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Supporting Information

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Highly Diastereoselective Alkylation of Aziridine-2-carboxylate Esters. Enantioselective Synthesis of LFA-1 Antagonist BIRT-377.

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General Experimental.

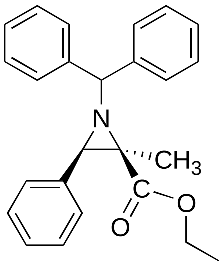
All solvents were reagent grade and were distilled under argon before use: dichloromethane, toluene and benzene from calcium hydride; tetrahydrofuran, diethyl ether and 1,2-dimethoxyethane from benzophenone ketyl. All reactions were performed under inert argon gas unless otherwise stated. NMR spectra were recorded on Varian 300 MHz spectrometers using ^{1}H and ^{13}C solvent peaks as an internal reference. Unless otherwise specified, all aziridines were alkylated as racemates.

General procedure for the preparation of racemic aziridines catalyzed by BF_3. Et_2O.

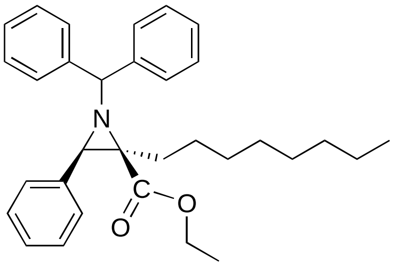
To a solution of benzhydralimine[1] in dry dichloromethane under Argon atmosphere was added BF_3. Et_2O (5 mol%) via a syringe followed by addition of ethyl diazoacetate (1.1equiv.) all at once. The reaction mixture was stirred at rt for 18h and was quenched with de-ionized water and extracted with 3 x 20 mL of dichloromethane. The organic phases were combined and dried over anhy. $MgSO_4$, filtered and the solvent removed on a rotary evaporator. The crude product was crystallized from 1:15 (dichloromethane : pentane) to give pure aziridine.

General Procedure For Alkylation Of Aziridines.

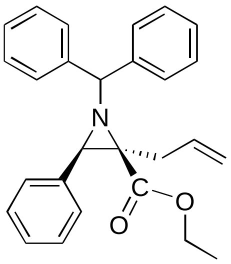
To a flame-dried round-bottomed flask equipped with a magnetic stir bar and a septa was added 4-ml dry 1,2-dimethoxyethane, 2 equiv dry diisopropylamine and 2 equiv *n*-butyl lithium at –78 °C. Then 1 equiv of the appropriate aziridine dissolved in a mixture of 1 mL DME and 1 mL diethyl ether was transferred to the reaction pot via a cannula. The final concentration of the aziridine is 0.08 M. Unless otherwise specified, the alkylation reactions were carried out on racemic aziridines. The color of the reaction turned to a transparent brown. The reaction was stirred at –78 °C for 30 min and then 3 equiv of the electrophile was added via syringe. The reaction was then gradually allowed to reach room temperature under constant stirring. The reaction was quenched with brine and extracted with 3 x 15 mL Et_2O. The ethereal phases were combined and dried over anhydrous $MgSO_4$, filtered and the solvent removed on a rotary evaporator. The crude product was then purified on a silica gel column eluting with a 9:1 mixtures of hexanes and ethyl acetate.



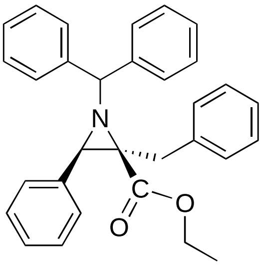
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-methyl-3-phenyl aziridine **(5a):** R$_f$=0.5 (9:1 hexanes: EtOAc). Yield 82 %. mp = 112 ^{o}C. ^{1}H NMR (300MHz, CDCl$_3$) δ = 0.88 (t, 3H, J = 7 Hz), 1.55 (s, 3H), 2.96 (s, 1H), 3.74-3.97 (m, 2H), 4.47 (s, 1H), 7.05-7.35 (m, 11 H), 7.47 (d, 2 H), 7.68 (d, 2 H); ^{13}C NMR (75MHz, CDCl$_3$) δ = 13.37, 13.83, 50.22, 52.71, 60.50, 70.50, 126.83, 126.87, 126.93, 127.30, 127.62, 127.86, 128.39, 136.24, 143.33, 143.65, 170.12 (2 aryl C's not located); IR (thin film) (cm^{-1}): 3030, 2980, 2363, 2336, 1705, 1450, 1147; MS (EI) m/z (% rel intensity) 372 (M+H)$^+$ (1), 371 M$^+$ (4), 266 (12), 265 (19), 168 (22), 167 (100), 165 (48), 152 (24), 105 (18); HRMS (FAB) calcd for $C_{25}H_{25}NO_2^+$ m/z 371.1885, meas 371.1880. Anal calcd for C, 80.83; H, 6.68; N, 3.77. Found: C, 80.58; H, 6.80; N, 3.80.



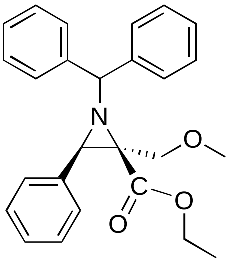
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-octyl-3-phenyl aziridine **(5b):** R$_f$=0.57 (9:1 hexanes: EtOAc), oil. Yield 50 %. ^{1}H NMR (300 MHz, CDCl$_3$) δ = 0.90 (t, 6H), 1.05-1.40 (m, 12 H), 1.6-1.8 (m, 1 H), 2.15-2.25 (m, 1 H), 2.95 (s, 1 H), 3.8-4.0 (m, 2 H), 4.55 (s, 1 H), 7.10-7.38 (m, 12 H), 7.50 (d, 2H, J = 6.8 Hz), 7.79 (d, 1H, J = 7.7 Hz); ^{13}C NMR (75MHz, CDCl$_3$) δ = 13.83, 14.09, 22.62, 26.91, 28.02, 29.03, 29.10, 29.71, 31.79, 50.76, 55.22, 60.26, 69.81, 126.80, 126.84, 126.93, 127.05, 127.21, 127.63, 127.86, 128.30, 128.37, 136.51, 143.38, 143.68, 169.44; IR (thin film) (cm^{-1}) 3028, 2926, 2855, 1743, 1454, 1147, 743, 700; MS (EI) m/z (% rel intensity) 470 (M+H) (0.04), 396 (1), 303 (26), 302 (100), 167 (24), 107 (31), 91 (24), 79 (15); HRMS calcd for $C_{32}H_{40}NO_2^+$ (M+H) m/z 470.3053, meas 470.3050.



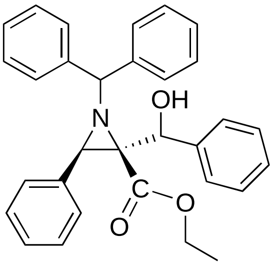
Cis-1-(N-1,1-diphenylmethyl)-2-allyl-2-carboxyethyl-3-phenyl aziridine **(5c):** R_f=0.43 (9:1 hexanes: EtOAc), oil. Yield 61 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, 3 H, *J* = 7 Hz), 2.58 (dd, 1 H, *J* = 10.0, 5.4 Hz), 2.92 (dd, 1 H, *J* = 8.3, 6.8 Hz), 3.03 (s, 1 H), 3.8-4.0 (m, 2 H), 4.60 (s, 1 H), 4.88 (dd, 1 H, *J* = 9.0, 1.0 Hz), 5.00 (dd, 1 H, *J* = 16.1, 1.0 Hz), 5.35-5.45 (m, 1 H), 7.12-7.38 (m, 11 H), 7.51 (d, 2 H, *J* = 8.3 Hz), 7.78 (d, 2 H, *J* = 7.6 Hz); ^{13}C NMR (75MHz, $CDCl_3$) δ = 13.85, 32.28, 50.87, 54.21, 60.37, 70,16, 117.47, 126.92, 126.95, 127.16, 127.24, 127.31, 127.66, 127.97, 128.38, 128.42, 134.26, 136.31, 143.29, 143.37, 169.03; IR (thin film) (cm^{-1}) 3063, 3028, 2980, 1742, 1495, 1125, 1146, 743, 698; MS (EI) m/z (% rel intensity) 230 (70), 167 (31), 131 (100), 91 (24), 77 (8); HRMS (FAB) calcd for $C_{27}H_{28}NO_2^+$ (M+H) m/z 398.2114, meas 398.2115.



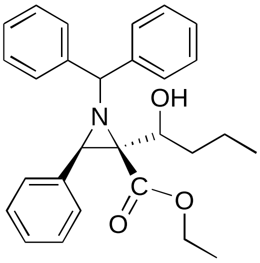
Cis-1-(N-1,1-diphenylmethyl)-2-benzyl-2-carboxyethyl -3-phenyl aziridine **(5d):** R_f=0.35 (9:1 hexanes: EtOAc), oil. Yield 33 %. ^{1}H NMR (500MHz, $CDCl_3$) δ = 0.95 (t, 3 H, *J* = 7 Hz), 3.1 (s, 1 H), 3.26 (d, 1 H, J = 15.7 Hz), 3.34 (d, 1 H, J = 15.7 Hz), 3.82 (m, 2 H), 4.68 (s, 1 H), 7.0-7.8 (m, 20 H); ^{13}C NMR (125MHz, $CDCl_3$) δ = 13.69, 33.39, 51.20, 54.94, 60.47, 70.11, 126.31, 126.92, 127.05, 127.12, 127.23, 127.61, 127.96, 128.04, 128.37, 129.33, 129.28, 136.25, 138.55, 143.15, 143.27, 169.63, (one aryl C not located); IR (thin film) (cm^{-1}) 3063, 3029, 2980, 1742, 1495, 1455, 1142, 745, 698; MS (EI) m/z (% rel intensity) 447 (M$^+$) (0.04), 386 (1), 280 (100), 206 (18), 167 (29), 165 (19), 91 (61); HRMS calcd for $C_{31}H_{28}NO_2^+$ (M-H) m/z 446.2115, meas 446.2092.



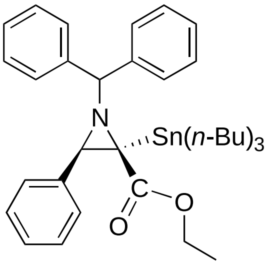
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-methoxymethyl-3-phenyl aziridine **(5e):** R_f=0.23 (9:1 hexanes: EtOAc). Yield 63 %. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, 3 H, *J* = 7.0 Hz), 3.29 (s, 3 H), 3.38 (s, 1 H), 3.95 (m, 4 H), 4.68 (s, 1 H), 7.1-7.4 (m, 11 H), 7.52 (d, 2 H, *J* = 7.7 Hz), 7.76 (d, 2 H, *J* = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.79, 48.03, 53.95, 58.36, 60.75, 68.27, 69.02, 126.75, 127.10, 127.22, 127.39, 127.68, 127.90, 128.27, 128.39, 135.75, 143.46, 168.65; IR (thin film) (cm^{-1}) 3063, 3029, 2982, 2930, 1746, 1719, 1495, 1453, 1152, 700; MS (EI) m/z (% rel intensity) 402 (M+H) (0.1), 306 (8), 234 (100), 167 (40), 131 (18), 91 (28), 77.0 (23), 45 (29); HRMS (FAB) calcd for $C_{26}H_{27}NO_3^+$ (M^+) m/z 401.1991, meas 401.1948.



Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-(hydroxy-phenyl-methyl)-3-phenyl aziridine **(5f):** R_f = 0.4 and 0.25 (9:1 hexanes: EtOAc). Yield 95 %. A mixture of diastereomers were produced in a ratio of 0.72 : 1..0 which could be readily separated. The following spectral data was taken on the major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.75 (t, 3 H, *J* = 7 Hz), 2.82 (d, 1 H, *J* = 9.6 Hz), 3.64-3.76 (m, 1 H), 3.84-4.00 (m, 1 H), 4.09 (s, 1 H), 4.49 (d, 1 H, *J* = 9.9 Hz), 4.65 (s, 1 H), 7.0-7.75 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.33, 52.41, 56.54, 61.29, 71.16, 71.76, 125.02, 126.81, 127.22, 127.34, 127.46, 127.68, 127.75, 127.87, 127.96, 128.24, 128.33, 128.45, 135.20, 141.24, 142.66, 142.82, 167.68; IR (thin film) (cm^{-1}) 3578, 3063, 2982, 1726, 1495, 1453, 1208, 1148, 1028, 700.



