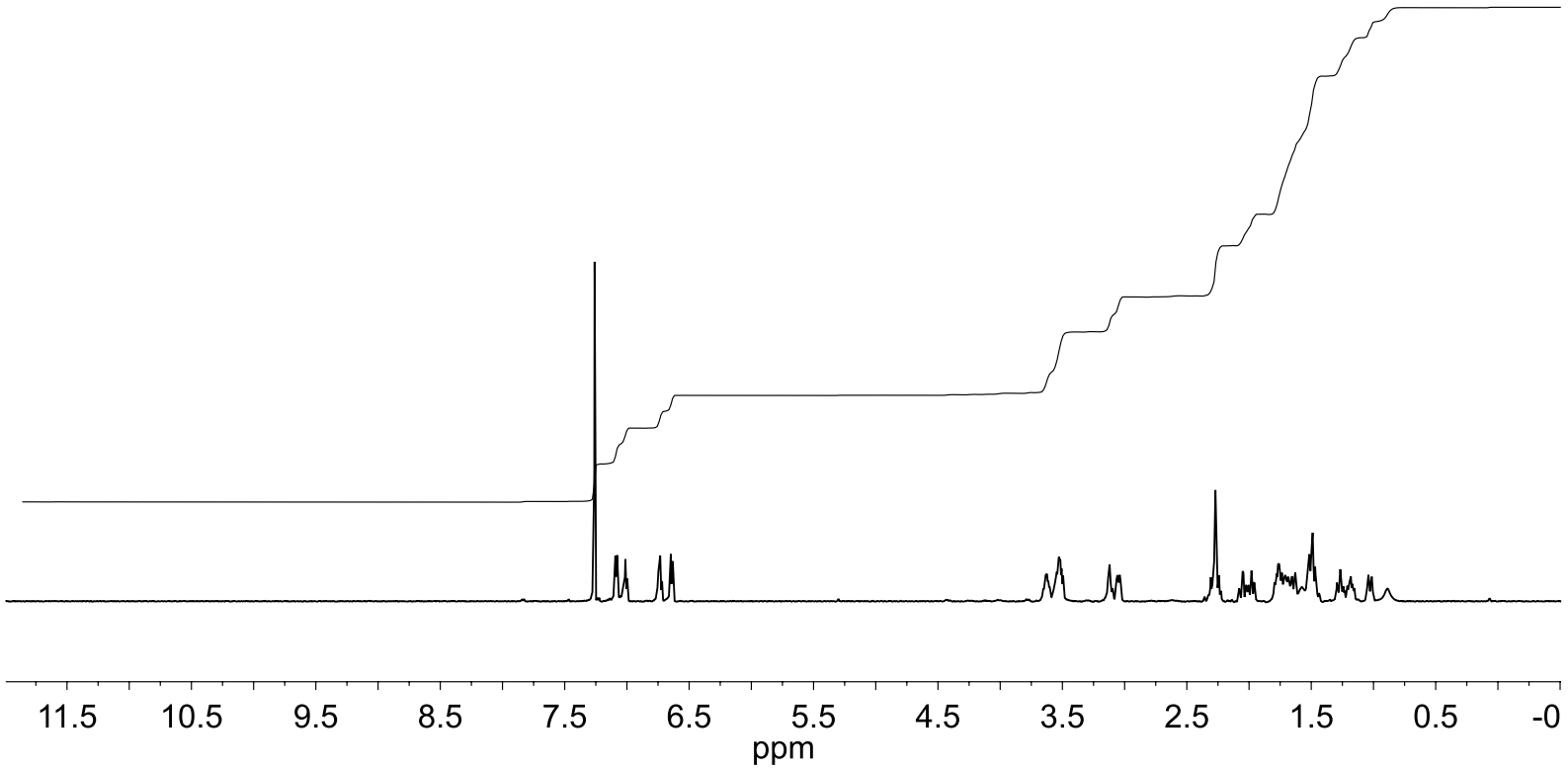


(–)-**S6**

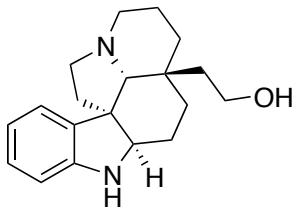
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



(+)-limaspermidine (**20**)

