# Asymmetric Total Synthesis of Batzelladine D

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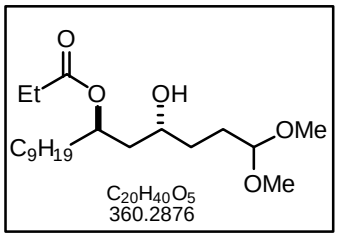
## Supporting Information[1]

### Experimental procedures and characterization data for new compounds reported in Schemes 2, 3 and 5




**(4*R*,6*R*)-1,1-Dimethoxy-6-propanoxypentadecane-4-o1 (9).** Following the general procedure of Evans and Hoveyda,[2] freshly prepared samarium(II) diiodide (15 mL of a ~0.1 M solution in THF) was added dropwise to a solution of β-hydroxy ketone **8**[3] (1.16 g, 3.84 mmol), propanal (1.1 mL, 15 mmol) and THF (37 mL) at –10 °C. After 1.5 h, the reaction was allowed to warm to rt. The yellow solution was then partitioned between saturated aqueous $NaHCO_3$ (100 mL) and EtOAc (100 mL), the aqueous phase was extracted with $Et_2O$ (3 × 100 mL) and the combined organic extracts were dried ($Na_2SO_4$) and concentrated to give a light yellow oil. This residue was purified by flash column chromatography (90:10:1 hexanes-EtOAc-$Et_3N$) to give 1.38 g (99%) of alcohol **9** as a colorless oil that solidified below 10 °C: $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.06–5.03 (m, 1H), 4.34 (app t, *J* = 5.6 Hz, 1H), 3.45–3.41 (broad m, 1H), 3.30 (s, 3H), 3.29 (s, 3H), 3.28–3.19 (broad s, 1H), 2.34 (q, *J* = 7.6 Hz, 2H), 1.80–1.73 (m, 1H), 1.66–1.40 (m, 7H), 1.4–1.2 (m, 14H), 1.13 (t, *J* = 7.4 Hz, 3H), 0.85 (t, *J* = 6.8 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 75 MHz) 175.7, 104.5, 71.6, 66.8, 52.9, 52.5, 42.9, 34.8, 31.8, 29.4, 29.3, 29.2, 28.9, 27.7, 25.4, 22.6, 14.0, 9.3 ppm; IR (film) 3506, 2927, 2855, 1735, 1463, 1379, 1278, 1194, 1129, 1070 $cm^{-1}$; MS (CI) m/z 383.2767 (383.2774 calcd for $C_{20}H_{40}O_5Na$, M+Na), 327, 311, 297, 253, 237, 223; $[\alpha]_D^{24}$ = –7.0, $[\alpha]_{577}^{24}$ = –6.22, $[\alpha]_{546}^{24}$ = –7.1, $[\alpha]_{435}^{24}$ = –12.3, $[\alpha]_{405}^{24}$ = –14.3 (*c* 1.0, $CHCl_3$).

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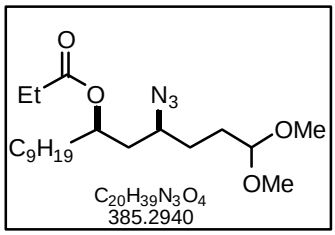
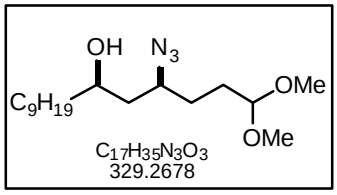
(1) General experimental details have been described: Minor, K. P.; Overman, L. E. *J. Org. Chem.* **1997**, *62*, 6379–6387. Morpholinium acetate was recrystallized from ether and dried *in vacuo* immediately prior to use.
(2) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447–6449.
(3) Details of the synthesis of the enantiomer of **8** have been described: Franklin, A. S.; Ly, S. K.; Mackin, G. H.; Overman, L. E.; Shaka, A. J. *J. Org. Chem.* **1999**, *64*, 1512–1519.