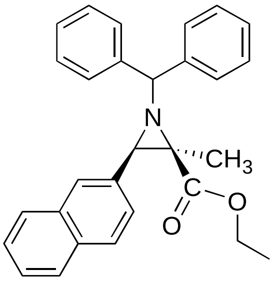
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-(1-hydroxy-butyl)-3-phenyl aziridine **(5g):** R_f=0.28 and 0.16 (9:1Hexanes: EtOAc). Yield 89 % (combined yield of a 1.1 : 1 of diastereomers). The diastereomers were separated on a silica gel column. The following spectral data was collected on the major isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.40 (t, 3 H, *J* = 7 Hz), 0.95-1.50 (m, 7 H), 2.40 (bs, 1 H, OH), 3.18 (d, 1 H, *J* = 9.6 Hz), 3.9-4.2 (m, 3 H), 4.62 (s, 1 H), 7.0-7.4 (m, 11 H), 7.55 (d, 2H, *J* = 8 Hz), 7.64 (d, 2 H, *J* = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.01, 13.86, 18.66, 35.52, 51.85, 54.46, 61.44, 70.68, 72.44, 127.15, 127.24, 127.37, 127.64, 127.75, 127.83, 127.92, 128.17, 128.42, 135.24, 142.67, 143.16, 168.52; IR (thin film) (cm^{-1}) 3588, 3030, 2961, 2872, 1726, 1454, 1205, 1153, 1030, 700; MS (EI) m/z (% rel intensity) 430 (M+H) (0.04), 386 (1), 356 (3), 262 (100), 167 (38), 162 (23), 91 (39), 71 (13); HRMS calcd for $C_{28}H_{32}NO_3^+$ (M+H) m/z 430.2376, meas 430.2375



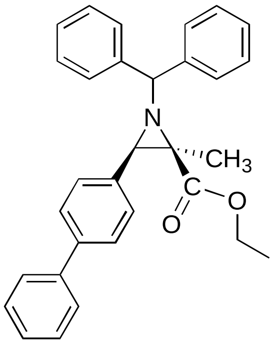
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-tributylstannanyl-3-phenyl aziridine **(5h):** R_f=0.5 (9:1 hexanes: EtOAc), oil. Yield 91 %. This product was isolated from the silica gel column with hexanes/ethyl acetate as eluent as an inseparable 4 : 1 mixture of isomers. The isomers could be separated on an HPLC silica column with 9 : 1 mixtures of hexanes and acetonitrile. Samples of each isomer could be obtained in pure form by silica gel column chromatography (97 : 3 mixture of hexanes and acetonitrile): R_f = 0.24 (minor), R_f = 0.16 (major) (95 : 5 hexanes and acetonitrile). The following spectral data was collected on pure samples of each isomer. The minor isomer was assigned as an O-alkylated product on the basis of carbon-tin coupling constants.

Spectral data for **5h**: (major) ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.70-1.02 (m, 18 H), 1.17-1.30 (m, 6 H), 1.31-1.48 (6H, m), 3.12 (s+d, 1 H, $^3J_{H\text{-}Sn}$ = 22.2 Hz), 3.68-4.00 (m, 2 H), 4.03 (s, 1H), 7.07-7.50 (m, 13 H), 7.78 (d, 2 H, J = 7.50 Hz); ^{13}C NMR (75 MHz) δ = 12.29 (s+d+d, $^1J_{C\text{-}Sn}$ = 331.8, 315.5 Hz), 13.62, 13.98, 27.35 (s+d, $^3J_{C\text{-}Sn}$ = 63.9 Hz), 28.87 (s+d, $^2J_{C\text{-}Sn}$ = 19.00 Hz), 50.07, 51.34 (s+d+d, $^1J_{C\text{-}Sn}$ = 246, 236 Hz),, 60.02, 75.85 (s+d, $J_{C\text{-}Sn}$ = 28.8 Hz), 126.99, 127.07, 127.23, 127.45, 127.63, 127.91, 127.97, 128.50, 128.59, 137.50, 142.81, 143.53, 172.14 (s+d, $^2J_{C\text{-}Sn}$ = 40 Hz); IR (Neat) (cm^{-1}) 3063, 3028, 2957, 2926, 2872, 28.53, 1726, 1495, 1454, 1300, 1297, 1192, 1076, 1030, 742, 698; MS (FAB) m/z (% rel intensity) 648 (M+H)$^+$ (6.5, ^{119}Sn), 590 (6.4, ^{119}Sn), 588 (5, ^{117}Sn), 480 (8), 478 (6), 430 (3), 423 (2.5). 395 (2), 356 (13), 291 (13), 289 (10), 235 (16), 233 (13), 179 (35), 177 (30), 167 (100).

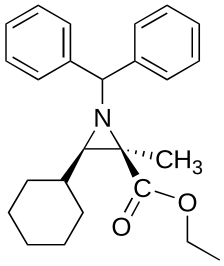
Spectral data for **5h**: (minor) ^{1}H NMR (300 MHz, CDCl$_3$) δ = 0.44-0.61 (m, 6H), 0.74-0.82 (m, 9 H, t, J = 6.60 Hz), 0.99-1.04 (3H, t, J = 7.20Hz), 1.08-1.28 (12H, m), 3.67 (s+d, 1H, $^5J_{H\text{-}Sn}$ = 8 Hz), 3.87-4.02 (m, 2 H), 5.09 (s, 1 H), 7.11-7.19 (m, 5 H), 7.21-7.29 (m, 7 H), 7.44-7.54 (t, 3H, J = 7.8 Hz); ^{13}C NMR (75 MHz) δ = 10.80 (s+d+d, $^1J_{C\text{-}Sn}$ = 338.6, 323.1 Hz), 13.62, 13.96, 27.39 (s+d, $^3J_{C\text{-}Sn}$ = 63.9 Hz), 28.84 (s+d, $^2J_{C\text{-}Sn}$ = 18.1 Hz), 47.71, 52.53 (s+d, $^3J_{C\text{-}Sn}$ = 7 Hz), 60.89, 70.03, 126.70, 127.03, 127.11, 127.46, 127.64, 127.89, 128.11, 128.14, 128.40, 139.05, 143.57, 144.07, 172.96 (s+d, $^2J_{C\text{-}Sn}$ = 41 Hz); IR (Neat) (cm^{-1}) 3028, 2955, 2924, 2870, 28.03, 1707, 1495, 1452, 1329, 1317, 1213, 1182, 1098, 1028, 754, 700; MS (FAB) m/z (% rel intensity) 648 (M+H)$^+$ (1.5, ^{119}Sn), 590 (27, ^{119}Sn), 589 (12), 588 (20, ^{117}Sn), 587 (10), 586 (11), 544 (0.7), 480 (2.3), 479 (1), 478 (1.8), 476 (2.8), 430 (1.3), 423 (2). 395(1.4), 393 (1.1), 356 (9), 291 (8), 257 (6), 235 (11), 233 (9), 167 (100).



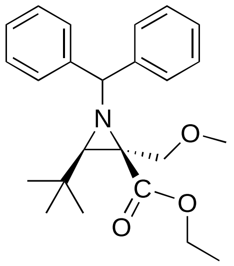
Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-methyl-3-napthyl aziridine **(5i):** R$_f$=0.31 (9:1 hexanes: EtOAc). Yield 70 %. ^{1}H NMR (300 MHz, CDCl$_3$) δ = 0.88 (t, 3 H, *J* = 7.1 Hz), 1.64 (s, 3 H), 3.17 (s, 1 H), 3.55-3.95 (m, 2 H), 4.60 (s, 1 H), 7.12-7.84 (m, 17 H); ^{13}C NMR (75 MHz, CDCl$_3$) δ = 13.76, 14.08, 50.92, 53.22, 60.78, 70.83, 125.65, 125.81, 125.97, 126.46, 127.14, 127.23, 127.43, 127.54, 127.78, 128.05, 128.13, 128.65, 128.67, 132.99, 133.25, 134.19, 143.57, 143.87, 170.36; IR (thin film) (cm^{-1}) 3061, 2980(s), 1740(s), 1453(s), 1148(s), 703(s); MS (EI) m/z (% rel intensity) 422 (M+H) (0.14), 421 (M$^+$) (0.4), 348 (1), 254 (100), 181 (75), 180 (81), 167 (39), 165 (29), 152 (20), 139 (38), 129 (32); HRMS: calcd for $C_{29}H_{27}NO_2^+$ (M$^+$) m/z 421.2042, meas 421.2030.



Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-2-methyl-3-(4-biphenyl) aziridine **(5j):** R_f=0.32 (9:1 hexanes: EtOAc). Yield 64 %. Solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.95 (t, 3 H, *J* = 7.1 Hz), 1.60 (s, 3 H), 3.09 (s, 1 H), 3.95 (m, 2 H), 4.58 (s, 1 H), 7.1-7.6 (m, 17 H), 7.75 (d, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.36, 13.85, 50.35, 52.47, 60.56, 70.49, 126.35, 126.85, 126.91, 127.03, 127.29, 127.72, 127.84, 128.42, 128.64, 135.40, 139.75, 140.94, 143.29, 143.61, 170.09 (2 aryl C's not located); IR (thin film) (cm^{-1}) 3061, 3029 (s), 1742 (s), 1489 (s), 1150 (s); MS m/z (% rel intensity) 447 (M^+) (0.03), 374 (0.7), 281 (100), 206 (32), 165 (35), 155 (12), 76 (7); HRMS (FAB) calcd for $C_{31}H_{30}NO_2^+$ (M+H) m/z 448.2271, meas 448.2275.

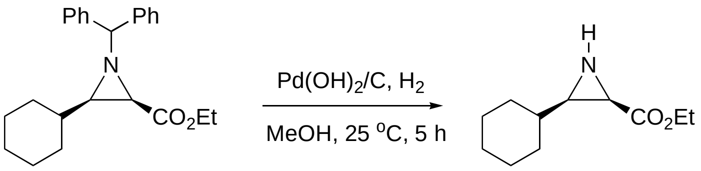


Cis-1-(N-1,1-diphenylmethyl)-2-carboxyethyl-3-cyclohexyl-2-methyl aziridine **(5l):** R_f=0.37 (15:1 hexanes: EtOAc). Yield 70 %. Waxy solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.84-1.16 (m, 6 H), 1.30 (t, 3 H, *J* = 7 Hz), 1.40 (s, 3 H), 1.48-1.68 (m, 6 H), 4.14-4.37 (m, 2 H), 4.19 (s, 1 H), 7.16-7.38 (m, 8 H), 7.61 (d, 2 H, *J* = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.53, 14.32, 25.44, 25.61, 26.15, 30.15, 30.37, 37.77, 46.27, 57.08, 60.72, 70.87, 126.59, 126.92, 127.31, 128.21, 128.79, 143.64, 171.82; IR (thin film) (cm^{-1}) 2980, 2930, 2851, 1742, 1719, 1451, 1146, 702; MS (EI) m/z (% rel intensity) 378 (M+H) (0.06), 377 (M^+) (0.03), 304 (1), 294 (1), 211 (15), 210 (100), 167 (40), 116 (57), 95 (53), 88 (19), 67 (22); HRMS calcd for $C_{25}H_{32}NO_2^+$ (M+H) m/z 378.2428, meas 378.2452.



Cis-1-(N-1,1-diphenylmethyl)-3-(*tert*-butyl)-2-carboxyethyl-2-methoxymethyl-aziridine **(5m):** R_f = 0.31 (15:1 hexanes: EtOAc). Yield 66 %. Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.64 (s, 9 H), 1.37 (t, 3 H, *J* = 7.0 Hz), 1.85 (s, 1 H), 3.18 (s, m3 H), 3.57 (d, 1 H, *J* = 11.3 Hz), 3.91 (d, 1 H, *J* = 11.5 Hz), 4.22 (m, 2 H), 4.34 (s, 1 H), 7.16-7.36 (m, 6 H), 7.44 (d, 2 H, *J* = 7.7 Hz), 7.80 (d, 2 H, *J* = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.97, 26.91, 31.39, 49.97, 56.25, 58.28, 60.76, 69.89, 70.21, 126.43, 126.97, 127.17, 127.87, 128.20, 128.57, 1432.50, 144.29, 170.49; IR (thin film) (cm^{-1}) 2953, 2870, 1747, 1719, 1453, 1152, 1115, 702; MS (EI) m/z (% rel intensity) 382 (M+H) (0.08), 381 (M^+) (0.03), 380 (M^+-H) (0.09), 308 (2), 292 (2), 214 (100), 167 (86), 165 (62), 152 (35), 108 (19), 98 (13), 69 (12); HRMS calcd for $C_{24}H_{32}NO_3^+$ (M+H) m/z 382.2377, meas 382.2383.

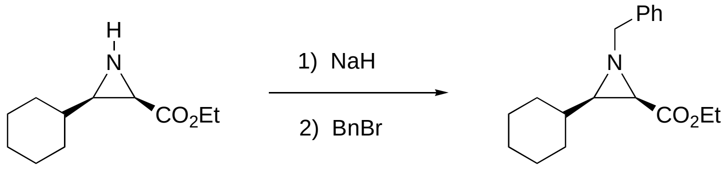
The synthesis and attempted alkylation of aziridine 9.