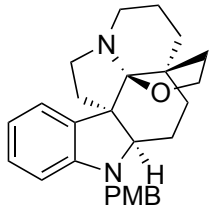


^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

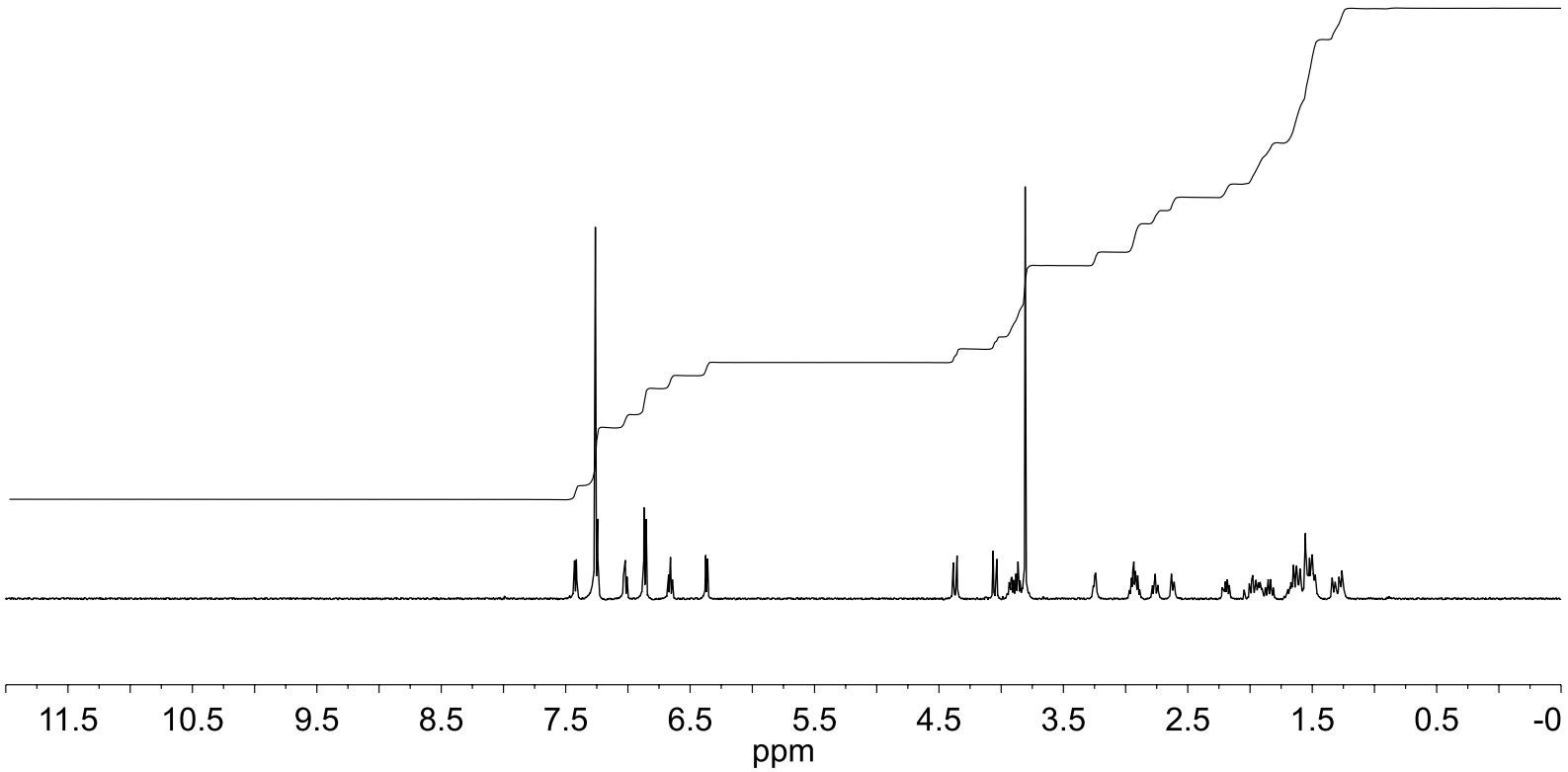


(+)-limaspermidine (**20**)

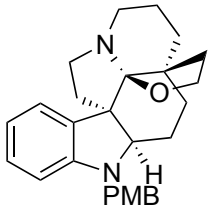
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



(+)-**21**

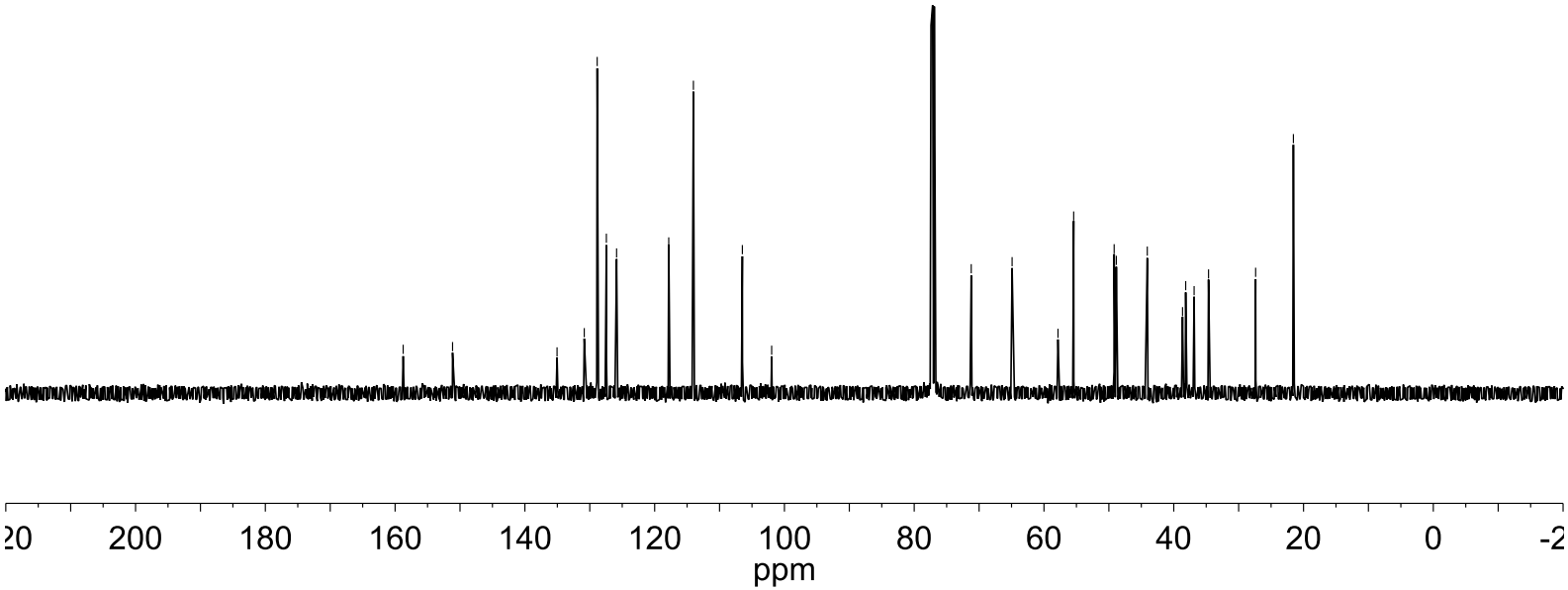


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

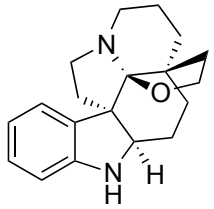


(+)-**21**

158.8
151.1
135.0
130.9
128.9
127.4
125.9
117.8
114.0
106.5
102.0
71.2
64.9
57.8
55.4
49.2
48.8
44.1
38.6
38.2
36.9
34.6
27.4
21.6

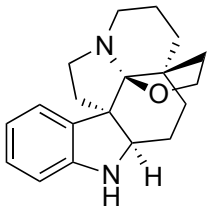


^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



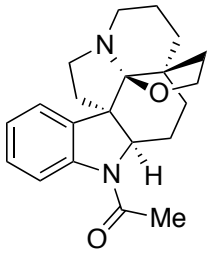
(+)-fendleridine (**3**)