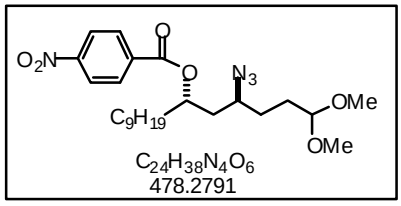

**(4*S*,6*R*)-4-Azido-1,1-dimethoxy-6-propanoxypentadecane (10).** Hydrazoic acid (28 mL of a 0.55 M solution in toluene, 15 mmol)[4] was added dropwise to a solution of alcohol **9** (2.25 g, 6.30 mmol), triphenylphosphine (4.13 g, 15.8 mmol) and benzene (100 mL) at 0 °C.[5] Diethyl azodicarboxylate (2.5 mL, 16 mmol) was then added dropwise over 30 min, and after 2 h, the yellow mixture was allowed to warm to rt. After concentration, the residue was purified by flash column chromatography (90:10:1 hexanes-EtOAc-$Et_3N$) to give 2.32 g (96%) of azido ester **10** as a colorless oil: $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.01–4.97 (m, 1H), 4.36 (app t, $J$ = 4.7 Hz, 1H), 3.31 (s, 6H), 3.27–3.26 (m, 1H), 2.32 (q, $J$ = 7.6 Hz, 2H), 1.88–1.81 (m, 1H), 1.77–1.49 (m, 7H), 1.4–1.2 (m, 14H), 1.14 (t, $J$ = 7.5 Hz, 3H), 0.85 (t, $J$ = 6.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 75 MHz) 174.1, 103.9, 71.3, 59.5, 52.9, 38.5, 34.4, 31.8, 29.5, 29.4, 29.3, 29.1, 28.8, 27.8, 25.1, 22.6, 14.1, 9.2 ppm; IR (film) 2927, 2855, 2102, 1736, 1187, 1128, 1070 cm$^{-1}$; MS (CI) m/z 408.2836 (408.2838 calcd for $C_{20}H_{39}N_3O_4Na$, M+Na), 326, 282, 268, 252, 237; $[\alpha]_D^{24}$ = +7.4, $[\alpha]_{577}^{24}$ = +6.4, $[\alpha]_{546}^{24}$ = +8.5, $[\alpha]_{435}^{24}$ = +13.5, $[\alpha]_{405}^{24}$ = +18.3 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{20}H_{39}N_3O_4$: C, 62.31; H, 10.20; N, 10.90. Found: C, 62.22; H, 10.16; N, 10.80.



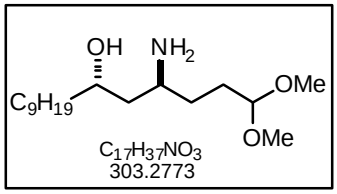

**(4*S*,6*R*)-4-Azido-1,1-dimethoxypentadecan-6-ol (11).** A mixture of azido ester **10** (2.4 g, 6.2 mmol), $K_2CO_3$ (2.4 g) and methanol (50 mL) was maintained at reflux for 5 h and then concentrated. The residue was partitioned between 20% EtOAc-hexanes (100 mL) and saturated aqueous $NaHCO_3$ (100 mL). The layers were separated, and the aqueous layer extracted with 20% EtOAc-hexanes (3 × 50 mL). The combined organic layers were washed with brine (150 mL), dried ($Na_2SO_4$) and concentrated to provide 2.0 g (100%) of azido alcohol **11** as a colorless oil: $^1$H NMR ($CDCl_3$, 500 MHz) δ 4.40 (t, $J$ = 4.8 Hz, 1H), 3.75 (m, 1H), 3.53 (m, 1H), 3.35 (s, 6H), 2.09 (broad s, 1H), 2.09–1.58 (m, 6H), 1.48–1.42 (m, 2H), 1.4–1.2 (m, 14H), 0.90 (t, $J$ = 6.2

(4) Wolff, H. *Org. React.* **1946**, *3*, 307.
(5) (a) Hassner, A.; Dehaen, W. *J. Org. Chem.* **1990**, *55*, 2243–2244. (b) Mitsunobu, O. Synthesis **1981**, 1–32.

Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) 104.1, 69.8, 60.6, 53.1, 52.8, 41.3, 37.7, 31.8, 29.6, 29.5, 29.3, 29.0, 28.8, 25.4, 22.6, 14.1 ppm; IR (film) 3444, 2926, 2854, 2100, 1455, 1360, 1255, 1129, 1065 cm$^{-1}$; $[\alpha]_D^{24}$ = +8.8, $[\alpha]_{577}^{24}$ = +10.1, $[\alpha]_{546}^{24}$ = +11.5, $[\alpha]_{435}^{24}$ = +20.7, $[\alpha]_{405}^{24}$ = +24.6 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{17}H_{35}N_3O_3$: C, 61.97; H, 10.71; N, 12.75. Found: C, 62.04; H, 10.77; N, 12.68.



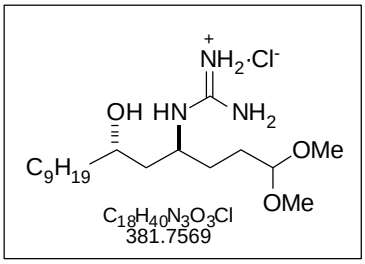

**(4*S*,6*S*)-4-Azido-6-(4-nitrobenzoyloxy)-1,1-dimethoxypentadecane (12).** Diethyl azodicarboxylate (1.96 mL, 12.4 mmol) was added dropwise to a 0 °C solution of triphenylphosphine (3.25 g, 12.4 mmol) and toluene (15 ml). The resulting yellow solution was added dropwise over 20 min to a mixture of alcohol **11** (2.04 g, 6.20 mmol), 4-nitrobenzoic acid (2.07 g, 12.4 mmol) and toluene (15 mL). One hour after addition was complete, Celite was added and the mixture was concentrated to a free-flowing powder. This residue was chomatographed (5 % then 10 % EtOAc-hexanes containing 1% $Et_3N$) to give 2.65 g (89%) of azido ester **12** as a colorless oil: $^1$H NMR ($CDCl_3$ 500 MHz) δ 8.30 (d, *J* = 8.9 Hz, 2H), 8.22 (d, *J* = 8.9 Hz, 2H), 5.40–5.30 (m, 1H), 4.35 (app t, *J* = 5.3 Hz, 1H), 3.42–3.36 (m, 1H), 3.31 (s, 3H), 3.30 (s, 3H), 1.94–1.86 (m 1H), 1.80–1.60 (m, 8H), 1.38–1.21 (m, 14H), 0.87 (app t, *J* = 6.9 Hz); $^{13}$C NMR ($CDCl_3$ 125 MHz) δ 164.2, 150.5, 135.7, 130.7, 123.6, 104.1, 73.4, 59.3, 53.3, 39.0, 34.6, 31.8, 29.9, 29.5, 29.4, 29.2, 29.0, 25.2, 22.6, 14.1 ppm; IR (film) 2927, 2855, 2104, 1724, 1607, 1529, 1349, 1274, 1118 cm$^{-1}$; $[\alpha]_D^{24}$ = +20.4, $[\alpha]_{546}^{24}$ = +27.4, $[\alpha]_{435}^{24}$ = +47.2, $[\alpha]_{405}^{24}$ = +58.2 (*c* 0.25, $CHCl_3$). Anal. Calcd for $C_{24}H_{38}N_4O_6$: C, 60.23; H, 8.00; N, 11.71. Found: C, 60.45; H, 8.00; N,11.59.




**(4*S*,6*S*)-4-Amino-1,1-dimethoxypentadecane-6-o1 (13).** A mixture of ester **12** (2.62 g, 5.47 mmol), aqueous NaOH (1M, 55 mL), and THF (55 mL) was refluxed with vigerous stirring for 18 h. The mixture was diluted with 20% EtOAc-hexanes (50 mL) and the layers were separated. The aqueous layer was extracted with 20% EtOAc-hexanes (3 × 20 mL). The combined organic layers

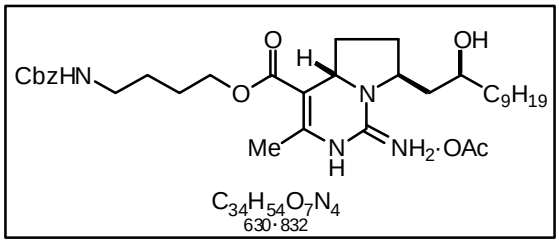
were washed with saturated aqueous $NaHCO_3$ (1 × 50 mL) and brine (1 × 50 mL), and dried ($Na_2SO_4$), and concentrated to a colorless oil.

