"Novel Selectfluor and Deoxo-Fluor Mediated Rearrangements. New 5(6)-Methyl and Phenyl Methanopyrrolidine Alcohols and Fluorides. "

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Experimental

General Methods. Reagent chemicals were obtained from commercial suppliers. ^1H NMR spectra were recorded at 300 or 400 MHz and ^{13}C NMR spectra were recorded at 75 or 100 MHz in CDCl_3 . The NMR spectra are often complicated by the presence of carbamate rotamers and pairs of ^1H and ^{13}C NMR lines due to a single carbon, identified using proton-carbon correlation experiments, have been presented as pairs. Chemical shifts are expressed in parts per million related to internal TMS. High resolving power accurate mass measurements were obtained at Drexel University and Merck Research Laboratories, Merck & Co, Inc., West Point, PA. Thin layer chromatography was performed on precoated plates of silica gel GF 250 microns (Analtec. Inc.). Solvents were removed under reduced pressure. *N*-(Benzyloxycarbonyl)-2-azabicyclo[2.2.0]hex-5-ene (**4**),⁹ 5-methyl-*N*-(benzyloxycarbonyl)-2-azabicyclo[2.2.0]hex-5-ene (**5**) and its epoxide **22b**,⁹ iodo fluoride **7**,^{2c} iodoalcohol **8**,^{2c} bromoalcohol **12**,^{2c} bromoselenide **13**,^{2c} and bromoalcohol **23**^{2f} were prepared as reported.

Preparation of 6-endo-fluoro-6-exo-iodo-5-exo-methyl-*N*-(benzyloxycarbonyl)-2-azabicyclo[2.2.0]hexane (9). HgF_2 (1.55 g, 6.53 mmol) and alkene **5** (400 mg, 1.75 mmol) were dissolved in MeNO_2 (20 mL) and stirred at 25 °C. I_2 (797 mg, 3.14 mmol) dissolved in CH_2Cl_2 (25 mL) was added dropwise over 20 min to the stirring solution. After all the I_2 was added, the reaction was allowed to stir for an additional 10 h at 25 °C. The reaction mixture was then filtered over celite and the liquid collected was washed with 10% $\text{Na}_2\text{S}_2\text{O}_3$ (3 x 25 mL), deionized H_2O (3 x 25 mL), dried over MgSO_4 , and the solvent was removed *in vacuo*. After column chromatography using silica gel (2:1

Supplementary: Krow, G. R., et al. "Novel Selectfluor and Deoxo-Fluor Mediated ... S-3 hexane/ether) there was obtained 486 mg (74%) of iodo fluoride **9** at $R_f = 0.35$ (1:1 hexane/ether): ^1H NMR (CDCl_3 , 400 MHz, 60 °C) δ 7.5 (m, 5H), 5.25 (d, $J = 9$ Hz, 1H), 5.15 (d, $J = 9$ Hz, 1H), 4.85 (d, $J = 17$ Hz, 1H), 4.52 and 4.50 (d, $J = 9$ Hz, 1H), 4.43 and 4.41 (d, $J = 6$ Hz), 4.18 and 4.08 (dd, $J = 2, 9$ Hz, 1H), 3.10 (dd, $J = 2, 6$ Hz, 1H), 1.55 (d, $J = 23$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 155.5, 136.6, 128.9, 128.6, 127.9, 93.5 ($J_{\text{FC}} = 225$ Hz), 67.9, 62.9, 49.8 and 49.0, 42.1 and 41.9, 30.7 and 30.4, 29.7; HRMS m/z 398.0029, calcd for $\text{C}_{14}\text{H}_{15}\text{NO}_2\text{FINa}$ (MNa^+) 398.0027.

Preparation of 5-endo-Hydroxy-6-exo-iodo-5-exo-methyl-N-(benzyloxycarbonyl)-2-azabicyclo[2.2.0]hexane (10). Alkene **5** (150 mg, 0.65 mmol) was dissolved in a 2:1 DMSO/ H_2O mixture (30 mL) and stirred at 25 °C. *N*-Iodosuccinimide (442 mg, 1.97 mmol) was added in one portion to the reaction mixture and stirring was continued for an additional 10 h. The crude reaction mixture was then washed with 10% $\text{Na}_2\text{S}_2\text{O}_3$ (3 x 25 mL), extracted with ether (3 x 25 mL), dried over MgSO_4 and the solvent was removed *in vacuo*. After column chromatography using silica gel (1:1 ether/hexane), there was afforded 165 mg (68%) of iodoalcohol **10** at $R_f = 0.25$ (3:1 ether/hexane): ^1H NMR (400 MHz, CDCl_3 , 60 °C) δ 7.5 (m, 5H), 5.25 (d, $J = 9$ Hz, 1H), 5.15 (d, $J = 9$ Hz, 1H), 4.65 (d, $J = 1$ Hz, 1H), 4.55 (dd, $J = 3, 9$ Hz, 1H), 4.46 (dd, $J = 1, 5$ Hz, 1H), 4.15 (dd, $J = 7, 9$ Hz, 1H), 3.05 (broad s, 1H), 3.05 (ddd, $J = 3, 5, 7$ Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 155.9, 136.7, 128.9, 128.5, 128.3, 73.4, 67.3, 63.8, 50.2 and 49.4, 43.1, 35.6 and 34.8, 33.1; HRMS m/z 396.0072, calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_3\text{INa}$ (MNa^+) 396.0083.