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

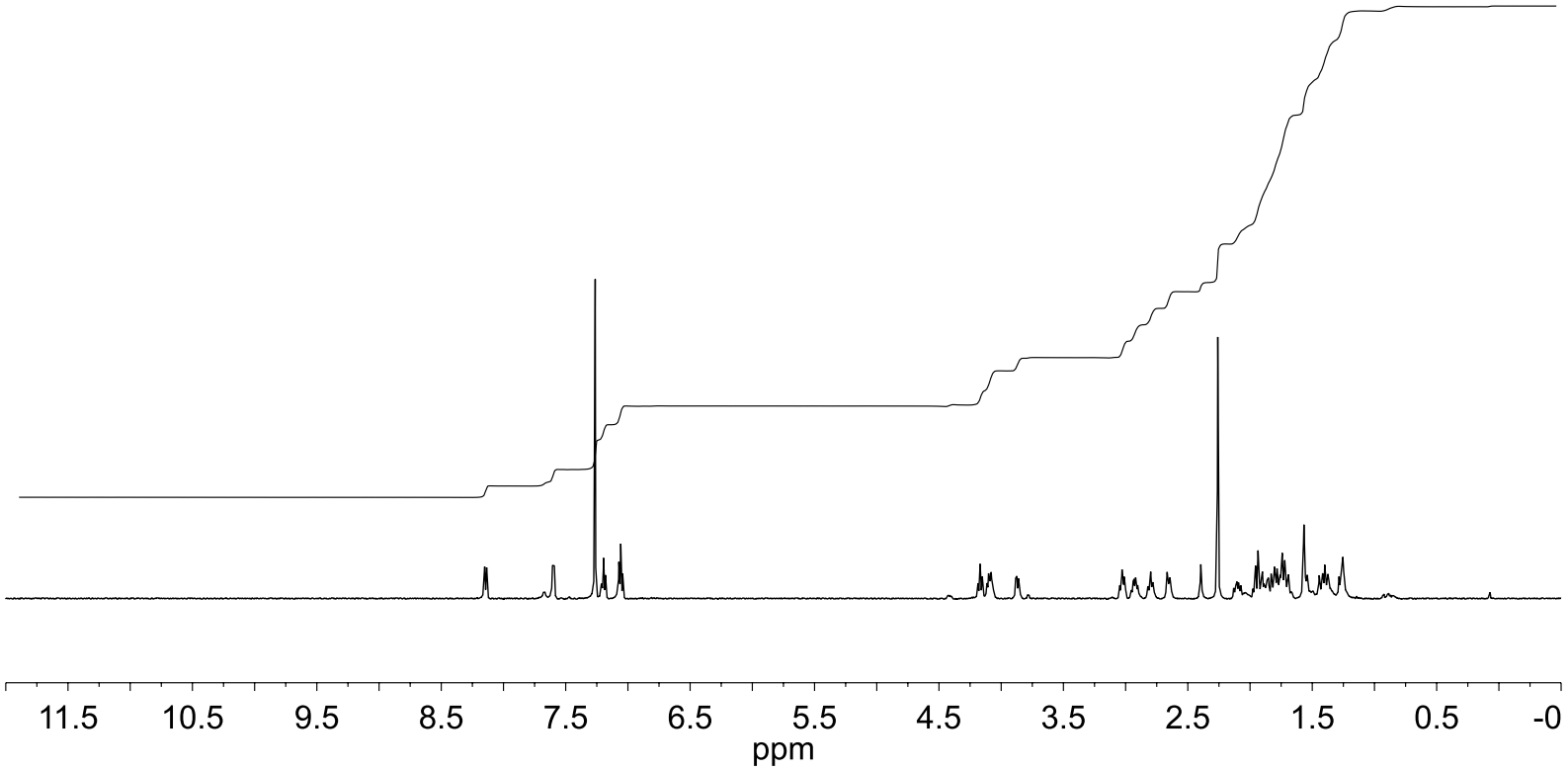


(+)-fendleridine (**3**)

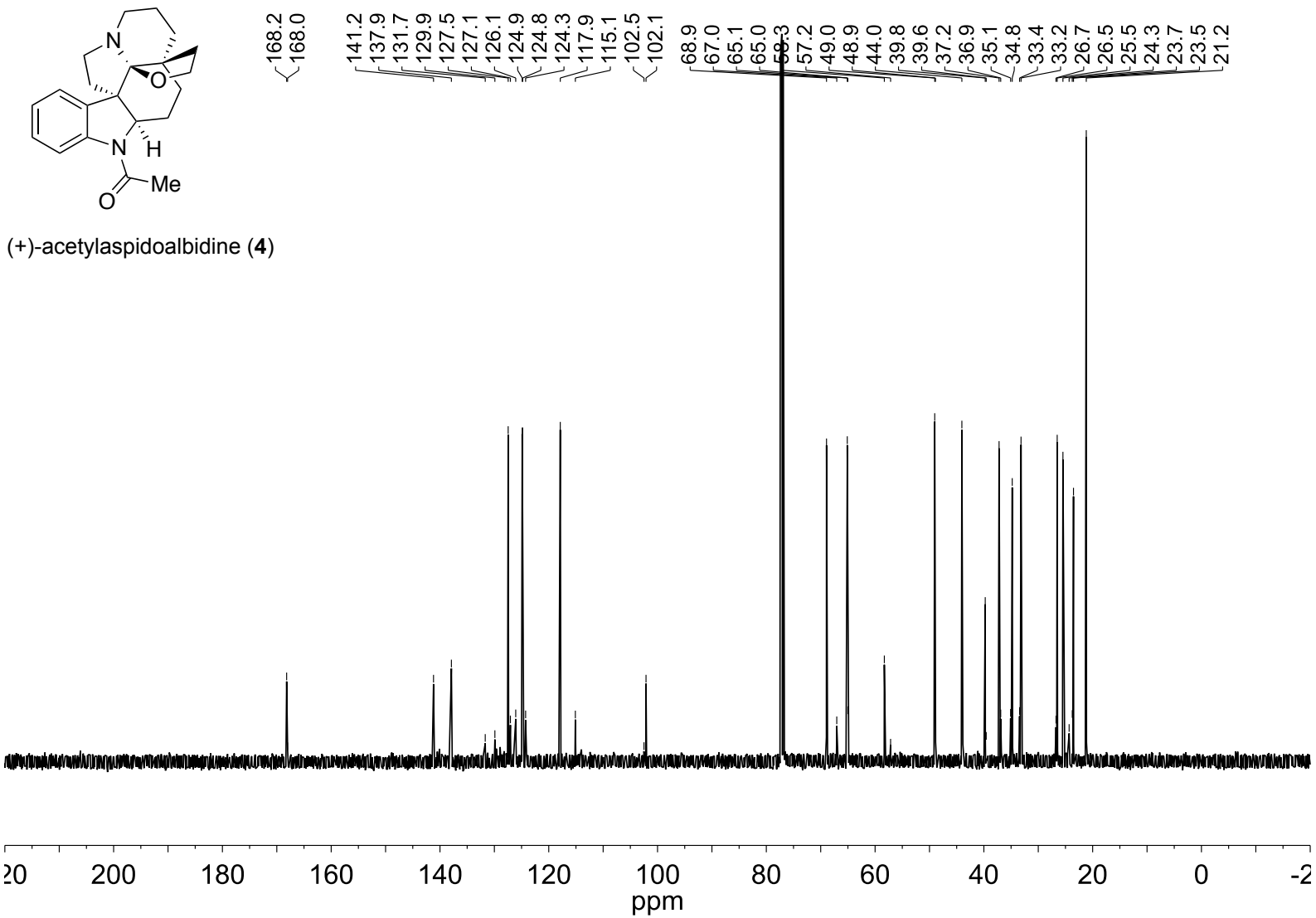
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



(+)-acetylaspidoalbidine (**4**)