The azido alcohol prepared above was combined with MeOH (25 mL), 10% Pd•C (200 mg) and maintained under 50 psi of $H_2$ for 5 h. The mixture was filtered through Celite, and the pad was washed with MeOH (50 mL). The solution was concentrated to give 1.60 g (98%) of amino alcohol **13** as a colorless oil: $^1$H NMR ($CDCl_3$, 300 MHz) δ 4.34 (app t, $J$ = 4.2 Hz, 1H), 3.82–3.81 (m, 1H), 3.29 (s, 3H), 3.28 (s, 3H), 3.10–3.05 (m, 1H), 2.86–2.55 (broad m, 2H), 1.64–1.31 (m, 8H), 1.4–1.2 (m, 14H), 0.84 (t, $J$ = 6.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 75 MHz) 104.3, 69.1, 52.8, 52.7, 48.8, 41.0, 37.7, 32.4, 31.8, 29.7, 29.6, 29.5, 29.3, 29.2, 25.8, 22.6, 14.0 ppm; IR (film) 3404, 3356, 3298, 2825, 2854, 1464, 1380, 1126, 1063 cm$^{-1}$; MS (CI) m/z 304.2852 (304.2551 calcd for $C_{17}H_{38}NO_3$, MH), 285, 275, 253, 242, 211, 194, 167, 154, 128; $[\alpha]_D^{24}$ = +0.1, $[\alpha]_{577}^{24}$ = +0.3, $[\alpha]_{546}^{24}$ = +1.2, $[\alpha]_{435}^{24}$ = +1.5, $[\alpha]_{405}^{24}$ = +1.5 (*c* 1.0, $CHCl_3$).



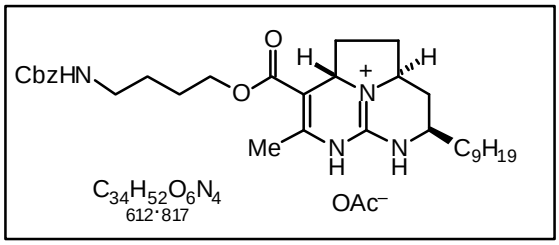

**(4*S*,6*S*)-1,1-Dimethoxy-4-(chloroguanidinium)-3-hydroxypentadecane (15).** Following the general procedure of Bernatowicz,[6] a solution of amino alcohol **13** (100 mg, 0.33 mmol), 1*H*-pyrazole-1-carboxamidine hydrochloride (51 mg 0.35 mmol), *i*-$Pr_2$NEt (61 μl, 0.35 mmol), and MeOH (165 μl) was maintained at rt for 24 h, then concentrated at 0.5 mm for 12 h to yield guanidine **15** as a colorless oil that was used without further purification: $^1$H NMR ($CDCl_3$, 500 MHz) δ 7.98 (broad s, 1H), 7.54 (broad d, $J$ = 8.6 Hz, 1H), 7.30–7.09 (m, 3H), 4.24 (app t, $J$ = 4.8 Hz, 1H), 3.58–3.52 (m, 2H), 3.05–3.01 (m, 1H), 3.18 (s, 6H), 1.63–1.25 (m, 8H), 1.4–1.2 (m, 14H), 0.74 (t, $J$ = 6.7 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) 158.1, 104.1, 67.3, 53.8, 53.1, 52.6, 42.1, 37.5, 31.5, 29.3, 29.2, 28.9, 25.2, 22.3, 18.2, 16.9, 13.7, 12.0 ppm; IR (film) 3356, 3168, 2926, 2854, 1652, 1463, 1129, 1065 cm$^{-1}$; MS (CI) m/z 346.3069 (346.3069 calcd for $C_{18}H_{40}N_3O_3$, M–Cl), 300, 282, 240, 222, 154, 136, 123.