23

24 95 %

Synthesis of aziridine ***24***: To an oven-dried 500 mL round bottom flask filled with argon was added aziridine **23**[2] (2.50 g, 6.89 mmol) and 800 mg $Pd(OH)_2/C$, followed by 250 mL of MeOH. The flask was briefly exposed to high-vacuum and then back-filled with hydrogen. This was repeated three times and then a hydrogen gas ballon was attached to the flask and the suspension was stirred for five hours at room temperature. After the reaction finished, the solution was filtered to remove the Pd catalyst and concentrated *in vacuo*. Silica gel chromatography (50:50 Et_2O/hexane to 100 % Et_2O) afforded **24** (1.291 g, 95 % yield) as white solid. Spectral data of **24**: $[\alpha]_D$ = -45.4 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.77 (br, 1 H), 0.99-1.20 (m, 6 H), 1.13 (t, 3 H, J = 7.1 Hz), 1.30-1.82 (m, 6 H), 2.48 (d, 1 H, J = 5.8 Hz), 4.07 (q, 2 H, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.20, 25.44, 26.05, 30.89, 31.67, 34.31, 36.96, 44.02, 61.12, 171.04 (one carbon not located); (75 MHz, C_6D_6) δ 14.20, 25.87, 26.44, 31.38, 31.97, 34.45, 37.33, 44.45, 60.87, 171.30 (one carbon not located); IR (thin film) 3165w, 2924vs, 2849s, 1730vs, 1194s, 1180s cm^{-1}; mass spectrum *m/z* (% rel intensity) 197 M^+ (4), 168 (32), 124 (100), 95 (84). Anal calcd for $C_{11}H_{19}NO_2$: C, 66.97; H, 9.71; N, 7.10. Found: C, 66.98; H, 9.30; N, 7.08. White solid, mp 59-61 °C, R_f = 0.16 (1:4 EtOAc/hexane)



24

9 85 %

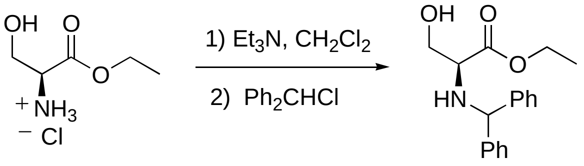
Synthesis of N-benzyl aziridine **9**: To an oven-dried 250mL flask filled with argon was added aziridine **24** (1.291 g, 6.55 mmol), 80 mL dry THF. The solution was stirred at 0^{o}C and NaH (943 mg of 60% dispersion, 23.58 mmol) was added. The mixture was stirred at 0^{o}C for 1 hour, then benzyl bromide (4.48 g, 26.19 mmol) and tetrabutyl ammonium iodide (4.94 g, 13.10 mmol) was added. The mixture was stirred at 0^{o}C for 15 minutes, then warmed up to room temperature and stirred for 48 hours. The reaction was quenched by adding 1 mL H_2O via syringe dropwisely, followed by addition of 50 mL saturated NH_4Cl solution. The mixture was loaded to separatory funnel, and extracted with 3 × 60 mL Et_2O. The combined organic layer was washed with brine, dried over $MgSO_4$, concentrated *in vacuo*. Silica gel chromatography (1:10 EtOAc/hexane) afforded **9** (1.605 g, 85% yield) as white solid. Spectral data of **9**: $[\alpha]_D$ = 47.3 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (dq, 2H, J = 11, 3 Hz), 1.04-1.71 (m, 10H), 1.22 (t, 3H, J = 7 Hz), 2.10 (d, 2H, J = 7 Hz), 3.51 (d, 2H, J = 4 Hz), 4.17 (m, 2H), 7.23-7.29 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.21, 25.38, 25.49, 26.11, 30.04, 31.30, 36.19, 42.43, 51.94, 60.73, 64.22, 127.18, 128.22, 128.33, 137.71, 169.84;; IR (thin film, cm^{-1}) 2926 vs, 2851 s, 1745 vs, 1720 s, 1178 vs; Mass spectrum *m/z* (% rel intensity) 287 M^{+} (7), 286 (7), 214 (51), 91 (100); Anal calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.63; H, 9.11; N, 4.75; White solid, mp 39-42 ^{o}C, Rf = 0.27 (1:9 EtOAc/hexane).

9

10 3 %

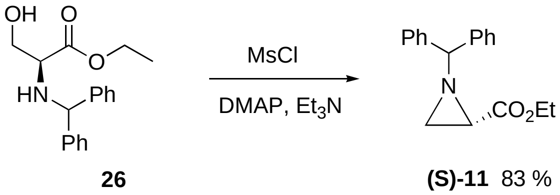
Attempted alkylation of ***9*****:** To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (449 mg, 4.5 mmol), followed by 25 mL DME. The solution was cooled to -78^{o} C, then *n*-BuLi (2.8 mL, 4.5 mmol) was added via syringe. The LDA solution was stirred at -78^{o} C for 5 min, then warmed up to 0^{o} C and stirred for 15 min. After cooling to -78^{o} C, a solution of pre-cooled (-78° C) aziridine **9** (800 mg, 2.7 mmol) in 15 mL DME and 8 mL Et_2O was transferred via cannula to the flask containing LDA gaving a light brown solution. After stirring at -78^{o} C for 30 min, iodomethane (950 mg, 6.7 mmol) was added via syringe. The solution was then stirred at -78^{o} C for 1 h, then allowed to warm up to room temperature slowly over 2h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 mixutre of CH2Cl2/hexane) afforded **10** (30 mg, 3% yield) as the only product that was mobile on silica gel. Spectral data of **10**: Colorless needle, mp = 119-120^o C (CH_2Cl_2/hexane); R_f = 0.26 (1:15 EtOAc/hexane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14-1.77 (m, 9 H), 1.23 (t, 3 H, J = 6.9 Hz), 2.43 (tt, 1 H, J = 1.6 Hz, J < 1 Hz), 4.18 (q, 2 H, J = 6.9 Hz), 5.3 (s, 2 H), 5.7 (s, 1H), 6.88 (d, 2 H, J = 7.5 Hz), 7.19-7.29 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.26, 25.82, 26.35, 33.26, 35.57, 47.87, 59.62, 77.20, 94.04, 104.72, 125.37, 126.86, 128.51, 139.12, 146.83 (one carbon not located); IR (thin film, cm^{-1}) 2928 vs, 1647vs, 1559vs; Mass spectrum *m/z* (% rel intensity) 327 M^+ (100), 281 (46), 91 (38). Anal calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 72.99; H, 7.48; N, 4.49. Crystallization of **10** was achieved by dissolving 30 mg of **10** in ~0.2 mL of CH_2Cl_2 and transferred to a NMR tube and then the CH_2Cl_2 solution was covered with 1 mL of hexane. After one week needle-like crystal was grown in the tube and an X-ray crystal structure was obtained.

Synthesis and Alkylaltion of aziridine 11.[2]

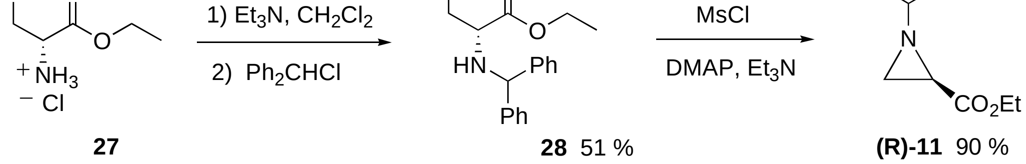


25 **26** 52 %

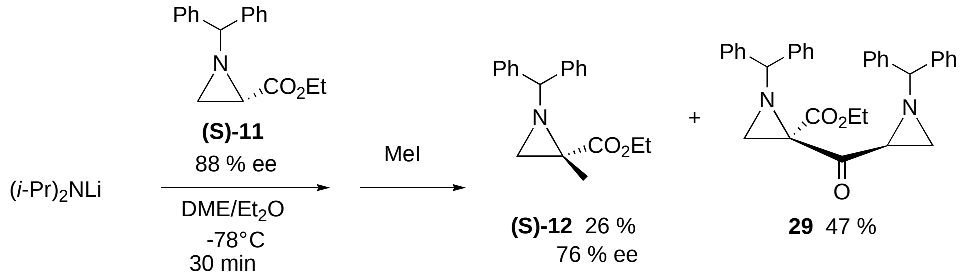
*Synthesis of N-benzhydryl L-serine ester **26**:* To a 25 mL Schlenk flask filled with argon was added L-serine ethyl ester hydrochloride **25** (1.2 g, 7.1 mmol) (purchased from Aldrich), followed by 12 mL $CHCl_3$. The suspension was stirred at 0^o C. Triethylamine (1.72 g, 16.8 mmol) was added via syringe. Then benzhydryl chloride (1.01 g, 4.86 mmol) was added via syringe drop-wise over 10 minutes. The flask was then sealed under argon and heated to reflux for 3 days. After cooling room temperature, the reaction mixture was quenched with saturated aqueous ammonium chloride solution and extracted with 3 × 30 mL CH_2Cl_2. The organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:3 EtOAc/hexane) afforded **26** (756 mg, 52 % yield) as a colorless oil. Spectral data of **26**: Colorless oil, R_f = 0.24 (1:3 EtOAc/hexane), $[\alpha]_D$ = -44.1 (*c* = 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, 3 H, J = 7.1 Hz), 2.65 (s, 2 H, br), 3.39 (m, 1 H), 3.63-3.77 (m, 2 H), 4.19 (q, 2 H, J = 7.1 Hz), 4.94 (s, 1 H), 7.22-7.43 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.15, 60.40, 61.13, 63.12, 65.23, 127.23, 127.29, 127.50, 128.53, 142.21, 143.53, 173.15 (two aryl carbon not located); IR (thin film, cm^{-1}) 3420vs, 1725vs, 1190vs; mass spectrum *m/z* (% rel intensity) 300 $(M+1)^+$ (<1), 226 (17), 182 (80), 167 (100). Anal calcd for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.10; H, 7.04; N, 4.77.



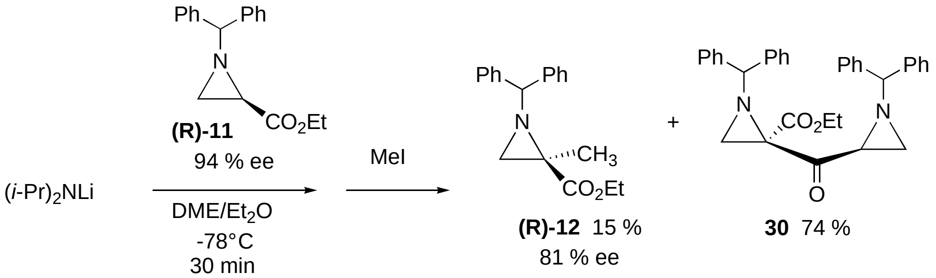
Synthesis of (2S)-aziridine ***11***: To a schlenk flask filled with argon was added N-benzhydryl serine ester **26** (756 mg, 2.53 mmol) and 40 mL chloroform, followed by 4-(dimethylamino)pyridine (32 mg, 0.27 mmol) and triethyl amine (614 mg, 6.07 mmol). The solution was cooled to 0^o C. Methanesulfonic anhydride (681 mg, 3.79 mmol) in 5 mL chloroform was added via syringe drop-wise over 30 minutes. The solution was stirred at 0^o C for 1 h, then allowed to reach room temperature and finally heated to reflux for 44 h. The solution was allowed to cool to room temperature and then quenched with water. The mixture was extracted with 3 × 50 mL CH_2Cl_2 and the combined organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:9 EtOAc/hexane) afforded **(S)-11** (588 mg, 83 % yield) as a white solid. Spectral data of (S)-**11**: White solid, mp = 93-95 °C, R_f = 0.24 (1:9 EtOAc/hexane), ^1H NMR (300 MHz, $CDCl_3$) δ 1.23 (t, 3 H, J = 7.1 Hz), 1.82 (d, 1 H, J = 6.3 Hz), 2.23 (dd, 1 H, J = 6.3, 3.0 Hz), 2.29 (d, 1 H, J = 2.8 Hz), 3.6 (s, 1 H), 4.19 (q, 2 H, J = 7.1 Hz), 7.20-7.42 (m, 10 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.12, 34.73, 38.26, 60.97, 77.76, 127.07, 127.16, 127.36, 127.60, 128.41, 142.41, 142.44, 170.52 (one aryl carbon not located); IR (thin film, cm^{-1}) 1728vs, 1186vs; mass spectrum *m/z* (% rel intensity) 281 M^+ (1), 280 (11), 252 (38), 167 (100), 165 (70). Anal calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.92; H, 6.61; N, 4.60. The optical purity by HPLC of aziridine **(S)-11** was found to be 88 % by using a Chiralpak AD column with the following conditions: 221nm, 0.5 mL/min, 99.6:0.4 mixture of hexane and 2-propanol. (t_R = 31.44 min for major isomer and t_R = 37.48 for minor isomer): optical rotation $[\alpha]_D$ = -84.5 (*c* = 1.0, $CHCl_3$).



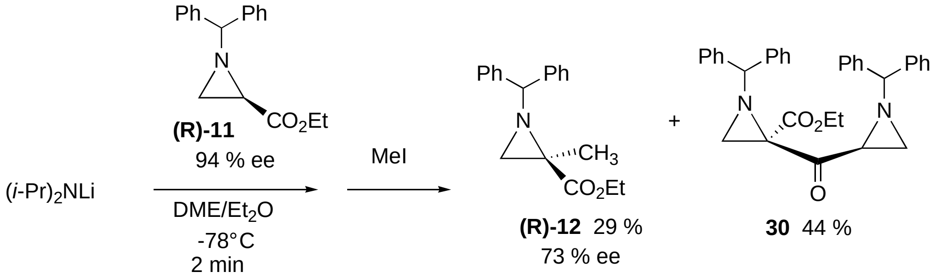
Synthesis of (2-R)-aziridine ***11***: Aziridine (R)**-11** was prepared from D-serine ethyl ester hydrochloride **27** (purchased from Senn Chemicals) according to the procedure used for the synthesis of aziridine **(S)-11**. The optical purity by HPLC of aziridine **(R)-11** was found to be 94 % ee by using a Chiralpak AD column with the following conditions: 221nm, 0.5 mL/min, 99.6:0.4 mixture of hexane and 2-propanol. (t_R = 31.44 min for minor isomer and t_R = 37.48 for major isomer). Optical rotation: $[\alpha]_D$ = +95.5 (*c* = 1.0, $CHCl_3$).