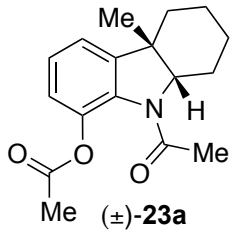


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C



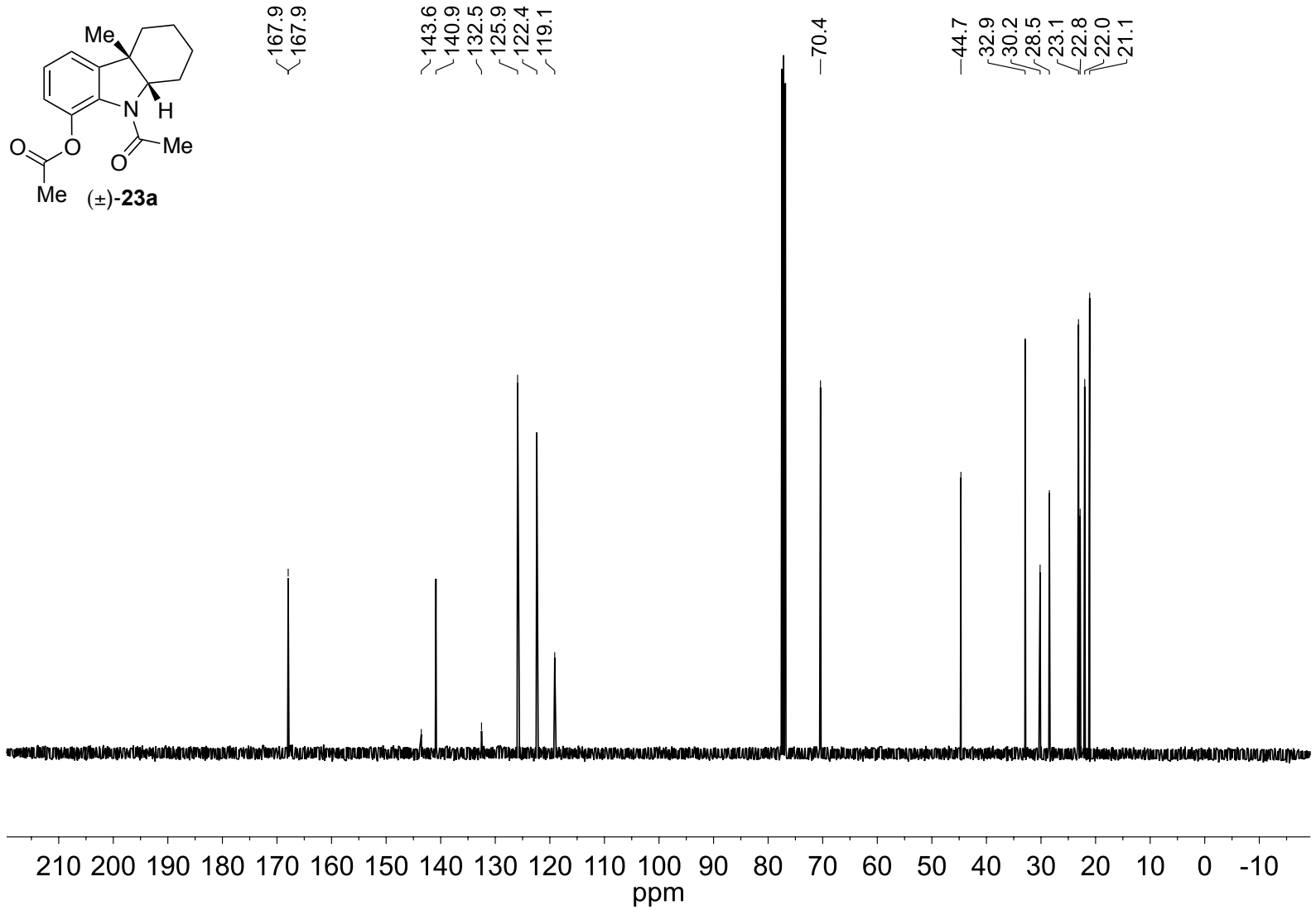
(+)-acetylaspidoalbidine (**4**)