(6) (a) Bernatowicz, M. Z.; Wu, Y.; Matsueda, G. R. *J. Org. Chem.* **1992**, *57*, 2497–2502. (b) Bernatowicz, M. S.; Wu, Y.; Matsueda, G. R. *Tetrahedron Lett.* **1993**, *34*, 3389–3392.




**(4a*R*,7*R*)-7-(2*S*-Hydroxyundecyl)-1-imino-3-methyl-1,2,4a,5,6,7,-hexahydropyrrolo-[1,2-*c*]pyrimidiniumacetate-4-carboxylic acid 4-(benzyloxycarbonylaminobutyl ester (17)**. Crude guanidine acetal **15** (0.33 mmol) was dissolved in 50% aqueous acetic acid (1 mL) and maintained at rt for 24 h. The clear solution was concentrated (35 °C/10 mmHg, then rt/0.5 mmHg 24 h) to give the corresponding crude hemi-aminal as colorless oil; diagnostic $^1$H NMR ($CDCl_3$, 500 MHz) δ 5.44–5.41 and 5.56–5.47 (multiplets, 1H total, C*H*(OH)N).

This intermediate, β-ketoester **16** (200 mg, 0.66 mmol),[7] morpholinium acetate (100 mg, 0.66 mmol), $Na_2SO_4$ (100 mg), and 2,2,2-trifluoroethanol were maintained at 70 °C for 40 h. The dark yellow mixture was diluted with $CHCl_3$, filtered, concentrated and purified by flash column chromatography (98:2:1 to 96:4:1 $CHCl_3$-MeOH-AcOH) to give 115 mg (55% overall from **12**) of Biginelli product **17** as a light yellow oil: $^1$H NMR ($CDCl_3$, 500 MHz) δ 9.41–9.32 (broad s, 1H), 8.13–7.95 (broad s, 1H), 7.35–7.38 (m, 5H), 6.98–6.63 (broad s, 1H), 5.16 (broad s, 1H), 5.09 (s, 2H), 4.83 (m, 1H), 4.39–4.35 (m, 2H), 4.18 (t, *J* = 6.2 Hz, 2H), 3.73–3.61 (m, 2H), 3.24–3.23 (m, 2H), 2.52 (broad m, 1H), 2.33 (s, 3H), 2.17–2.14 (m, 1H), 1.71–1.50 (m, 8H), 1.4–1.2 (m, 14H), 0.87 (t, *J* = 7.1 Hz, 3H) ; $^{13}$C NMR ($CDCl_3$, 125 MHz) 165.2, 156.5, 151.0, 143.5, 136.3, 128.6, 128.2, 128.1, 101.3, 68.2, 66.8, 64.1, 56.7, 56.3, 41.5, 40.6, 37.6, 34.3, 31.9, 29.7, 29.5, 29.4, 29.3, 28.2, 26.7, 25.9, 25.3, 22.7, 17.5, 14.1 ppm; IR (film) 3288, 3190, 2926, 2855, 1714, 1662, 1538, 1266, 1129, 1083 $cm^{-1}$; MS (CI) m/z 571.3849 (571.3859 calcd for $C_{32}H_{51}N_4O_5$, M–OAc), 440, 380, 348, 328, 307, 282, 272, 240, 222, 207; $[\alpha]_D^{24}$ = –8.7, $[\alpha]_{577}^{24}$ = –10.8, $[\alpha]_{546}^{24}$ = –12.2, $[\alpha]_{435}^{24}$ = –5.7, $[\alpha]_{405}^{24}$ = –6.5 (*c* 1.0, MeOH).

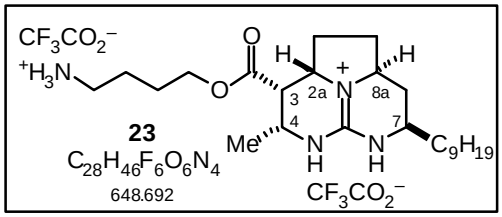



**(2a*S*,7*R*,8a*S*)-3-[4-(*N*-Benzyloxycarbonylamino)butoxycarbonyl]-4-methyl-7-nonyl-**

(7) Prepared in 91% yield from methyl acetoacetate and *N*-benzyloxycarbonyl-4-aminobutanol using the procedure of Taber: Taber, D. F.; Amedio, J. J. C.; Pate, Y. K. *J. Org. Chem.* **1985**, *50*, 3618–3619.