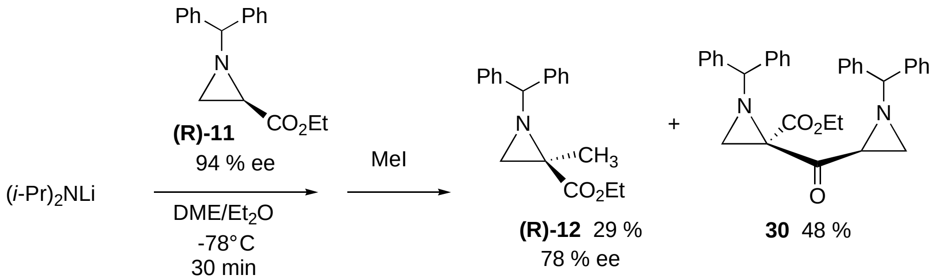
*Alkylation of aziridine **(S)-11** with methyl iodide:* To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (627 mg, 6.2 mmol), followed by 33 mL DME. The solution was cooled to -78° C, then *n*-BuLi (3.85 mL, 6.2 mmol) was added via syringe. The LDA solution was stirred at -78° C for 5 min, then warmed up to 0° C and stirred for 15 min then cooled down to -78° C. A solution of aziridine **(S)-11** (847 mg, 3.03 mmol, 88 % ee) in 22 mL DME and 11 mL Et_2O was also cooled to -78° C and transferred via cannula to the flask containing LDA gaving a light brown solution. After stirring at -78° C for 30 min, iodomethane (1.31 g, 9.2 mmol) was added via syringe. The solution was then stirred at -78° C for 1 h and then allowed to warm up to room temperature slowly over 2 h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and then the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 to 1:5 EtOAc/hexane) afforded **(S)-12** (200 mg, 26 % yield) as a colorless oil and **29** (367 mg, 47 % yield) as a white solid. Spectral data of **(S)-12**: Colorless oil, R_f = 0.29 (1:15 EtOAc/hexane), $[\alpha]_D$ = -35.4 (*c* = 2.13, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) (2:1 ratio of N-invertomers) major N-invertomer: δ 0.93 (t, 3 H, J = 6.9 Hz), 1.52 (s, 3 H), 2.01 (s, 1 H), 2.44 (s, 1 H), 3.90 (m, 2 H), 4.66 (s, 1 H), 7.19-7.50 (m, 10 H); minor N-invertomer: ^1H NMR (300 MHz, $CDCl_3$) 1.29 (t, 3 H, J = 6.9 Hz), 1.42 (s, 3 H), 4.66 (m, 2 H), other proton signals were obscured by major inveromer: ^{13}C NMR of major invertomer (75 MHz, $CDCl_3$) δ 13.62, 20.33, 39.59, 41.26, 60.90, 69.17, 126.70, 127.00, 127.10, 127.67, 128.04, 128.33, 143.20, 143.61, 170.29; Upon heating the sample d_8-toluene to 110°C, the two invertomers emerged: ^1H NMR 300 Mhz (d_8-toluene) δ 0.83 (t, J = 6.8 Hz), 1.38 (s, 3 H), 1.60 (s, 1 H), 2.32 (s, 1 H), 3.81 (q, 2 H, J = 6.8 Hz), 7.05-7.44 (m, 10 H); IR (thin film, cm^{-1}) 2980 s, 1720 vs, 1176 vs; mass spectrum *m/z* (% rel intensity) 295 M^+ (2), 294 (11), 266 (32), 180 (55), 167 (100). Anal calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found:C, 77.11; H, 7.21; N, 4.77. The optical purity by HPLC of aziridine **(S)-12** was found to be 76 % by using a Chiracel OD-H column with the following conditions: 254 nm, 0.6 mL/min, 99.5:0.5 mixture of hexane and 2-propanol. (t_R = 5.52 min for major isomer and t_R = 6.63 for minor isomer). Spectral data of **29**: mp = 52-56 °C (decomposed), R_f = 0.28 (1:5 EtOAc/Hexane), $[\alpha]_D$ = 17.9 (*c* = 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, 3 H, J = 7.3 Hz), 1.88 (d, 1 H, J = 6.3 Hz), 1.98 (s, 1 H), 2.41 (d, 1 H), 2.42 (s, 1 H), 2.82 (dd, 1 H, J = 6.3, 2.9 Hz), 3.64 (s, 1 H), 3.99 (m, 2 H), 4.51 (s, 1 H), 7.22-7.50 (m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.51, 37.60, 39.01, 40.41, 51.84, 61.73, 69.33, 78.14, 127.19, 127.21, 127.28, 127.40, 127.42, 128.28, 128.34, 128.36, 128.44, 142.17, 142.40, 142.55, 142.60, 165.88, 199.73 (three aryl carbon not located); IR (thin film, cm^{-1}): 3028 s, 1720 vs; mass spectrum *m/z* (% rel intensity) 516 M+ (<1), 349 (8), 248 (31), 167 (100), 165 (100), HRMS calcd for $C_{34}H_{33}N_2O_3$ (M+H) m/z 517.2491, meas 517.2495(FAB). Anal calcd for $C_{34}H_{32}N_2O_3$: C, 79.04; H, 6.24; N, 5.42. Found: C, 78.82; H, 6.10; N, 5.38;



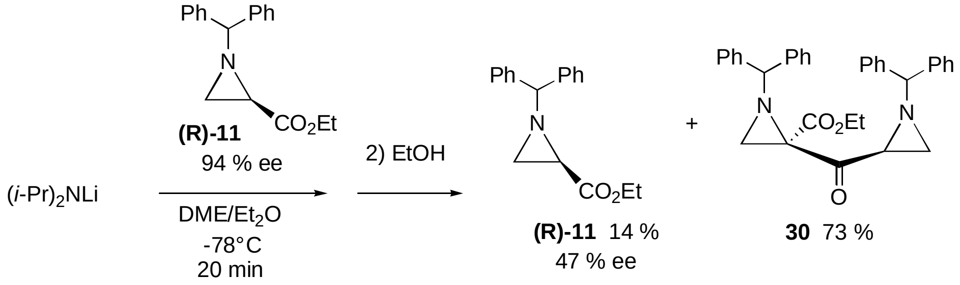
*Alkylation of aziridine **(R)-11** with methyl iodide***:** To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (314 mg, 3.1 mmol), followed by 16 mL DME. The solution was cooled to -78° C, then *n*-BuLi (1.93 mL, 3.1 mmol) was added via syringe. The LDA solution was stirred at -78° C for 5 min, then warmed up to 0° C and stirred for 15 min and finally cooled to -78° C. The solution of aziridine **(R)-11** (423 mg, 1.51 mmol) in 11 mL DME and 5 mL Et_2O was also cooled to -78° C and transferred via cannula to the flask containing LDA giving a light brown solution. After stirring at -78° C for 30 min, iodomethane (642 mg, 4.6 mmol) was added via syringe. The solution was then stirred at -78° C for 1 h, then allowed to warm up to room temperature slowly over 2 h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 to 1:5 EtOAc/hexane) afforded (R**)-12** (65 mg, 15 % yield) as colorless oil and **30** (290 mg, 74 % yield) as white solid. The optical purity by HPLC of aziridine **(R)-12** was found to be 81% with the same method as described above for **(S)-12**.



Alkylation of aziridine ***(R)-11*** *with methyl iodide (short enolate formation time).* To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (314 mg, 3.1 mmol), followed by 16 mL DME. The solution was cooled to -78° C, then *n*-BuLi (1.93 mL, 3.1 mmol) was added via syringe. The LDA solution was stirred at -78° C for 5 min, then warmed up to 0° C and stirred for 15 min finally cooled to -78° C. The solution of aziridine (**R)-11** (423 mg, 1.51 mmol) in 11 mL DME and 5 mL Et_2O was also cooled to -78° C and transferred via cannula to the flask containing LDA gaving a light brown solution. After stirring at -78° C for 2 min, iodomethane (642 mg, 4.6 mmol) was added via syringe. The solution was then stirred at -78° C for 1 h, then allowed to warm up to room temperature slowly over 2 h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 to 1:5 EtOAc/hexane) afforded (**R)-12** (128 mg, 29 % yield) as a colorless oil and **30** (177 mg, 44 % yield) as a white solid. The optical purity of (**R)-12** was found to be 73% ee by HPLC by the method described above for **(S)-12**.

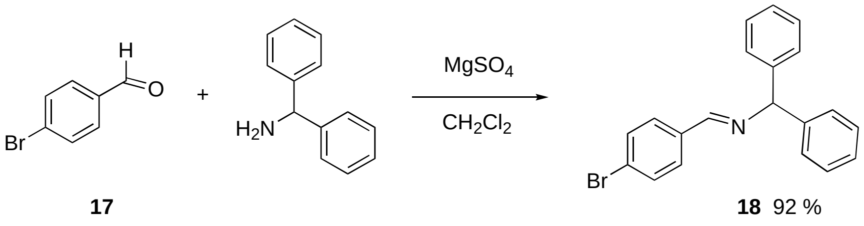


Alkylation of aziridine ***(R)-11*** *with methyl iodide (slow addition of aziridine* ***(R)-11).*** To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (314 mg, 3.1 mmol), followed by 16 mL DME. The solution was cooled to -78° C, then *n*-BuLi (1.93 mL, 3.1 mmol) was added via syringe. The LDA solution was stirred at -78° C for 5 min, then warmed up to 0° C and stirred for 15 min then cooled down to -78° C. The solution of aziridine (**R)-11** (423 mg, 1.51 mmol) in 11 mL DME and 5 mL Et_2O was added via syringe pump through a -78° C cooling coil to the flask containing LDA over a 30 minute period gaving a light brown solution. After the addition was finished the enolate solution was stirred at -78° C for 30 min and then iodomethane (642 mg, 4.6 mmol) was added via syringe. The solution was then stirred at -78° C for 1 h, then allowed to warm up to room temperature slowly over 2 h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 to 1:5 EtOAc/hexane) afforded (**R)-12** (130 mg, 29 % yield) as a colorless oil and **30** (188 mg, 48 % yield) as a white solid. The optical purity of (**R)-12** was found to be 78 % ee by HPLC by the method described above for **(S)-12**.



*Deprotonation/protonation of aziridine **(R)-11.*** To a flame-dried 100 mL flask cooled under argon was added diisopropylamine (314 mg, 3.1 mmol), followed by 16 mL DME. The solution was cooled to -78° C, then *n*-BuLi (1.93 mL, 3.1 mmol) was added via syringe. The LDA solution was stirred at -78° C for 5 min, then warmed up to 0° C and stirred for 15 min then finally cooled to -78° C. A solution of aziridine (**R)-11** (423 mg, 1.51 mmol) in 11 mL DME and 5 mL Et_2O was also cooled to -78° C and transferred via cannula to the flask containing LDA gaving a light brown solution. After stirring at -78° C for 20 min, ethanol (348 mg, 7.55 mmol) was added via syringe. The solution was then stirred at -78° C for 1 h, then allowed to warm up to 0° C slowly over 2 h before quenching with saturated $NaHCO_3$ solution. The mixture was extracted with 3 × 100 mL Et_2O and the combined organic solution was dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (1:15 to 1:5 EtOAc/hexane) afforded (**R)-11** (60 mg, 14 % yield) as a colorless oil and **30** (285 mg, 73 % yield) as a white solid. HPLC analysis of **(R)-11** indicated its optical purity was 47 % ee as described above. Optical rotation of recovered (**R)-11**: $[\alpha]_D = +45.0$ ($c = 1.0$, $CHCl_3$)

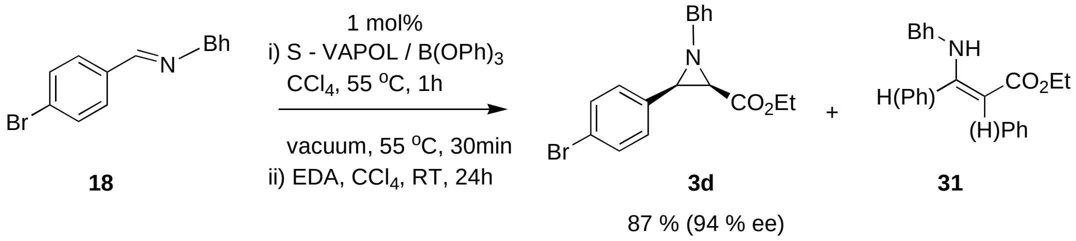
Synthesis of Benzhydryl Imine 18.[1]



To a magnetically stirred solution of diphenylaminomethane (4.575 g, 25 mmol) in dichloromethane (30 mL) was added $MgSO_4$ (4.5 g). After stirring for 10 min, *p*-bromobenzaldehyde **17** (4.625 g, 45 mmol) in dichloromethane (5 mL) was added to the mixture over a 2 minute period. After stirring for 24 h at rt, the reaction mixture was filtered through filter paper and the

$MgSO_4$ was washed with dichloromethane (20 mL). The combined filtrates were concentrated in *vacuo* to yield *p*-bromophenyl benzhydralimine **18** as a colorless solid. Crude product was taken up in a 9:1 mixture of hexanes and dicholormethane (50 mL) and heated on hot plate until all was dissolved. The solution was allowed to cool on the bench top overnight. The crystals were collected and subjected to a second crystallization (50 mL of hexanes and dichloromethane) to give pure crystalline *p*-bromophenyl benzhydralimine (8.02 g, 92 %), which was dried under high vacuum and stored in a dessicator. Spectral data for **18**: ^{1}H NMR (500 MMz, $CDCl_3$) $\delta = 5.23$ (s, 1 H), 7.15-7.35 (m, 10 H), 7.47 (d, 2 H, J = 7 Hz), 7.64 (d, 2 H, J = 7 Hz), 8.28 (s, 1 H).