Preparation of *N*-(Benzyloxycarbonyl)-5-*syn*-fluoro-6-*anti*-hydroxy-5-*anti*-methyl-2-

azabicyclo[2.1.1]hexane (18). *Method A (Moist HgF₂).* The iodofluoride **12** (72 mg, 0.19 mmol) was dissolved in nitromethane (10 mL). Moist HgF₂ (114 mg, 0.48 mmol), formed by brief exposure of hygroscopic HgF₂ to air, was added in one portion to the mixture and the temperature was raised to 60°C. The reaction was allowed to stir for 16 h and was monitored by TLC. Upon completion the solvent removed *in vacuo* and the crude oil was chromatographed using silica gel (1:1 ether/hexane) to afford 27 mg (53%) of rearranged fluoroalcohol **18** at R_f = 0.15 (3:1 ether/hexane): ¹H NMR (DMSO-*d*₆, 400 MHz, 104 °C) δ 7.5 (m, 5H), 5.25 (d, *J* = 9 Hz, 1H), 5.15 (d, *J* = 9 Hz, 1H), 4.05 (dd, *J* = 7, 2 Hz, 1H), 3.82 (dd, *J* = 27, 2 Hz, 1H), 3.55 (d, *J* = 8.5 Hz, 1H), 3.3 (dd, *J* = 8.5, 1 Hz, 1H), 2.63 (dd, *J* = 7, 1 Hz, 1H), 1.93 (broad s, 1H), 1.89 (d, *J* = 25 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.7, 139.0, 131.9, 131.5, 131.2, 93.1 (*J*_{F,C} = 220 Hz), 73.9, 69.3, 67.2, 51.3, 46.8, 19.2; HRMS *m/z* 288.1011, calcd for C₁₄H₁₆NO₃FNa (MNa⁺) 288.1020. *Method B (Selectfluor).* **General Procedure.** Iodofluoride **9** (26 mg, 0.07 mmol) was dissolved in a 1:1 water/acetonitrile mixture (8 mL). Selectfluor (61 mg, 0.17 mmol) was added in one portion and the temperature was raised to 60 °C. The reaction was allowed to stir for 20 h and was monitored by TLC. Upon completion the reaction mixture was extracted with ether (5 x 25 mL), dried over MgSO₄, and the solvent was removed *in vacuo*. After column chromatography using silica gel (2:1 ether/hexane) there was obtained 13.2 mg (71%) of rearranged fluoroalcohol **18**. *Control experiment.* The iodofluoride **9** (52 mg, 0.14 mmol) was dissolved in a 1:1 water/acetonitrile mixture (16 mL) and the temperature was raised to 60 °C. After 16 hours the reaction was

Supplementary: Krow, G. R., et al. "Novel Selectfluor and Deoxo-Fluor Mediated ... S-5 monitored by both ^1H NMR and by TLC. Both analyses revealed that no reaction had occurred and there was a quantitative recovery of unreacted iodofluoride **9**.