**1,2,2a,5,6,7,8,8a-octahydro-5,6,8b-triazaacephthylinium acetate (18).** A solution of methanesulfonyl chloride (1.6 mL, 22 mmol) and $CH_2Cl_2$ (12 mL) was added to a solution of **17** (500 mg, 0.79 mmol), triethylamine (1.4 mL, 10 mmol) and $CH_2Cl_2$ (60 mL) at 0 °C. After 2.5 h, the reaction was allowed to warm to rt and was quenched with 1 M aqueous HCl (100 mL). The aqueous phase was extracted with $CHCl_3$ (3 × 50 mL) and the combined organic phases were extracted further with 1 M aqueous HCl (3 × 50 mL), dried ($Na_2SO_4$), and concentrated to give a yellow solid. This residue was filtered through a short pad of silica gel (80:20:1 hexanes-*i*-PrOH-AcOH) to provide 450 mg of the crude mesylate as a yellow oil that was used without futher purification.

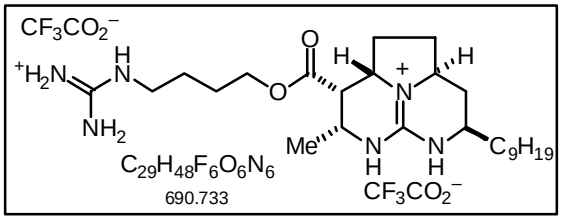
A solution of this crude mesylate, triethylamine (10 mL, 72 mmol), and $CHCl_3$ (100 mL, purified by filtering through basic A-3 alumina) was placed in an aluminum foil-covered flask and heated at reflux (bath temperature 90 °C) for 36 h. After cooling to rt, the yellow mixture was concentrated, the residue was partitioned between $CHCl_3$ (100 mL) and 1 M aqueous HCl (150 mL) and the layers were separated. The aqueous phase was extracted with $CHCl_3$ (3 × 50 mL) and the combined organic extracts were dried ($Na_2SO_4$) and concentrated to give a yellow solid. This residue was purified by column chromatography (80:20:1 hexanes-*i*-PrOH-AcOH to *i*-PrOH to MeOH) to provide 290 mg (60% from **17**) of tricyclic guanidine **18** as a light yellow oil: $^1$H NMR ($CD_3OD$, 500 MHz) δ 7.33–7.27 (m, 5H), 5.10 (broad s, 1H), 5.05 (s, 2H), 4.19–4.10 (broad m, 3H), 3.75–3.72 (m, 1H), 3.57–3.51 (m, 1H), 3.15 (t, J = 6.7 Hz, 2H), 2.61–2.55 (m, 1H), 2.35–2.31 (m, 1H), 2.26 (s, 3H), 1.94 (s, 3H), 1.92–1.84 (m, 1H), 1.60–1.39 (m, 9H), 1.4–1.2 (m, 14H), 0.89 (t, *J* = 5.1 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz) 166.8, 166.3, 158.9, 150.3, 148.3, 138.5, 129.5, 128.9, 128.7, 105.6, 67.3, 65.2, 58.2, 56.6, 53.3, 41.3, 35.8, 33.4, 33.1, 32.6, 30.6, 30.6, 30.4, 27.7, 27.1, 26.3, 26.2, 23.7, 17.7, 14.5 ppm; IR (film) 3335, 2930, 2860, 1686, 1655, 1600, 1518, 1196, 1134 cm$^{-1}$; MS (FAB) m/z 553.3756 (553.3753 calcd for $C_{32}H_{48}N_4O_4$, M–OAc), 346, 330, 307, 289, 267, 193; $[\alpha]_D^{24}$ = +18.5, $[\alpha]_{577}^{24}$ = +21.3, $[\alpha]_{546}^{24}$ = +26.4, $[\alpha]_{435}^{24}$ = +71.1, $[\alpha]_{405}^{24}$ = +104 (*c* 1, MeOH).