Catalytic asymmetric aziridination of *p*-bromophenyl benzhydral imine 18 with S-VAPOL catalyst prepared from $B(OPh)_3$.

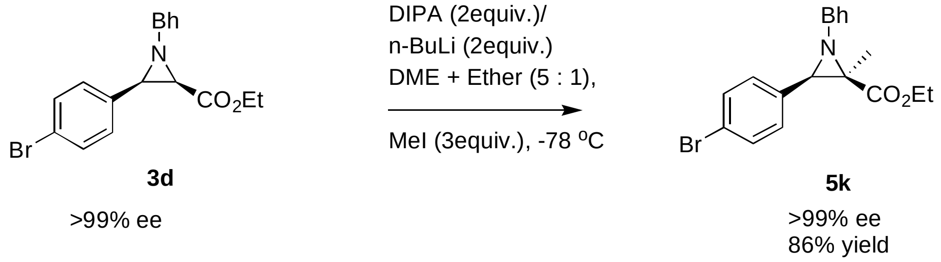


The following procedure for the preparation of the aziridine **3d** is taken from the published method.[3] To a flame-dried 25 mL Schlenk flask equipped with a stir bar and filled with argon was added S-VAPOL (0.054 g, 0.10 mmol), $B(OPh)_3$ (0.087 g, 0.3 mmol) and dry dichloromethane (3 mL). The flask was flushed with argon and closed with a stopper. The flask was placed in a pre-heated oil bath at 55 ^{o}C and the catalyst mixture was stirred for 1 h. The flask was allowed cool to room temperature and then the volatiles were removed under vacuum rt and then under high vacuum (0.5 mm Hg) for 30 min with heating at 55 ^{o}C. The catalyst was dissolved in 2 x 1 mL portions of carbon tetrachloride and transferred by syringe to a solution of *p*-bromophenyl benzhydral imine **18** (0.698 g, 2 mmol) in 2 mL of dichloromethane and the resulting solution was stirred for 10 min. Ethyl diazoacetate (0.23 mL, 2.2 mmol) was then added rapidly. After stirring 5-10 min some bubbling was noticed and then stirring was continued at rt for 24 h. The reaction mixture was diluted with hexanes (3 mL) and the solvents were removed by rotary evaporator to give the crude aziridine **3d** as a solid, which was dried under high vacuum. A ^{1}H NMR spectrum was taken to measure the ratio of diastereomers. The crude product was subjected to column chromatography on silica gel (hexanes/ ethyl acetate 95 : 5) to give 0.68 g of pure *cis*-aziridine **3d** (78 % yield) which was found to be 94 % ee by HPLC by a published method.[3] The spectral data for **3d** match that published for this compound.[3]

The pure *cis*-aziridine (0.68 g) was dissolved in hot hexanes and dichloromethane (75 mL of hexanes and few drops of CH_2Cl_2) and allowed to cool on the bench top for 2 h. Collection of this first crop gave **3d** as cotton like needles of *cis*-aziridine

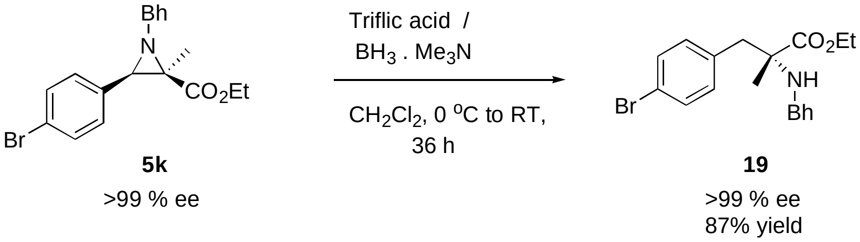
(0.488 g, 72 %) which was found to be > 99 % ee. Evaporation of the solvents from the mother liquor gave *cis*-aziridine of 68 % ee.

Methylation of aziridine 3d.



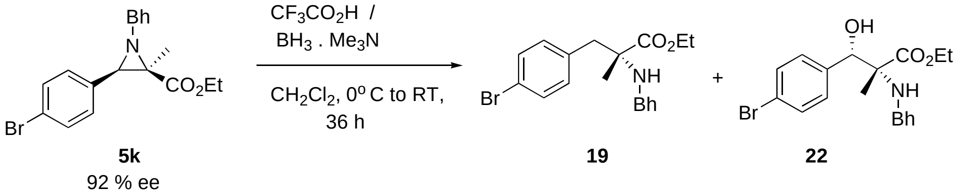
A flame dried 25 mL round-bottomed flask was equipped with a stir bar and a septa pierced with an argon inlet needle. The flask was charged with dry ethylene glycol dimethyl ether (DME) (7 mL), dry diethyl ether (2 mL) and dry diisopropylamine (DIPA) (0.28 mL, 2 mmol) at –78 °C. To this solution was added *n*-BuLi (0.8 mL, 2.5 M in hexanes) and after 5 min, aziridine **3d** (0.436 g, 1 mmol in 3 mL of DME) was added. The color of the reaction immediately turned brown. After 30 min methyl iodide (0.187 mL, 3 mmol) was added via syringe and the reaction was continued to stir as the temperature was gradually raised to rt. The reaction mixture was quenched with saturated brine (25 mL) and extracted with diethyl ether (2x15 mL). The combined organic layers were dried over anhyd Na_2SO_4, filtered and solvents removed on rotary evaporator. The crude product was purified by silica gel column chromatography (10 % ethyl acetate in hexanes) to give pure methylated product **5k**; 0.388 g, 86 % yield, R_f: 0.38 (10 % ethyl acetate in hexanes), white solid mp = 128 – 9 °C. The enantiomeric excess of >99 % ee was determined by HPLC on a Chiralcel OD-H column (9 : 1 hexanes / *i*-Pr-OH ; 1 mL / min). t_R (R,R, major) = 6.56 min; t_R (S,S, minor) = 5.26 min. Spectral data for **5k**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.99 (t, 3 H, J = 7.0 Hz), 1.57 (s, 3 H), 2.95 (s, 1H), 3.78-3.99 (m, 2 H), 4.51 (s, 1 H), 7.16 – 7.39 (m, 10 H), 7.22 (d, 2 H, J = 6.8 Hz), 7.49 (d, 2 H, J = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.31, 13.91, 50.49, 51.92, 60.67, 70.36, 120.87, 126.80, 126.92, 127.09, 127.37, 127.77, 128.42, 129.08, 130.72, 135.28, 143.08, 143.32, 169.76; IR (thin film) 3028, 2980, 2936, 1741, 1720, 1489, 1452, 1149, 1012, 744, 702 cm^{-1}; mass spectrum (FAB) m/z (% rel intensity) 451 M^+ (21, ^{81}Br), 449 M^+ (27, ^{79}Br), 373 (6, ^{81}Br), 371 (5, ^{79}Br), 284 (12), 283 (70, ^{81}Br), 282 (11), 281 (70, ^{79}Br), 168 (45), 167 (100), 165 (30). Anal Calcd for $C_{25}H_{24}BrNO_2$: C, 66.67; H, 5.37; N, 3.11. Found: C, 66.92; H, 5.10; N, 3.06. $[\alpha]^{25}_D$: +69.0° (*c* = 1, in CH_2Cl_2).

Reductive cleavage of aziridine 5k with triflic acid / borane- trimethyl amine complex.[4]



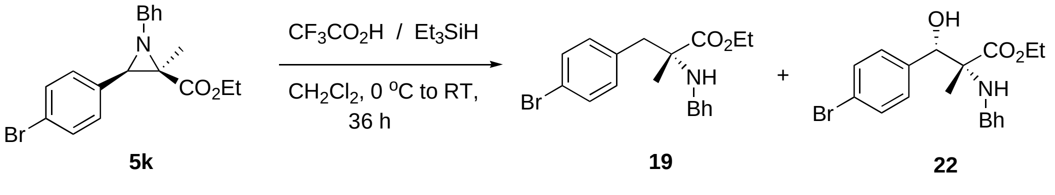
To a cold solution (0 °C) of aziridine **5k** (0.3 g, 0.67 mmol, >99 % ee) in dry dichloromethane (4 mL) in a 10 mL round-bottomed flask was added a solution of $BH_3.Me_3N$ complex (0.741 g, 8.04 mmol) in 2 mL dry dichloromethane. Triflic acid (177 μL, 2.01 mmol) was added drop-wise via syringe over two minutes and the reaction mixture was continued to stir as the temperature was gradually raised to ambient. After 12 h, the reaction mixture was cooled to 0° C and an additional portion of triflic acid (177 μL, 2.01 mmol) was added. The final dose of triflic acid (177 μL, 2.01 mmol) was added after an additional 12 h and the resulting solution was stirred at 0° C for 12 h. The reaction mixture was quenched with sat aq $NaHCO_3$ (5 mL) and after stirring for 15 min was extracted with dichloromethane (3x10 mL). The combined organic extracts were dried over anhyd Na_2SO_4 and concentrated on a rotary evaporator. The crude product was subjected to silica gel column chromatography (5 % ethyl acetate in hexanes) to give the pure product **19** (R_f = 0.44 in 10 % ethyl acetate in hexanes) as an oil (262 mg, 87 % yield) along with 24 mg of the starting material (R_f = 0.36 in 10 % ethyl acetate in hexanes). The enantiomeric excess was determined to be > 99 % ee by HPLC on a Chiralcel OD-H column (9 : 1 hexanes / *i*-Pr-OH ; 1 mL / min): t_R (R, major) = 5.70 min; t_R (S, minor) = 6.36 min. The retention time of the S-enantiomer of **19** was determined on material obtained from the reaction of 5k that was only 92 % ee. Spectral data for **19**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.07 (s, 3 H), 1.18 (t, 3 H, J = 7.2 Hz), 2.27 (s, 1 H, -NH-), 2.89 (d, 1 H, J = 13.2 Hz), 2.94 (d, 1 H, J = 13.2 Hz), 4.03 (dq, 2 H, J = 7.1, 2.1 Hz), 4.87 (s, 1 H), 7.07 (d, 2 H, J = 8.1 Hz), 7.30-7.19 (m, 8 H), 7.45-7.38 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 14.09, 21.63, 46.64, 60.78, 63.07, 63.83, 120.72, 126.57, 126.91, 127.17, 127.41, 128.15, 128.49, 131.02, 132.09, 135.47, 145.17, 145.58, 175.83; IR (Neat) 3344, 3063, 3026, 2984, 2939, 2867, 1725, 1599, 1489, 1452, 1404, 1379, 1182, 1111, 1072, 1012, 744, 702 cm^{-1}. MS (FAB) m/z (% rel intensity) 454 $(M+H)^+$ (20, ^{81}Br), 452 $(M+H)^+$ (25, ^{79}Br), 433 (10), 419 (35), 391 (30), 380 (30), 378 (30), 280 (100), 168 (80), 167 (100), 149 (100), 71 (65), 57 (62). Anal Calcd for $C_{25}H_{26}BrNO_2$: C, 66.37; H, 5.79; N, 3.10. Found: C, 66.39; H, 5.96; N, 3.04. HRMS (FAB) Calcd for $C_{25}H_{27}{}^{79}BrNO_2$ $(M+H)^+$ m/z 452.1225, meas 452.1216. $[\alpha]^{25}_D$: -39.1° (*c* = 1, in CH_2Cl_2).

Reductive cleavage of aziridine 5k with trifluoroacetic acid / borane- trimethyl amine complex.