^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

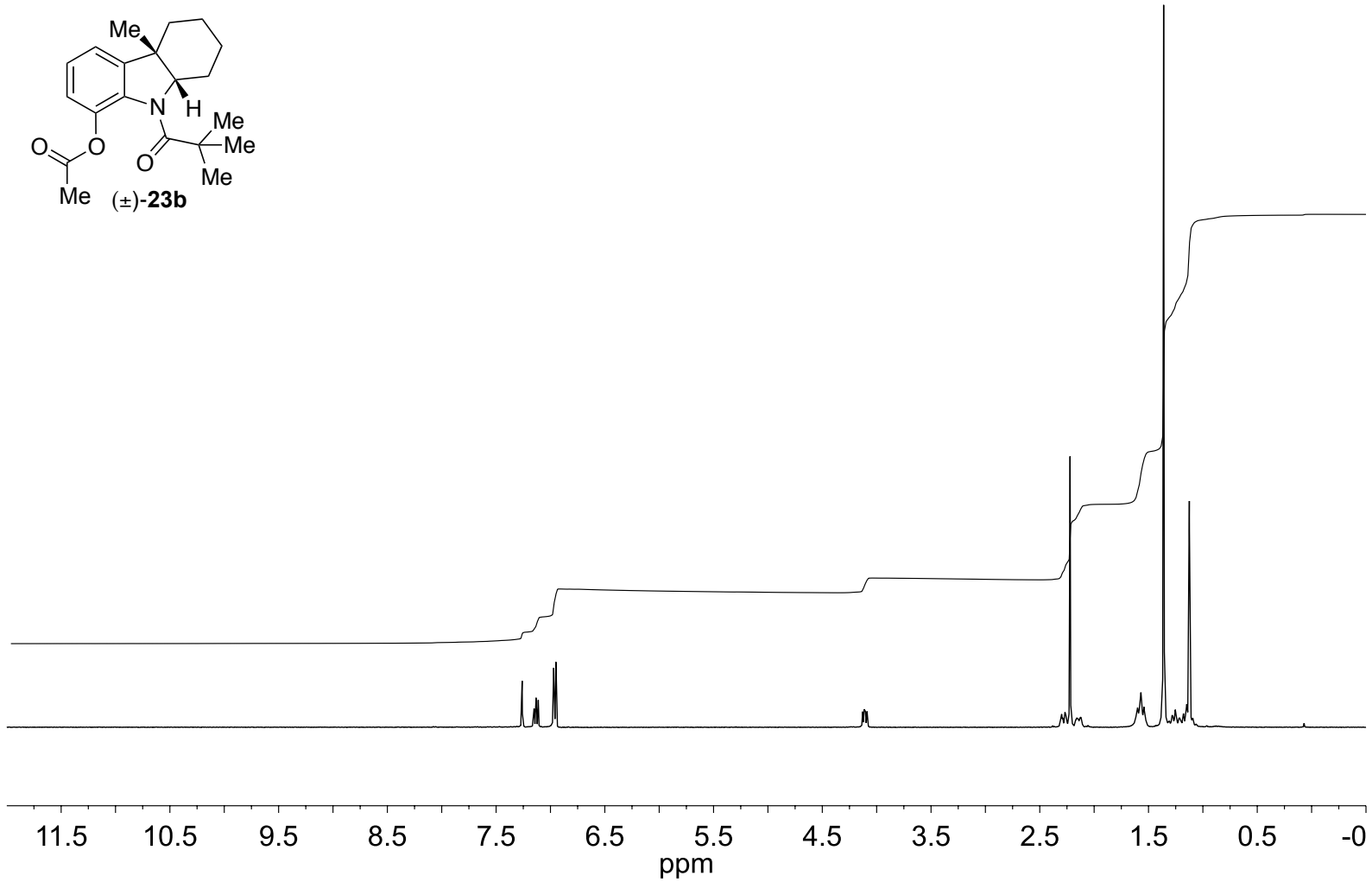


(±)-**23a**

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

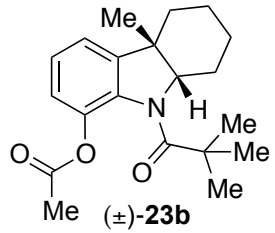


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



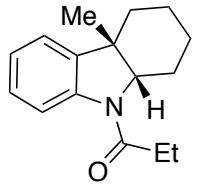
(±)-**23b**

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C

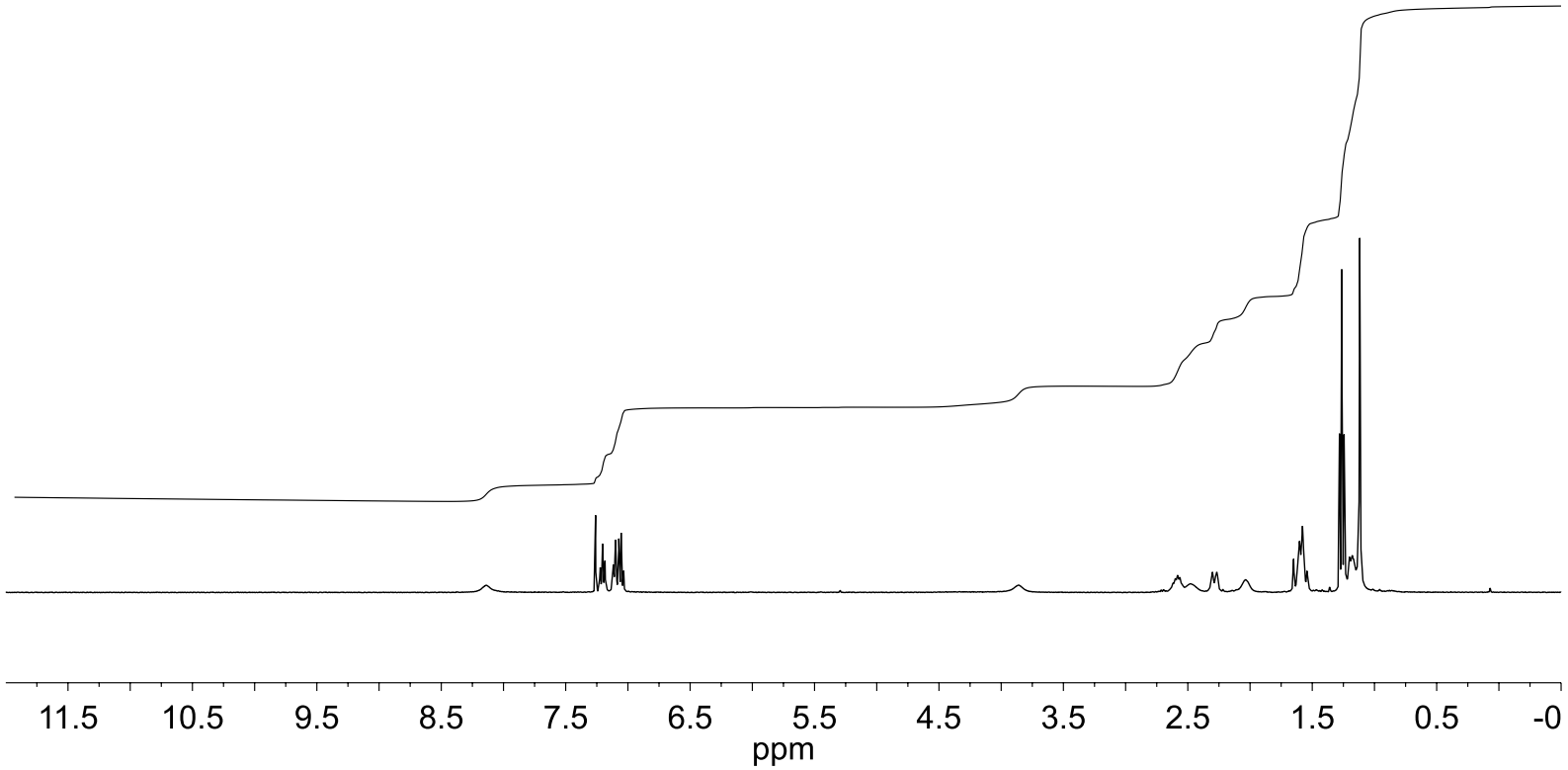


(±)-**23b**

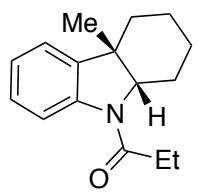
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