**23**
$C_{28}H_{46}F_6O_6N_4$
648.692

**(2a*S*,3*S*,4*R*,7*R*,8a*S*)-3-[4-(Trifluoroacetoxyammonium)butoxycarbonyl]-4-methyl-7-nonyl-1,2,2a,3,4,5,6,7,8,8a-decahydro-5,6,8b-triazanaphthylinium trifluoroacetate (23) and Isomer 24.** A solution of **18** (100 mg, 0.163 mmol), formic acid (88% aqueous, 200 μL), 5%

$Rh/Al_2O_3$ (600 mg), MeOH (5 mL) and $H_2O$ (15 mL) was maintained under 80 psi of $H_2$ for 12 h.[8] The reaction was filtered through a pad of Celite (pre-washed with 20 mL of MeOH) and concentrated to give a yellow oil. This residue was purified by HPLC (5 μ Alltima reverse phase C18 silica column, 10:14:0.1 $CH_3CN$-$H_2O$-TFA) to give 44 mg (38%) of pure **24** and 34 mg (30%) of an inseparable 10:1 mixture of **23** and **25**, all as colorless oils. Characterization data for **23**: $^1$H NMR ($CD_3OD$, 500 MHz) δ 4.18–4.17 (m, 2H), 4.01–3.95 (m, 1H, H2a), 3.87–3.84 (m, 1H, H4), 3.57–3.48 (m, 2H, H7 and H8a), 3.14 (broad s, 1H, H3), 2.96 (broad s, 2H), 2.37–2.32 (m, 1H), 2.25–2.19 (m, 2H), 1.75–1.42 (m, 9H), 1.4–1.2 (m, 17H), 0.90 (t, $J$ = 4.7 Hz, 3H); $^{13}$C NMR ($CD_3OD$, 125 MHz) 170.2, 151.5, 65.2, 57.8, 57.3, 53.2, 50.2, 45.4, 40.3, 37.0, 34.2, 33.0, 31.4, 30.6, 30.4, 29.3, 26.7, 26.2, 25.3, 23.7, 18.5, 14.4 ppm; IR (film) 3381, 3200, 3114, 2927, 2858, 1725, 1681, 1641, 1202, 1134 $cm^{-1}$; MS (FAB) m/z 421.3544 (421.3543 calcd for $C_{24}H_{45}N_4O_2$, M–$C_4F_6O_4H$), 391, 369, 350. Isomer **24** showed the following diagnostic signals in its $^1$H NMR spectrum: 4.40–4.07 (m, H2a), 3.80–3.78 (m, H4), 3.65–3.60 (m, H8a), 3.51–3.49 (m, H7), 2.96–2.91 (m, H3). Assignments for the methine hydrogens of **23** and **24** were made by analogy to their methyl ester congeners, whose structures had been previously established using double-pulsed field gradient spin echo NOE experiments.[3] The structure of the minor dehydro product **25** was established by chemical correlation.[9]




**Batzelladine D ditrifluoroacetate (2).** A solution of this impure sample of **23** (10 mg, 0.015 mmol), *i*-$Pr_2NEt$ (0.15 mL, 0.86 mmol), 1*H*-pyrazole-1-carboxamidine hydrochloride (40 mg, 0.27 mmol) and DMF (0.25 mL) was maintained at rt for 18 h.[6] The reaction was partitioned between $CHCl_3$ (10 mL) and 1 M aqueous HCl (10 mL), the aqueous layer was extracted with $CHCl_3$ (3 × 10 mL) and the combined organic phases were extracted with 1 M aqueous HCl ( 3 × 10 mL), dried ($Na_2SO_4$) and concentrated to give 13 mg of a crude residue. This residue was purified by HPLC (5μ Alltima reverse phase C18 silica column, 10:14:0.1 $CH_3CN$-$H_2O$-TFA then 10:16:0.1 $CH_3CN$-$H_2O$-TFA) to give 8 mg (75%) of pure batzelladine D ditrifluoroacetate (**2**) as a colorless oil: $[\alpha]_D^{24}$ = –4.6, $[\alpha]_{577}^{24}$ = –13.4, $[\alpha]_{546}^{24}$ = –18.0 (*c* 0.6, MeOH). This sample showed spectroscopic and mass spectral data in accord with those of an authentic sample of the natural

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product.[10]

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