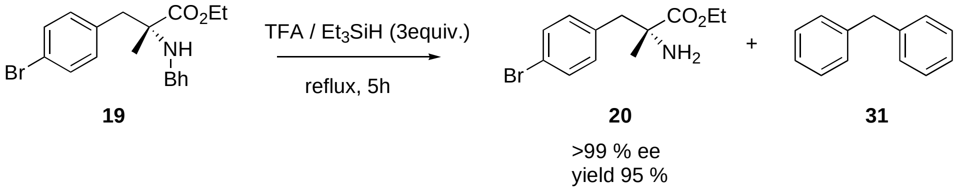
This reaction was carried out with the procedure described above for the ring cleavage with triflic acid / borane-trimethylamine complex except that trifluoroacetic acid (TFA) was substituted for triflic acid. Reaction with 4 equiv TFA and 12 equiv of borane-trimethylamine complex gave 90 % conversion and a 6.3 : 1 ratio of the desired product **19** and the undesired hydroxy-opened product **22**. With 4 equiv of TFA and 4 equiv of borane-trimethyamine complex **19** and **22** were obtained in a 1:2 ratio in 100 % conversion. Spectral data for **22**: Oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.97 (s, 3 H), 1.14 (t, 3 H, J = 7.2 Hz), 2.79 (br s, 1 H, -NH-), 3.88 (br s, 1 H, OH), 3.97 (q, 2 H, J = 7.2 Hz), 4.78 (s, 1 H), 4.93 (s, 1H), 7.33 – 7.19 (m, 10 H), 7.39 (d, 2H, J = 7.5 Hz), 7.46 (d, 2 H, J = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 13.94, 15.10, 61.15, 62.44, 67.46, 77.47, 121.79, 126.82, 126.92, 127.25, 127.57, 128.31, 128.61, 129.16, 130.82, 137.44, 143.91, 144.42, 174.94; IR (Neat) 3478 (br), 3064, 3026, 2984, 1716, 1597, 1488, 1450, 1383, 1234, 1176, 1109, 1062, 1010, 912, 839, 744, 702 cm^{-1}. MS (FAB) m/z (% rel intensity) 480 (M+H) (7, ^{81}Br), 468 (7, ^{79}Br), 396 (2, ^{81}Br), 394 (2, ^{79}Br), 282 (15), 167 (100). Anal Calcd for $C_{25}H_{26}BrNO_2$: HRMS (FAB) Calcd for $C_{25}H_{27}BrNO_3$ (M+H) m/z 468.1174, meas 468.1173. $[\alpha]^{25}_D = -21.6^o$ (*c* = 1.0, EtOH) taken on material that was prepared from a sample of **5k** that was 92 % ee.

Reductive cleavage of aziridine 5k with trifluoroacetic acid / Et_3SiH.



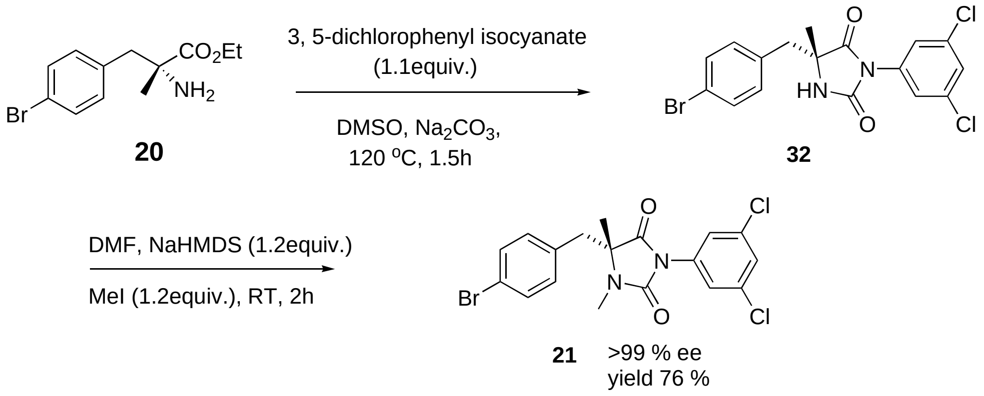
To a solution of aziridine **5k** (0.056 g, 0.125 mmol) in dry dichloromethane (3 mL) in a 10 mL round-bottomed flask was added Et_3SiH (19 8μL, 1.25 mmol). The mixture was cooled to 0 °C and then TFA (10 μL, 0.125 mmol) was added via syringe and then reaction mixture was allowed to gradually rise to rt with stirring. After 12 h, the reaction mixture was quenched with a few drops of sat aq $NaHCO_3$. After stirring for 10 min, the reaction mixture was diluted with water (10 mL) and extracted with dichloromethane (2x10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated on rotary evaporator. The crude product was subjected to silica gel column chromatography (5 to 10 % ethyl acetate in hexanes) to give a small amount of the desired product **19** (R_f = 0.44 in 10 % ethyl acetate in hexanes) as an oil and the hydroxy-opened product **22** (R_f = 0.28 in 10 % ethyl acetate in hexanes) as the major product.

Deprotection of benzhydral group to give the amino-ester 20.



To a solution of **19** (0.214 g, 0.47 mmol) in trifluoroacetic acid (5 mL) was added Et_3SiH (0.224 mL, 1.41 mmol) and the resulting solution refluxed for 5 h. The reaction mixture was cooled to rt and the excess trifluoroacetic acid was removed under reduced pressure. The crude reaction mixture was diluted with dichloromethane (5 mL), exposed to sat aq $NaHCO_3$ (3 mL) for 10 min, extracted with dichloromethane (3x10 mL), dried over anhyd Na_2SO_4 and concentrated on a rotary evaporator. The residue was loaded onto a silica gel column and eluted with first with 10 % ethyl acetate in hexanes to give diphenylmethane (**31**) (0.074 g, 94 %) and then with 10 % MeOH in CH_3CN to give pure amino ester **20** as a solid: 0.124 g, 95 % yield, mp 43-44 ^{o}C. Enantiomeric excess was determined to be > 99 % ee by HPLC on a Chiralcel OD-H column (9 : 1 of hexanes / *i*-Pr-OH ; 1 mL / min); t_R (S, minor) = 6.52 min; t_R (R, major) = 5.22 min. Spectral data for **20**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.28 (t, 3 H, J = 7.2 Hz), 1.41 (s, 3 H), 2.1-2.4 (bs, 2 H, -NH_2), 2.80 (d, 1 H, J = 13.2 Hz), 3.10 (d, 1 H, d, J = 13.2 Hz), 4.16 (q, 2 H, J = 7.2 Hz), 7.07 (d, 2 H, J = 8.1 Hz), 7.41 (d, 2 H, J = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 14.11, 26.18, 45.81, 58.56, 61.25, 121.00, 131.34, 131.69, 135.31, 176.30; IR (Neat) 3375, 3321, 2980, 2932, 2870, 1728, 1593, 1489, 1451, 1406, 1373, 1196, 1113, 1072, 1012, 846, 788 cm^{-1}; MS (FAB) m/z (% rel intensity) 288 $(M+H)^+$ (99, ^{81}Br), 286 (100, ^{79}Br), 214 (50, ^{81}Br), 212 (50, ^{79}Br), 154 (15), 149 (10), 133 (15), 117 (60), 116 (50), 95 (25), 69 (40), 57 (45), 55 (45); $[\alpha]^{25}_{D\,:}$ +6.2^{o} (*c* = 1, in C_2H_5OH). HRMS (FAB) calcd for $C_{12}H_{16}{}^{79}BrNO_2$ $(M+H)^+$ m/z 286.0443, meas 286.0439.

Synthesis of BIRT – 377 (21).



To a stirred solution amino acid **20** (0.114 g, 0.42 mmol) in dry DMSO (1.5 mL) was added 3,5-dichlorophenylisocyante (0.086 g, 0.46 mmol) at rt and resulting mixture was stirred for 1.5 h. To this was added Na_2CO_3 (0.118 g, 0.84 mmol) and reaction mixture was heated at 120 °C for 1.5 h. The reaction mixture was cooled to rt and diluted with ethyl acetate (10 mL). The mixture was washed with water (2x5 mL) and brine (2x5 mL) and the dried over anhyd Na_2SO_4. The mixture was concentrated on a rotary evaporator and dried under high vacuum to give the product as a solid which was subjected to next step without further purification.

The crude product was dissolved in dry DMF (1.5 mL), treated with NaHMDS (0.5 mL, 1 M in THF) and then stirred for 20 min at rt. Methyl iodide (31 µL, 0.5 mmol) was added and stirred for 2 h at rt. The reaction was quenched with ice-c old water (2 mL) and diluted with ethyl acetate (10 mL). The organic layer was separated and washed with sat brine (10 mL), dried over anhyd Na_2SO_4 and concentrated on rotary evaporator. The crude product was purified by silica gel column chromatography (20 % ethyl acetate in hexanes) to give pure **21** (R_f = 0.23 in 20 % ethyl acetate in hexanes): 0.143 g, 76 % yield; white solid, mp 135 – 136 °C. Enantiomeric excess was determined to be >99 % ee by HPLC on a Chiralcel OD-H column (9 : 1 of hexanes / *i*-Pr-OH ; 1 mL / min). t_R (R, major) = 15.6 min; t_R (S, minor) = 21.5 min. Spectral data for **21**: ^{1}H NMR (300 MHz, $CDCl_3$) δ = 1.63 (s, 3 H), 2.98 (d, 1 H, J = 14.1 Hz), 3.09 (s, 3 H), 3.12 (d, 1 H, J = 14.1 Hz), 6.86 (m, 2 H), 6.96 (d, 2 H, J = 7.7 Hz), 7.30 (m, 1 H), 7.44 (d, 2 H, J = 7.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 20.98, 25.25, 40.63, 65.61, 121.92, 124.46, 128.26, 131.06, 131.79, 132.77, 132.94, 135.00 153.38, 173.28; IR (thin film) 3086, 2981, 2932, 1778, 1724, 1587, 1574, 1489, 1454, 1400, 1379, 1145, 1107, 1012, 804, 740 cm^{-1}; MS (FAB) m/z (% rel intensity) 447 (3, ^{81}Br, ^{37}Cl, ^{37}Cl), 445 (18, ^{x}Br, ^{y}Cl, ^{z}Cl), 443 (38, ^{x}Br, ^{y}Cl, ^{z}Cl), 441 (30, ^{79}Br, ^{35}Cl, ^{35}Cl), 273 (15), 271 (20), 154 (100), 137 (60); HRMS (FAB) calcd for $C_{18}H_{15}{}^{79}Br^{35}Cl_2N_2O_2$ $(M+H)^+$ m/z 440.9772, meas 440.9770. Anal Calcd for $C_{18}H_{15}BrCl_2N_2O_2$: C, 48.90; H, 3.42; N, 6.34. Found: C, 49.02; H, 3.30; N, 6.21. $[\alpha]^{25}_{D}$: +130.2° (*c* = 1, in C_2H_5OH).

References.

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3) Antilla, J. C.; Wulff, W. D., *Angew. Chem. Int. Ed. Engl.*, **2000**, *39*, 4518.

4) a) Vedejs, E.; Klapars, A.; Warner, D. L.; Weiss, A. H., *J. Org. Chem.*, **2001**, *66*, 7542. b) Carboni, B.; Monnier, *Tetrahedron*, **1999**, *55*, 1197.

Crystal Structure of Aziridine 5a

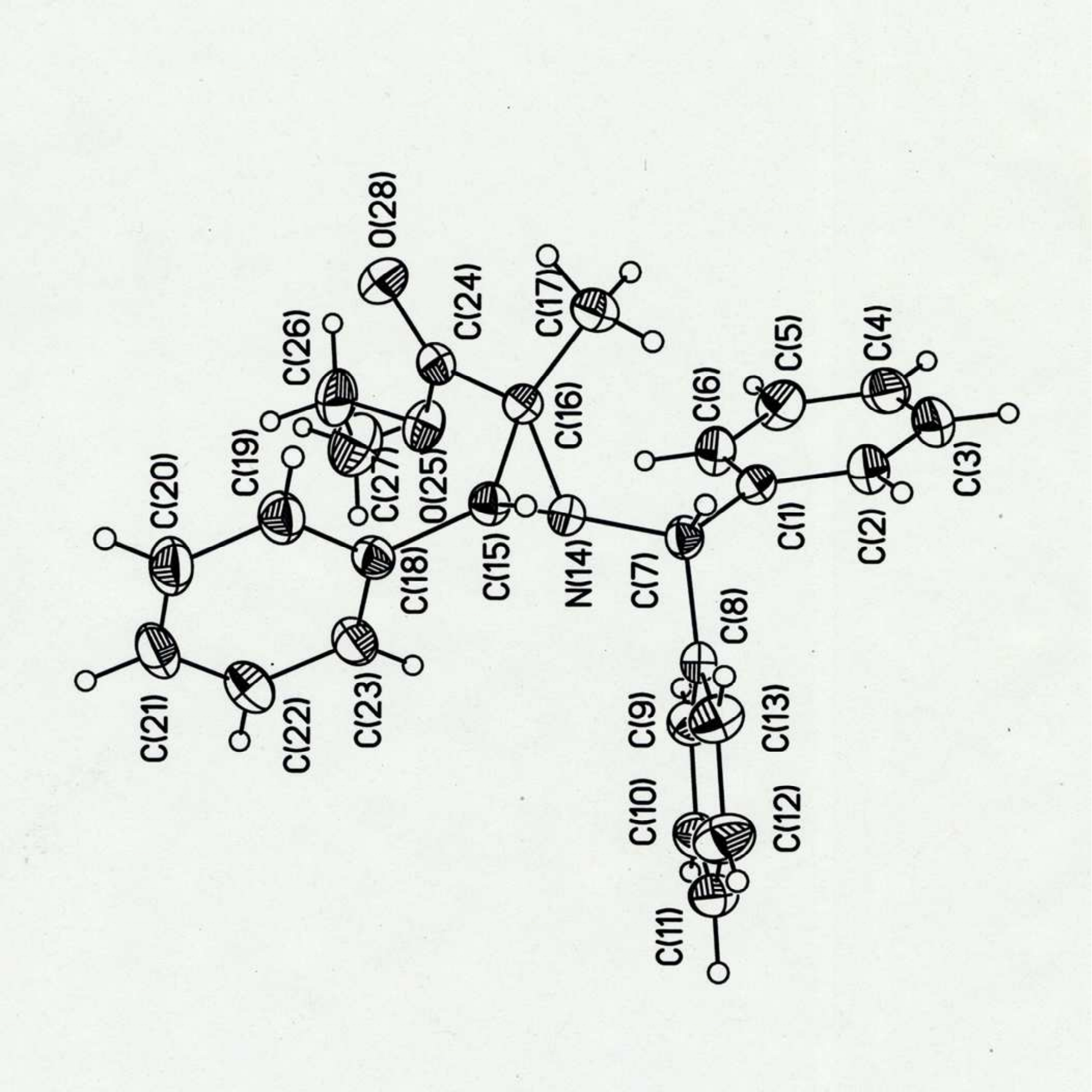

Figure I. ORTEP of 5a

Table 1. Crystal data and structure refinement for 5a (1-benzhydryl–2-methyl-3-phenyl aziridine-2-carboxylic acid ethyl ester)