(±)-**22c**

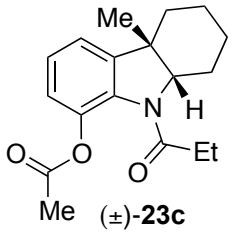


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C



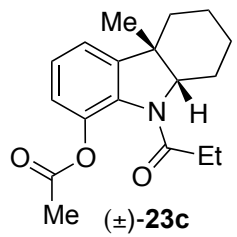
(±)-**22c**

^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



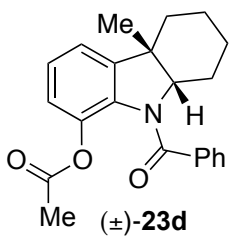
(±)-**23c**

^{13}C NMR, 100 MHz, $CDCl_3$, 25 °C



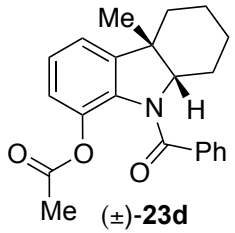
(±)-**23c**

^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



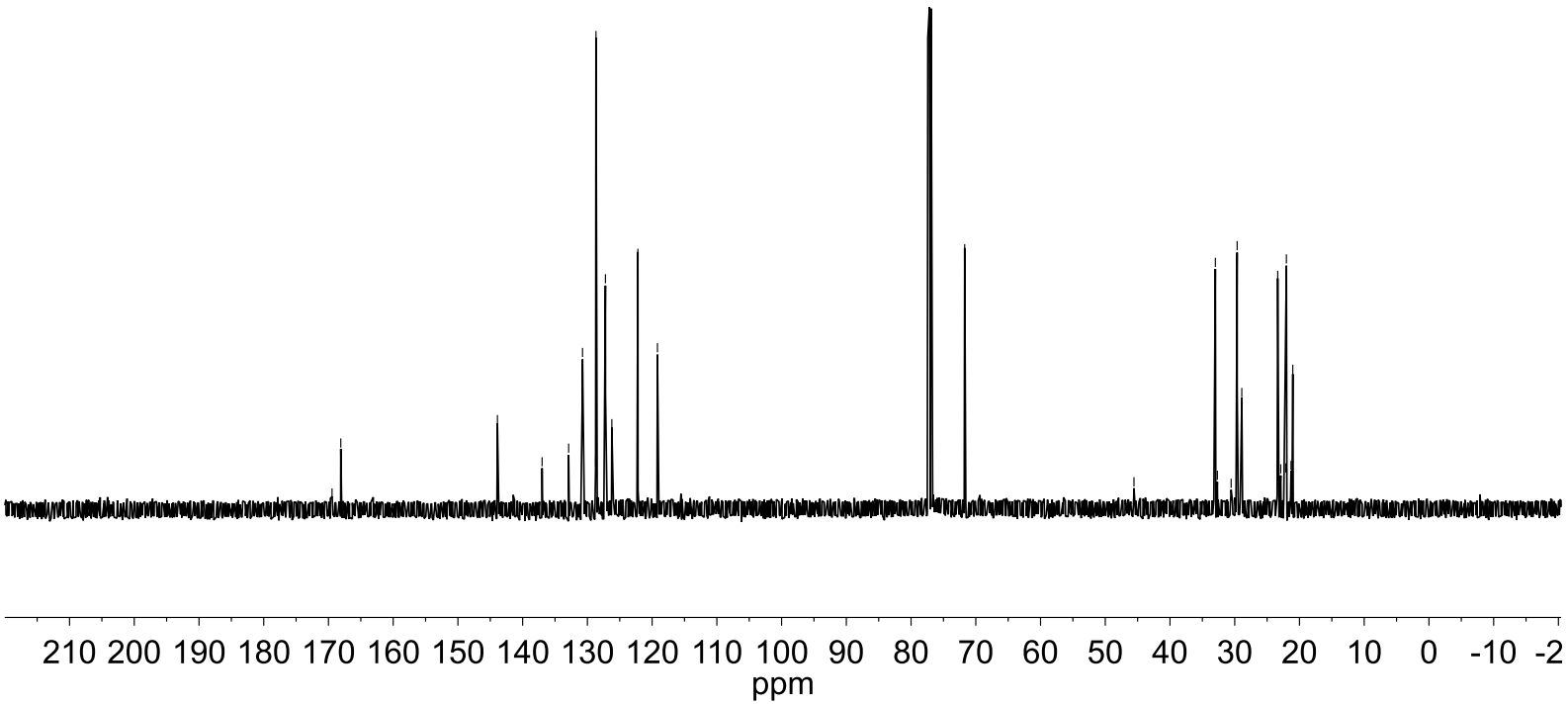
(±)-**23d**

^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

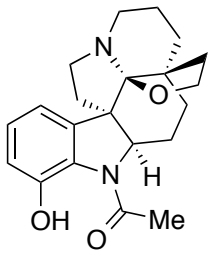


(±)-**23d**

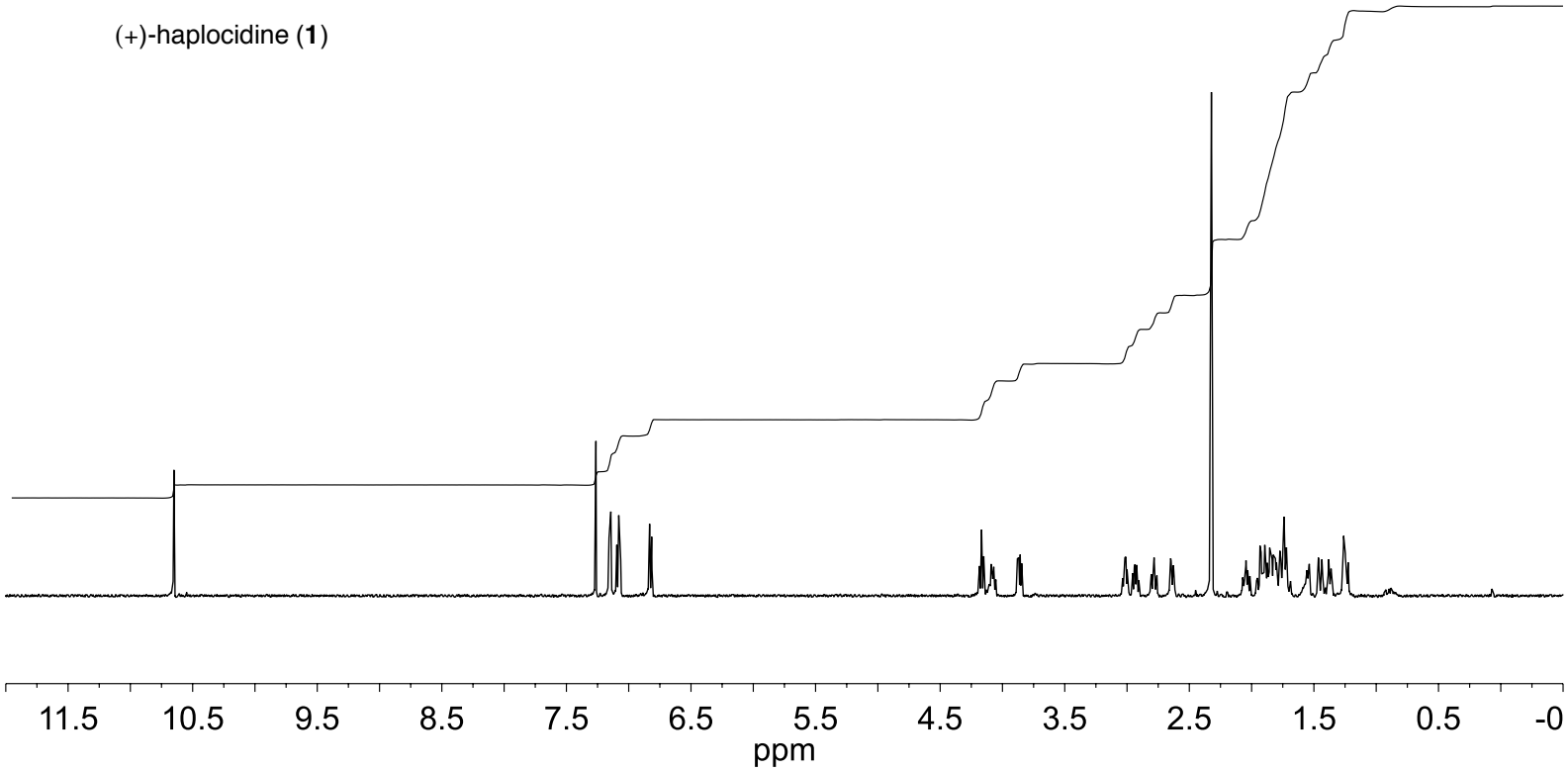
169.4
168.1
143.9
137.0
132.9
130.8
128.7
128.7
127.2
126.2
122.2
119.2
71.7
45.6
33.0
32.7
30.6
29.6
28.9
23.4
22.9
22.1
22.0
21.3
21.0