Preparation of *N*-(Benzyloxycarbonyl)-5-*syn*,6-*anti*-dihydroxy-5-*anti*-methyl-2-azabicyclo[2.1.1]hexane (19**).** *Method A.* By the general method Iodoalcohol **10** (150 mg, 0.40 mmol) in nitromethane (10 mL) with HgF_2 (238 mg, 1.0 mmol) at 60 °C for 16 h afforded after chromatography using silica gel (2:1 ethyl acetate/hexane) 37.5 mg (37%) of the rearranged diol **19** at $R_f = 0.5$ (4:1 ethyl acetate/hexane): ^1H NMR (CDCl_3 , 400 MHz, 60 °C) δ 7.5 (m, 5H), 5.25 (d, $J = 9$ Hz, 1H), 5.15 (d, $J = 9$ Hz, 1H), 3.95 (d, $J = 7$ Hz, 1H), 3.85 (s, 1H), 3.5 (dd, $J = 9, 1$ Hz, 1H), 3.25 (d, $J = 9$ Hz, 1H), 2.4 (dd, $J = 7, 1$ Hz, 1H), 2.05 (br s, 1H), 1.90 (br s, 1H), 1.82 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 157.8, 137.3, 129.1, 73.3, 70.2 and 69.1, 67.8, 65.1, 47.5, 45.8 and 44.1, 17.6; HRMS m/z 286.1055, calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_4\text{Na}$ (MNa^+) 286.1054. *Method B.* By the general method iodoalcohol **10** (101 mg, 0.270 mmol) in 1:1 water/acetonitrile (8 mL) with Selectfluor (239 mg, 0.675 mmol) at 60 °C for 20 h afforded after chromatography on silica gel (2:1 ethyl acetate/hexane) 44 mg (62%) of the rearranged diol **19**.

Attempted Reactions of Iodofluoride **9 and Iodoalcohol **10** with HgCl_2 and $\text{Hg}(\text{OAc})_2$.** ($\text{HgCl}_2/\text{nitromethane}$) Iodofluoride **9** (52 mg, 0.14 mmol) in nitromethane (6 mL) and HgCl_2 (114 mg, 0.42 mmol) were heated to 80 °C for 16 h. No reaction of starting material was observed. Iodoalcohol **10** (67 mg, 0.21 mmol) in nitromethane (6 mL) and HgCl_2 (171 mg, 0.63 mmol) also failed to react under the above conditions. [$\text{Hg}(\text{OAc})_2/\text{nitromethane}$] Iodofluoride **9** (52 mg, 0.14 mmol) in nitromethane (6 mL) and $\text{Hg}(\text{OAc})_2$ (134 mg, 0.42 mmol) were heated to 80 °C for 16 h. No reaction was

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 observed. Iodoalcohol **10** (67 mg, 0.21 mmol) in nitromethane (6 mL) and Hg(OAc)₂ (202 mg, 0.63 mmol) were heated to 80 °C for 16 h. No reaction of starting material was observed. [Hg(OAc)₂/HOAc] Iodofluoride **9** (52 mg, 0.14 mmol) in glacial acetic acid (5 mL) and Hg(OAc)₂ (134 mg, 0.42 mmol) were heated to 80 °C for 16 h. No reaction of starting material was observed. Iodoalcohol **10** (67 mg, 0.21 mmol) in glacial acetic acid (5 mL) and Hg(OAc)₂ (202 mg, 0.63 mmol) were heated to 80 °C for 16 h. No reaction was observed.

***N*-(Benzyloxycarbonyl)-5-*syn*-fluoro-6-*anti*-hydroxy-2-azabicyclo[2.1.1]hexane (**14**).**

By Method B, to iodofluoride **7** (181 mg, 0.5 mmol) in CH₃CN (6 mL) there was added Selectfluor (354 mg, 1 mmol). After 5 min H₂O (5 mL) was added and the solution was stirred for an additional 12 h at room temperature, extracted with ether (3 x 100 mL), and dried over MgSO₄. The customary workup and chromatography on silica gel (1:1 hexane/ether) afforded 105.4 mg (84%) of known fluoroalcohol **14** at R_f = 0.36 (1:3 hexane/ether).^{2b}

***N*-(Benzyloxycarbonyl)-5-*anti*,6-*syn*-dihydroxy-2-azabicyclo[2.1.1]hexane (**20**).** By the general procedure of Method B, the iodoalcohol **8** (179.5 mg, 0.5 mmol) in 6:5 CH₃CN/water (11 mL) and Selectfluor (354 mg, 1 mmol) after chromatography (1:2 hexane/ether) afforded 85 mg (68%) of diol **20** at R_f = 0.35 (1:4 hexane/ether): ¹H NMR (CDCl₃, 400Hz) δ 7.24 (m, 5H), 5.07 (s, 2H), 4.65(s, 1H), 4.23 (d, J = 6.9 Hz, 1H), 3.82(s, 1H), 3.23 (d, J = 9.0 Hz, 1H), 3.12 (d, J = 9.0 Hz, 1H), 2.71 (m, 1H), 2.0-2.7 (br, 2H); ¹³C NMR (CDCl₃, 400 Hz) δ 157.2, 72.6 (two C), 69.4 (two C), 67.1, 66.2, 48.1, 44.5; HRMS *m/z* 272.0902, calcd for C₁₃H₁₅NO₄Na (MNa⁺) 272.0898.