Identification code	5a
Empirical formula	C25 H25 N O2
Formula weight	371.46
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P21/c
Unit cell dimensions	a = 10.419(2) A b = 22.506(5) A c = 8.7510(18) A alpha = 90 deg. beta = 98.27(3) deg. gamma = 90 deg.
Volume	2030.6(7) A^3
Z	4
Density (calculated)	1.215 Mg/m^3
Absorption coefficient	0.076 mm^-1
F(000)	792
Crystal size	0.6 x 0.3 x 0.25 mm
Theta range for data collection	1.81 to 28.33 deg.
Index ranges	-13<=h<=13, -27<=k<=29, -11<=l<=9
Reflections collected / unique	12867 / 4811 [R(int) = 0.0250]
Completeness to theta = 28.33	94.9%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4811 / 0 / 261
Goodness-of-fit on F^2	0.944
Final R indices [I>2sigma(I)]	R1 = 0.0449, wR2 = 0.1279
R indices (all data)	R1 = 0.0694, wR2 = 0.1421
Largest diff. peak and hole	0.263 and -0.222 e.A^-3

Table 2. Atomic coordinates (x 10^4), equivalent isotropic displacement parameters (A^2 x 10^3), and occupancies for 5a

	x	y	z	U(eq)	Occ.
C(1)	4014(1)	3426(1)	458(2)	26(1)	1
C(2)	5191(1)	3177(1)	209(2)	34(1)	1
C(3)	6142(2)	3041(1)	1428(2)	41(1)	1
C(4)	5926(2)	3146(1)	2921(2)	41(1)	1
C(5)	4768(2)	3393(1)	3189(2)	41(1)	1
C(6)	3811(2)	3536(1)	1964(2)	34(1)	1
C(7)	2998(1)	3552(1)	-930(2)	25(1)	1
C(8)	3273(1)	4103(1)	-1834(2)	26(1)	1
C(9)	3536(2)	4645(1)	-1103(2)	32(1)	1
C(10)	3710(2)	5153(1)	-1959(2)	36(1)	1
C(11)	3643(2)	5119(1)	-3542(2)	38(1)	1
C(12)	3400(2)	4581(1)	-4278(2)	42(1)	1
C(13)	3216(2)	4075(1)	-3424(2)	35(1)	1
N(14)	1709(1)	3631(1)	-446(1)	24(1)	1
C(15)	609(1)	3430(1)	-1549(2)	26(1)	1
C(16)	1022(1)	3090(1)	-73(2)	26(1)	1
C(17)	1601(2)	2475(1)	-144(2)	34(1)	1
C(18)	-599(1)	3799(1)	-1808(2)	26(1)	1
C(19)	-1755(1)	3529(1)	-2442(2)	34(1)	1
C(20)	-2893(2)	3858(1)	-2686(2)	39(1)	1
C(21)	-2880(2)	4453(1)	-2312(2)	39(1)	1
C(22)	-1732(2)	4725(1)	-1708(2)	40(1)	1
C(23)	-588(2)	4397(1)	-1446(2)	34(1)	1
C(24)	145(1)	3153(1)	1141(2)	30(1)	1
O(25)	246(1)	3670(1)	1881(1)	36(1)	1
C(26)	-718(2)	3774(1)	2920(2)	44(1)	1
C(27)	-249(2)	4254(1)	3997(2)	57(1)	1
O(28)	-595(1)	2762(1)	1372(2)	46(1)	1

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 3. Bond lengths [A] and angles [deg] for 5a

C(1)-C(6)	1.387(2)
C(1)-C(2)	1.393(2)
C(1)-C(7)	1.5189(19)
C(2)-C(3)	1.382(2)
C(3)-C(4)	1.378(3)
C(4)-C(5)	1.379(2)
C(5)-C(6)	1.392(2)
C(7)-N(14)	1.4751(17)
C(7)-C(8)	1.5189(18)
C(8)-C(13)	1.385(2)
C(8)-C(9)	1.3866(19)
C(9)-C(10)	1.393(2)
C(10)-C(11)	1.379(2)
C(11)-C(12)	1.378(2)
C(12)-C(13)	1.390(2)
N(14)-C(15)	1.4601(17)
N(14)-C(16)	1.4726(17)
C(15)-C(18)	1.4977(19)
C(15)-C(16)	1.5090(19)
C(16)-C(24)	1.505(2)
C(16)-C(17)	1.5153(19)
C(18)-C(23)	1.383(2)
C(18)-C(19)	1.391(2)
C(19)-C(20)	1.387(2)
C(20)-C(21)	1.379(2)
C(21)-C(22)	1.379(2)
C(22)-C(23)	1.393(2)
C(24)-O(28)	1.2059(18)
C(24)-O(25)	1.3278(18)
O(25)-C(26)	1.4675(19)
C(26)-C(27)	1.471(3)
C(6)-C(1)-C(2)	118.60(13)
C(6)-C(1)-C(7)	122.80(13)
C(2)-C(1)-C(7)	118.59(13)
C(3)-C(2)-C(1)	121.20(15)
C(4)-C(3)-C(2)	119.76(15)
C(3)-C(4)-C(5)	119.84(15)
C(4)-C(5)-C(6)	120.60(16)
C(1)-C(6)-C(5)	119.99(14)
N(14)-C(7)-C(8)	107.44(10)
N(14)-C(7)-C(1)	110.59(11)
C(8)-C(7)-C(1)	114.07(11)
C(13)-C(8)-C(9)	118.66(13)
C(13)-C(8)-C(7)	120.17(12)
C(9)-C(8)-C(7)	121.12(13)
C(8)-C(9)-C(10)	120.47(14)
C(11)-C(10)-C(9)	120.12(14)
C(12)-C(11)-C(10)	119.92(14)
C(11)-C(12)-C(13)	119.86(15)
C(8)-C(13)-C(12)	120.96(14)
C(15)-N(14)-C(16)	61.93(9)
C(15)-N(14)-C(7)	115.71(11)

C(16)-N(14)-C(7)	117.16(10)
N(14)-C(15)-C(18)	119.42(12)
N(14)-C(15)-C(16)	59.44(9)
C(18)-C(15)-C(16)	122.70(12)
N(14)-C(16)-C(24)	116.28(11)
N(14)-C(16)-C(15)	58.63(8)
C(24)-C(16)-C(15)	115.44(11)
N(14)-C(16)-C(17)	122.51(12)
C(24)-C(16)-C(17)	113.60(12)
C(15)-C(16)-C(17)	119.64(13)
C(23)-C(18)-C(19)	119.63(13)
C(23)-C(18)-C(15)	121.72(13)
C(19)-C(18)-C(15)	118.65(13)
C(20)-C(19)-C(18)	120.04(14)
C(21)-C(20)-C(19)	120.16(15)
C(22)-C(21)-C(20)	120.04(14)
C(21)-C(22)-C(23)	120.15(15)
C(18)-C(23)-C(22)	119.96(14)
O(28)-C(24)-O(25)	124.39(14)
O(28)-C(24)-C(16)	121.17(14)
O(25)-C(24)-C(16)	114.42(12)
C(24)-O(25)-C(26)	115.39(12)
O(25)-C(26)-C(27)	108.71(14)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for 5a

	U11	U22	U33	U23	U13	U12
C(1)	23(1)	23(1)	33(1)	1(1)	4(1)	-1(1)
C(2)	28(1)	35(1)	40(1)	0(1)	8(1)	4(1)
C(3)	27(1)	40(1)	56(1)	5(1)	4(1)	6(1)
C(4)	30(1)	44(1)	46(1)	11(1)	-7(1)	-2(1)
C(5)	37(1)	53(1)	33(1)	4(1)	2(1)	-5(1)
C(6)	26(1)	42(1)	33(1)	0(1)	5(1)	2(1)
C(7)	22(1)	24(1)	28(1)	-2(1)	6(1)	2(1)
C(8)	19(1)	28(1)	31(1)	2(1)	5(1)	2(1)
C(9)	34(1)	29(1)	34(1)	-1(1)	6(1)	0(1)
C(10)	33(1)	27(1)	47(1)	0(1)	4(1)	1(1)
C(11)	32(1)	36(1)	45(1)	13(1)	3(1)	-3(1)
C(12)	48(1)	46(1)	31(1)	6(1)	5(1)	-8(1)
C(13)	39(1)	33(1)	33(1)	-1(1)	7(1)	-6(1)
N(14)	21(1)	25(1)	27(1)	1(1)	4(1)	0(1)
C(15)	23(1)	25(1)	28(1)	0(1)	2(1)	0(1)
C(16)	23(1)	24(1)	32(1)	2(1)	2(1)	-1(1)
C(17)	33(1)	26(1)	43(1)	4(1)	3(1)	1(1)

C(18)	25(1)	29(1)	25(1)	4(1)	3(1)	2(1)
C(19)	28(1)	34(1)	39(1)	-1(1)	0(1)	1(1)
C(20)	24(1)	51(1)	41(1)	3(1)	-1(1)	2(1)
C(21)	30(1)	51(1)	36(1)	7(1)	5(1)	16(1)
C(22)	41(1)	35(1)	44(1)	0(1)	4(1)	11(1)
C(23)	31(1)	31(1)	39(1)	0(1)	0(1)	4(1)
C(24)	22(1)	32(1)	34(1)	9(1)	1(1)	3(1)
O(25)	29(1)	44(1)	38(1)	-4(1)	12(1)	-2(1)
C(26)	31(1)	59(1)	45(1)	-3(1)	16(1)	4(1)
C(27)	53(1)	69(1)	52(1)	-14(1)	21(1)	-4(1)
O(28)	37(1)	38(1)	66(1)	12(1)	20(1)	-3(1)

The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

Table 5. Hydrogen coordinates (x 10^4), isotropic displacement parameters (A^2 x 10^3), and occupancies for 5a

	x	y	z	U(eq)	Occ.
H(2)	5339	3101	-796	41	1
H(3)	6927	2879	1241	49	1
H(4)	6559	3051	3745	49	1
H(5)	4625	3465	4197	50	1
H(6)	3036	3706	2156	40	1
H(7)	2968(14)	3204(6)	-1664(17)	24(4)	1
H(9)	3596	4670	-35	39	1
H(10)	3871	5516	-1462	43	1
H(11)	3762	5458	-4111	46	1
H(12)	3358	4556	-5345	50	1
H(13)	3053	3713	-3926	42	1
H(15)	835(16)	3223(7)	-2504(19)	32(4)	1
H(17A)	2147	2464	-937	51	1
H(17B)	916	2189	-371	51	1
H(17C)	2104	2381	834	51	1
H(19)	-1765	3128	-2703	41	1
H(20)	-3666	3676	-3102	47	1
H(21)	-3645	4671	-2468	47	1
H(22)	-1722	5128	-1475	48	1
H(23)	183	4580	-1028	41	1
H(26A)	-844	3414	3490	53	1
H(26B)	-1542	3885	2327	53	1
H(27A)	-870	4326	4687	85	1
H(27B)	-135	4610	3426	85	1
H(27C)	566	4141	4582	85	1