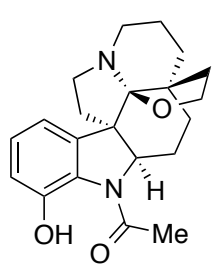
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



(+)-haplocidine (**1**)

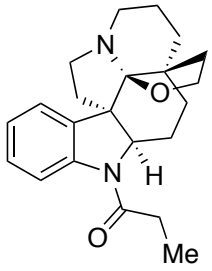


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

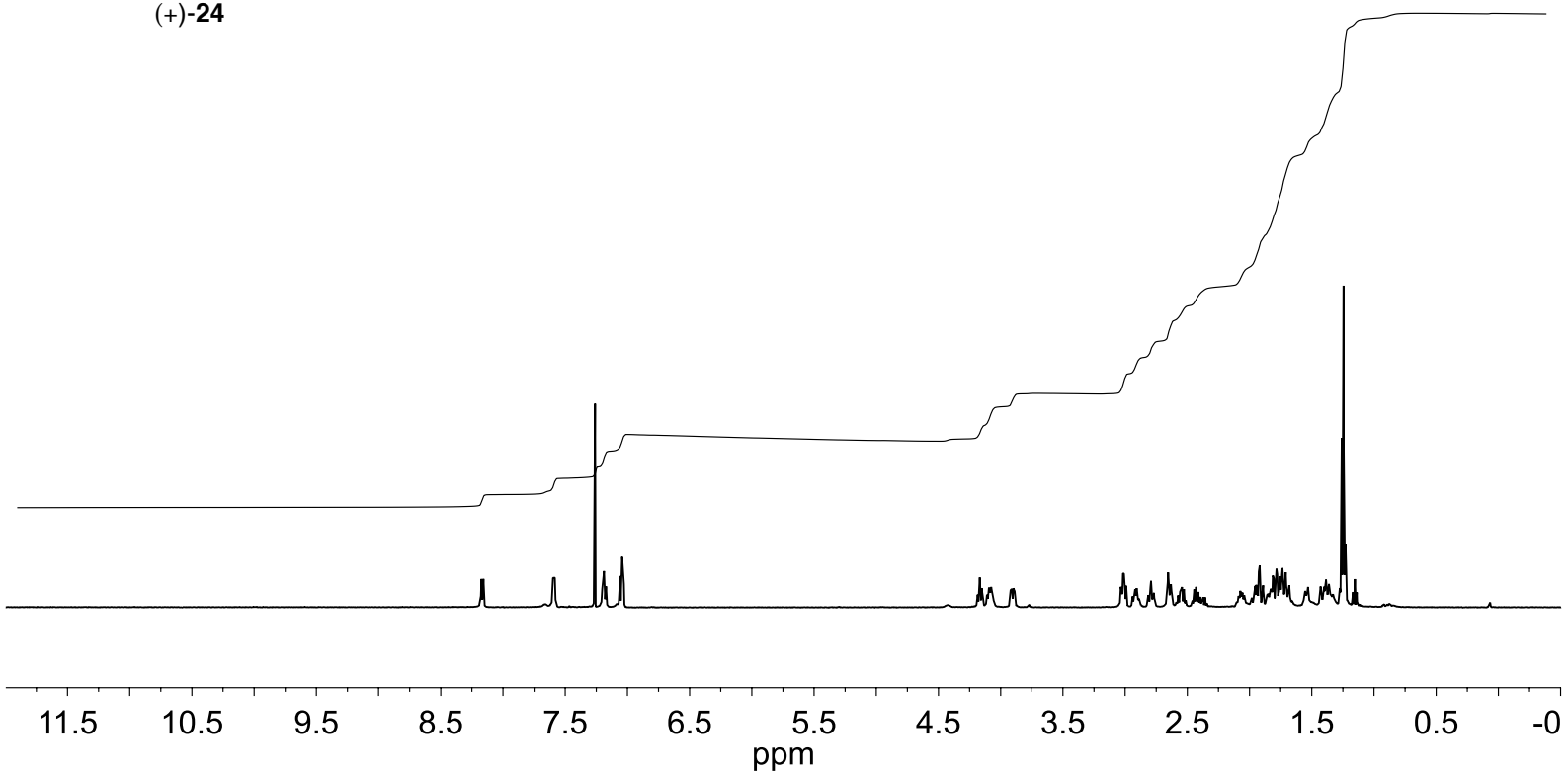


(+)-haplocidine (**1**)