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Preparation of *N*-(Benzyloxycarbonyl)-5-*endo*-chloro-6-*exo*-iodo-2-azabicyclo[2.2.0]-hexane (11). The olefin **4** (1.5 g, 7.0 mmol) was dissolved in methylene chloride (25 mL) and the solution was cooled to 0 °C. Iodine monochloride (1.4 g, 8.3 mmol) was dissolved in methylene chloride (25 mL) and was added dropwise to the stirred solution at 0 °C. After 10 hours the reaction had reached completion and was diluted with 25 mL of methylene chloride. The solution was washed with 10% Na₂S₂O₃ (2 x 25 mL), deionized H₂O (2 x 25 mL), dried over MgSO₄, and the solvent was removed *in vacuo*. Following chromatography 1.9 g (72%) of the iodochloride **11** was obtained at R_f = 0.48 (1:1 hexane/ether): ¹H NMR (400 MHz, CDCl₃, 60 °C), δ 7.5 (m, 5H), 5.02 (d, *J* = 9 Hz, 1H), 4.99 (d, *J* = 9 Hz, 1H), 4.75 and 4.7 (d, *J* = 6 Hz, 1H), 4.55 (d, *J* = 4 Hz, 1H), 4.50 (d, *J* = 9 Hz, 1H), 4.40 (dd, *J* = 9, 3 Hz, 1H), 4.11 (dd, *J* = 7, 6 Hz, 1H), 3.22 (ddd, *J* = 7, 4, 3 Hz, 1H); ¹³C NMR δ 155.2, 137.1, 128.7, 128.4, 128.1, 67.8, 67.2, 62.9 and 62.5, 51.3 and 50.0, 38.2, 25.1 and 24.6; HRMS *m/z* 377.9746, calcd for C₁₃H₁₄NO₂ICl (MH⁺) 377.9752.

Preparation of *N*-Benzyloxycarbonyl-5-*syn*-chloro-6-*anti*-hydroxy-2-azabicyclo[2.1.1]hexane (21). By the General Method B, the iodochloride **11** (382 mg, 1.0 mmol) was dissolved in a 1:1 water/acetonitrile mixture (20 mL), Selectfluor (1.07 g, 3.05 mmol) was added in one portion to the mixture, and the temperature was raised to 35 °C for 16 h. Following the usual workup and chromatography, 200 mg (75%) of the rearranged chloroalcohol **21** was obtained at R_f = 0.07 (1:1 ether/hexane): ¹H NMR (400 MHz, CDCl₃, 60 °C) δ 7.5 (m, 5H), 5.35 (d, *J* = 9 Hz, 1H), 5.25 (d, *J* = 9 Hz, 1H), 4.95 (s, 1H), 4.50 (d, *J* = 7 Hz, 1H), 4.30 (s, 1H), 3.70 (d, *J* = 9 Hz, 1H), 3.40 (d, *J* = 9 Hz,

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1H), 2.95 (d, $J = 7$ Hz, 1H); ^{13}C NMR δ 157.2, 137.1, 128.7, 128.4, 128.1, 76.8, 68.2, 67.9, 58.5, 51.3, and 45.3; HRMS m/z 268.0725, calcd for $\text{C}_{13}\text{H}_{15}\text{ClINO}_3$ 268.0740.

Experiment with Acetic Acid. The iodochloride **11** (382 mg, 1.0 mmol) was dissolved in a 1:1 acetic acid/water mixture (10 mL)¹⁵ and the temperature was raised to 95 °C (reflux) for 2 days while being monitored by both ^1H NMR and by TLC. Both analyses indicated that no reaction had occurred; there was complete retention of the iodochloride **11**.

Experiment with ammonium chloride. The iodochloride **11** (255 mg, 0.67 mmol) was dissolved in 1:1 acetonitrile/water (8 mL). Ammonium chloride (108 mg, 2.0 mmol) was added in one portion and the temperature was raised to 60 °C for 16 h. Monitoring of the reaction by both ^1H NMR and by TLC indicated that no reaction of iodochloride **11** occurred.

Experiment with sulfuric acid. The iodochloride **11** (100 mg, 0.265 mmol) was dissolved in 1:1 acetonitrile/water (5 mL) and Selectfluor (281 mg, 0.795 mmol) was added. The pH as measured by pHDrion paper was about 7. The mixture was heated at 35 °C for 24 h to afford chloroalcohol **21**; the reaction mixture had pH = 1. To see if the rearrangement was proton induced the iodochloride **11** (100 mg, 0.265 mmol) was dissolved in 1:1 acetonitrile/water (5 mL) and 0.009 M sulfuric acid (140 μL) was added to make a pH = 1. The reaction was heated to 35 °C for 12 h. Workup afforded quantitative recovery of iodochloride **11**. There was also no cleavage of the benzyl protecting group under these conditions.