Table 6. Torsion angles [deg] for 5a

C(6) C(1) C(2) C(3)	0.0(2)
C(7) C(1) C(2) C(3)	-178.75(13)
C(1) C(2) C(3) C(4)	0.7(2)
C(2) C(3) C(4) C(5)	-0.8(3)
C(3) C(4) C(5) C(6)	0.2(3)
C(2) C(1) C(6) C(5)	-0.7(2)
C(7) C(1) C(6) C(5)	178.08(14)
C(4) C(5) C(6) C(1)	0.5(2)
C(6) C(1) C(7) N(14)	-16.59(18)
C(2) C(1) C(7) N(14)	162.15(12)
C(6) C(1) C(7) C(8)	104.63(15)
C(2) C(1) C(7) C(8)	-76.63(16)
N(14) C(7) C(8) C(13)	-106.47(14)
C(1) C(7) C(8) C(13)	130.58(14)
N(14) C(7) C(8) C(9)	71.06(15)
C(1) C(7) C(8) C(9)	-51.89(17)
C(13) C(8) C(9) C(10)	1.4(2)
C(7) C(8) C(9) C(10)	-176.15(13)
C(8) C(9) C(10) C(11)	-1.1(2)
C(9) C(10) C(11) C(12)	0.2(2)
C(10) C(11) C(12) C(13)	0.3(3)
C(9) C(8) C(13) C(12)	-0.9(2)
C(7) C(8) C(13) C(12)	176.69(14)
C(11) C(12) C(13) C(8)	0.0(2)
C(8) C(7) N(14) C(15)	87.84(13)
C(1) C(7) N(14) C(15)	-147.09(11)
C(8) C(7) N(14) C(16)	157.97(11)
C(1) C(7) N(14) C(16)	-76.96(14)
C(16) N(14) C(15) C(18)	112.78(14)
C(7) N(14) C(15) C(18)	-138.71(12)
C(7) N(14) C(15) C(16)	108.51(12)
C(15) N(14) C(16) C(24)	-105.07(13)
C(7) N(14) C(16) C(24)	148.73(12)
C(7) N(14) C(16) C(15)	-106.20(12)
C(15) N(14) C(16) C(17)	107.35(15)
C(7) N(14) C(16) C(17)	1.15(19)
C(18) C(15) C(16) N(14)	-107.38(14)
N(14) C(15) C(16) C(24)	106.51(13)
C(18) C(15) C(16) C(24)	-0.87(19)
N(14) C(15) C(16) C(17)	-112.17(14)
C(18) C(15) C(16) C(17)	140.44(14)
N(14) C(15) C(18) C(23)	21.1(2)
C(16) C(15) C(18) C(23)	91.71(17)
N(14) C(15) C(18) C(19)	-159.49(13)
C(16) C(15) C(18) C(19)	-88.86(17)
C(23) C(18) C(19) C(20)	-1.0(2)
C(15) C(18) C(19) C(20)	179.53(14)
C(18) C(19) C(20) C(21)	0.5(2)
C(19) C(20) C(21) C(22)	0.6(3)

C(20)	C(21)	C(22)	C(23)	-1.2(3)
C(19)	C(18)	C(23)	C(22)	0.4(2)
C(15)	C(18)	C(23)	C(22)	179.84(14)
C(21)	C(22)	C(23)	C(18)	0.7(2)
N(14)	C(16)	C(24)	O(28)	169.37(13)
C(15)	C(16)	C(24)	O(28)	103.45(16)
C(17)	C(16)	C(24)	O(28)	-40.19(19)
N(14)	C(16)	C(24)	O(25)	-9.18(17)
C(15)	C(16)	C(24)	O(25)	-75.10(16)
C(17)	C(16)	C(24)	O(25)	141.26(13)
O(28)	C(24)	O(25)	C(26)	-6.4(2)
C(16)	C(24)	O(25)	C(26)	172.11(12)
C(24)	O(25)	C(26)	C(27)	162.12(15)

Symmetry transformations used to generate equivalent atoms:

Crystal Structure of Pyrrole 10.

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Figure 2. ORTEP of 10.

Table 1. Crystal data and structure refinement for 10

Identification code	p21n
Empirical formula	C20 H25 N O3
Formula weight	327.41
Temperature	173(2) K
Wavelength	0.71073 A
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 8.7829(18) A b = 6.1391(12) A c = 32.373(7) A alpha = 90 deg. beta = 93.08(3) deg. gamma = 90 deg.
Volume	1743.0(6) A^3
Z	4
Density (calculated)	1.248 Mg/m^3
Absorption coefficient	0.083 mm^-1
F(000)	704
Crystal size	0.7 x 0.3 x 0.15 mm
Theta range for data collection	2.37 to 28.28 deg.
Index ranges	-11<=h<=11, -7<=k<=7, -41<=l<=41
Reflections collected / unique	19969 / 4167 [R(int) = 0.0331]
Completeness to theta = 28.28	96.6%
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4167 / 0 / 317
Goodness-of-fit on F^2	0.868
Final R indices [I>2sigma(I)]	R1 = 0.0393, wR2 = 0.1116
R indices (all data)	R1 = 0.0657, wR2 = 0.1268
Largest diff. peak and hole	0.245 and -0.228 e.A^-3

Table 2. Atomic coordinates (x 10^4), equivalent isotropic displacement parameters (A^2 x10^3), and occupancies for **10**.

`

	x	y	z	U(eq)	Occ.
C(1)	4556(1)	-2288(2)	1536(1)	24(1)	1
C(2)	5268(1)	-4136(2)	1392(1)	28(1)	1
C(3)	5051(1)	-4145(2)	961(1)	27(1)	1
C(4)	4217(1)	-2310(2)	840(1)	26(1)	1
N(5)	3929(1)	-1161(2)	1203(1)	25(1)	1
O(6)	5574(1)	-5741(2)	716(1)	36(1)	1
C(7)	3067(1)	872(2)	1222(1)	26(1)	1
C(8)	1352(1)	582(2)	1188(1)	25(1)	1
C(9)	644(2)	-1325(2)	1306(1)	31(1)	1
C(10)	-946(2)	-1463(3)	1289(1)	40(1)	1
C(11)	-1825(2)	288(3)	1152(1)	41(1)	1
C(12)	-1123(2)	2177(3)	1032(1)	38(1)	1
C(13)	454(2)	2330(2)	1049(1)	32(1)	1
C(14)	4425(2)	-1559(2)	1976(1)	25(1)	1
C(15)	4561(2)	-3509(2)	2273(1)	34(1)	1
C(16)	4394(2)	-2819(3)	2722(1)	40(1)	1
C(17)	5541(2)	-1066(3)	2853(1)	40(1)	1
C(18)	5428(2)	877(2)	2560(1)	35(1)	1
C(19)	5612(2)	175(2)	2111(1)	30(1)	1
C(20)	3751(2)	-1829(2)	416(1)	30(1)	1
O(21)	2921(1)	-24(2)	352(1)	34(1)	1
C(22)	2404(2)	406(3)	-77(1)	40(1)	1
C(23)	1560(2)	2520(3)	-83(1)	52(1)	1
O(24)	4107(1)	-3031(2)	135(1)	41(1)	1

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 3. Bond lengths [A] and angles [deg] for**10**.

C(1)-N(5)	1.3714(16)
C(1)-C(2)	1.3874(18)
C(1)-C(14)	1.5030(17)
C(2)-C(3)	1.3990(18)
C(3)-C(4)	1.3884(18)
C(3)-O(6)	1.3561(16)
C(4)-N(5)	1.4032(16)
C(4)-C(20)	1.4420(18)
N(5)-C(7)	1.4626(16)
C(7)-C(8)	1.5153(18)
C(8)-C(9)	1.3881(19)
C(8)-C(13)	1.3922(19)
C(9)-C(10)	1.398(2)
C(10)-C(11)	1.382(2)
C(11)-C(12)	1.380(2)
C(12)-C(13)	1.387(2)
C(14)-C(15)	1.5367(19)
C(14)-C(19)	1.5366(18)
C(15)-C(16)	1.527(2)
C(16)-C(17)	1.520(2)
C(17)-C(18)	1.524(2)
C(18)-C(19)	1.5320(19)
C(20)-O(24)	1.2263(16)
C(20)-O(21)	1.3364(17)
O(21)-C(22)	1.4611(16)
C(22)-C(23)	1.494(3)
N(5)-C(1)-C(2)	108.57(11)
N(5)-C(1)-C(14)	123.16(11)
C(2)-C(1)-C(14)	128.27(12)
C(1)-C(2)-C(3)	107.33(12)
C(4)-C(3)-O(6)	127.69(12)
C(4)-C(3)-C(2)	108.59(11)
O(6)-C(3)-C(2)	123.71(12)
C(3)-C(4)-N(5)	106.80(11)
C(3)-C(4)-C(20)	123.56(12)
N(5)-C(4)-C(20)	129.63(12)
C(1)-N(5)-C(4)	108.71(10)
C(1)-N(5)-C(7)	125.76(10)
C(4)-N(5)-C(7)	125.51(10)
N(5)-C(7)-C(8)	114.31(10)
C(9)-C(8)-C(13)	118.98(12)
C(9)-C(8)-C(7)	122.54(11)
C(13)-C(8)-C(7)	118.43(12)
C(8)-C(9)-C(10)	120.11(14)
C(11)-C(10)-C(9)	120.36(15)
C(10)-C(11)-C(12)	119.60(14)
C(13)-C(12)-C(11)	120.38(14)
C(12)-C(13)-C(8)	120.57(14)
C(1)-C(14)-C(15)	110.73(11)
C(1)-C(14)-C(19)	113.04(10)
C(15)-C(14)-C(19)	109.44(11)
C(16)-C(15)-C(14)	111.81(12)
C(15)-C(16)-C(17)	111.50(13)
C(18)-C(17)-C(16)	111.09(12)
C(17)-C(18)-C(19)	111.35(12)
C(18)-C(19)-C(14)	111.12(11)
O(24)-C(20)-O(21)	122.81(12)
O(24)-C(20)-C(4)	120.87(13)
O(21)-C(20)-C(4)	116.31(11)

C(20)-O(21)-C(22)	115.92(11)
O(21)-C(22)-C(23)	107.37(13)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for **10**.

	U11	U22	U33	U23	U13	U12
C(1)	21(1)	27(1)	24(1)	2(1)	0(1)	-3(1)
C(2)	26(1)	29(1)	29(1)	0(1)	1(1)	1(1)
C(3)	22(1)	31(1)	29(1)	-6(1)	4(1)	-1(1)
C(4)	23(1)	32(1)	25(1)	-4(1)	1(1)	-2(1)
N(5)	24(1)	28(1)	23(1)	-2(1)	0(1)	1(1)
O(6)	37(1)	40(1)	31(1)	-9(1)	3(1)	9(1)
C(7)	27(1)	25(1)	25(1)	-2(1)	-2(1)	0(1)
C(8)	27(1)	31(1)	18(1)	-4(1)	0(1)	2(1)
C(9)	29(1)	35(1)	29(1)	1(1)	-1(1)	0(1)
C(10)	33(1)	49(1)	36(1)	0(1)	2(1)	-10(1)
C(11)	26(1)	64(1)	32(1)	-8(1)	0(1)	2(1)
C(12)	34(1)	48(1)	33(1)	-4(1)	-4(1)	14(1)
C(13)	34(1)	34(1)	28(1)	-1(1)	-1(1)	5(1)
C(14)	26(1)	26(1)	24(1)	1(1)	1(1)	0(1)
C(15)	46(1)	27(1)	29(1)	2(1)	6(1)	-3(1)
C(16)	54(1)	36(1)	29(1)	7(1)	9(1)	2(1)
C(17)	50(1)	44(1)	24(1)	1(1)	-4(1)	6(1)
C(18)	44(1)	34(1)	28(1)	-3(1)	-6(1)	-3(1)
C(19)	34(1)	30(1)	25(1)	2(1)	-3(1)	-5(1)
C(20)	25(1)	38(1)	26(1)	-3(1)	1(1)	-4(1)
O(21)	36(1)	42(1)	23(1)	1(1)	-2(1)	4(1)

C(22)	38(1)	57(1)	23(1)	5(1)	-4(1)	-3(1)
C(23)	58(1)	58(1)	38(1)	13(1)	-6(1)	3(1)
O(24)	45(1)	53(1)	27(1)	-11(1)	2(1)	6(1)

The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

Table 5. Hydrogen coordinates (x 10^4), isotropic displacement parameters (A^2 x 10^3), and occupancies for **10**.

	x	y	z	U(eq)	Occ.
H(2)	5821(17)	-5240(20)	1569(5)	31(4)	1
H(6)	5280(20)	-5400(40)	448(7)	72(7)	1
H(7A)	3328(15)	1550(20)	1483(4)	25(3)	1
H(7B)	3368(15)	1850(20)	1002(4)	22(3)	1
H(9)	1245(18)	-2470(30)	1397(5)	37(4)	1
H(10)	-1420(20)	-2840(30)	1365(6)	51(5)	1
H(11)	-2920(20)	180(30)	1139(5)	51(5)	1
H(12)	-1670(20)	3380(30)	930(5)	49(5)	1
H(13)	954(19)	3630(30)	960(5)	43(4)	1
H(14)	3412(18)	-910(30)	2002(5)	38(4)	1
H(15A)	5570(20)	-4190(30)	2242(5)	41(4)	1
H(15B)	3790(20)	-4560(30)	2188(5)	50(5)	1
H(16A)	3340(20)	-2260(30)	2758(5)	50(5)	1
H(16B)	4510(20)	-4110(30)	2905(6)	53(5)	1
H(17A)	6600(20)	-1650(30)	2855(6)	57(5)	1
H(17B)	5340(18)	-610(30)	3138(5)	43(4)	1
H(18A)	4343(19)	1580(30)	2582(5)	38(4)	1

H(18B)	6200(20)	2020(30)	2640(5)	46(5)	1
H(19A)	5519(19)	1470(30)	1924(6)	46(4)	1
H(19B)	6639(18)	-510(20)	2082(5)	33(4)	1
H(22A)	1710(20)	-820(30)	-170(5)	47(5)	1
H(22B)	3300(20)	450(30)	-238(6)	55(5)	1
H(23A)	710(30)	2500(40)	96(8)	79(7)	1
H(23B)	1150(20)	2820(30)	-367(6)	58(5)	1
H(23C)	2230(30)	3640(40)	-3(8)	89(8)	1

Table 6. Hydrogen-bonds [A and deg.] for **10.**

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)