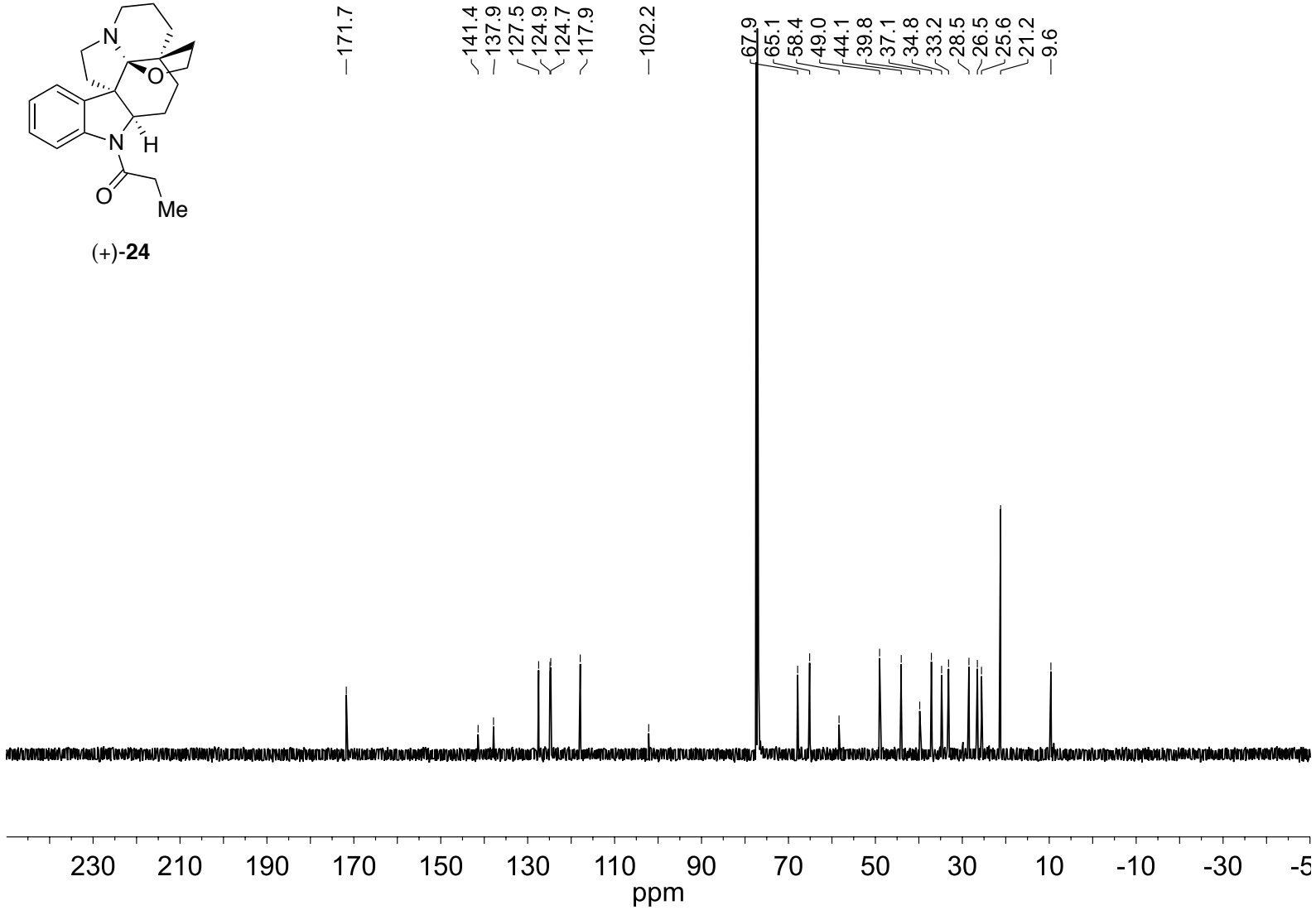
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



(+)-**24**

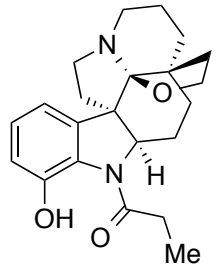


^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C

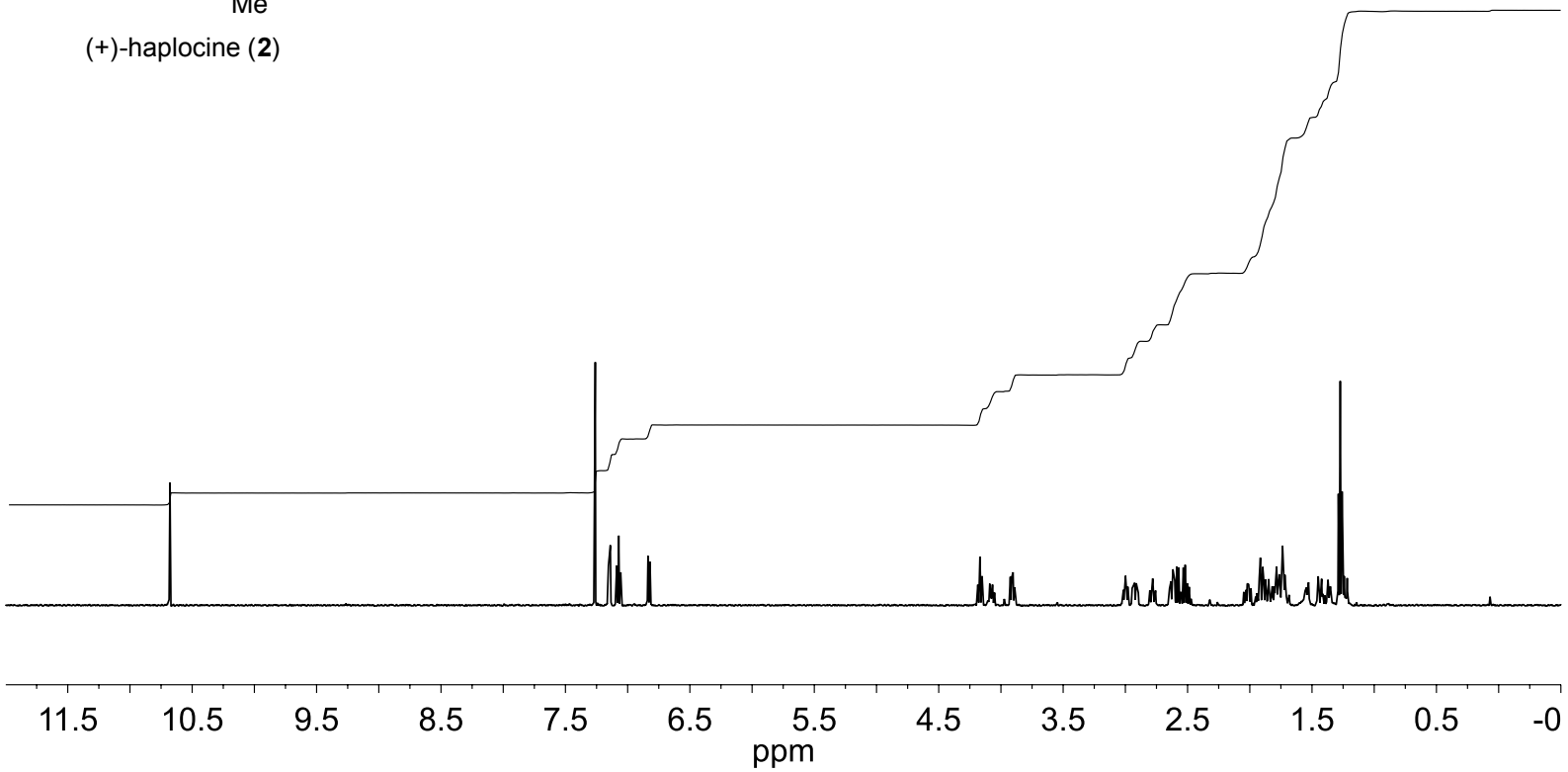


(+)-**24**

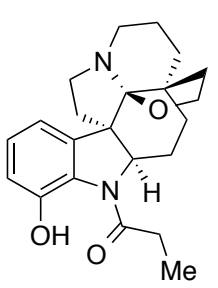
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



(+)-haplocine (**2**)



^{13}C NMR, 125 MHz, $CDCl_3$, 25 °C



(+)-haplocine (**2**)