Attempted Reaction of Selectfluor with *N*-(Benzyloxycarbonyl)-6-*exo*-bromo-5-*endo*-hydroxy-2-azabicyclo[2.2.0]hexane (12). According to Method B, the bromoalcohol^{2c} **12** (104 mg, 0.333 mmol) was dissolved in 1:1 water/acetonitrile (16

Supplementary: Krow, G. R., et al. "Novel Selectfluor and Deoxo-Fluor Mediated ... S-9 mL). Selectfluor (354 mg, 1 mmol) was added in one portion to the solution and the temperature was raised successively after 16 h intervals from 40 °C to 60 °C and then to 80 °C. Monitoring of the mixture by both ¹H NMR and by TLC showed that no reaction of bromide **12** occurred.

Attempted Reaction of Selectfluor with *N*-(Benzyloxycarbonyl)-5-*endo*-bromo-6-*exo*-phenylselenyl-2-azabicyclo[2.2.0]hexane (13). According to Method B, the bromoselenide **13** (94 mg, 0.208 mmol) was dissolved in 1:1 water/acetonitrile (16 mL). Selectfluor (221 mg, 0.624 mmol) was added in one portion to the solution and the temperature was raised successively after 16 h intervals from 40 °C to 60 °C and then to 80 °C. Monitoring of the mixture by both ¹H NMR and by TLC showed that no reaction of selenide **13** occurred.

Preparation of *N*-(Ethoxycarbonyl)-5-*syn*-bromo-6-*anti*-fluoro-2-azabicyclo[2.1.1]hexane (26). General Procedure for Reactions of N,N-di(methoxyethyl)sulfur trifluoride (Deoxo-Fluor). To a solution of 5-*endo*-bromo-6-*exo*-hydroxy-2-azabicyclo[2.2.0]hexane^{2f} **23** (125.0 mg, 0.5 mmol) in dry CH₂Cl₂ (20 mL) under argon at -78 °C Deoxo-Fluor (221 mg, 1.0 mmol) was added dropwise. The mixture was warmed slowly and stirred for 2 h at room temperature, then refluxed for 12 h. The reaction was quenched with water (5 mL) and the aqueous layer was extracted with CH₂Cl₂ (4 x 10 mL). The combined organic layer was washed with water (5 mL), brine (5 mL) and was dried over sodium sulfate. Removal of solvent in *vacuo* and flash chromatography (1:1 hexane/ether) gave 76 mg (60%) of bromofluoride **26** at R_f = 0.43 (1:2 hexane/ether): ¹H NMR (400 Hz) δ = 5.07 (d, J = 60.62 Hz, 1H), 4.82 (m, 1H), 4.43

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(b, 1H, H₆), 4.12 (q, J = 7.18 Hz, 2H, CH₂ CH₃), 3.57 (b, 1H, H₃), 3.31 (d, J = 10.27 Hz, 1H), 3.06 (b, 1H), 1.21 (br, 3H); ¹H NMR (400 Hz, DMSO-d₆, 70 °C), δ 5.31 (d, J = 60.5 Hz, 1H), 4.99 (m, 1H), 4.56 (d, J = 7.2 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.44 (br, 2H), 3.24 (b, 1H), 1.23 (t, J = 7.1 Hz, 3H); ¹³C NMR (400 Hz) δ 155.6, 93.8 (d, J = 216.0 Hz), 66.3 and 66.1, 61.6, 49.2 and 49.0, 47.9, 45.4 and 45.1, 14.6; HRMS *m/z* 273.9847 and 275.9839, calcd for C₈H₁₁NO₂FBr⁷⁹Na (MBr⁷⁹Na⁺) 273.9854 and C₈H₁₁NO₂FBr⁸¹Na (MBr⁸¹Na⁺) 275.9834.

Preparation of *N*-(Benzyloxycarbonyl)-6-*exo*-hydroxy-5-*endo*-methyl-2-azabicyclo[2.2.0]hexane (24). Copper(I) iodide (373 mg, 1.9 mmol) was placed in an oven-dried vial under argon and dry diethyl ether (5 mL) was added. The slurry was cooled to 0 °C and methyllithium (2.44 mL, 3.8 mmol) was added dropwise until the end point was reached. When methyllithium is added to the slurry the color immediately turns bright orange, supposedly “methylcopper”. As more methyllithium is gradually added to the mixture the color fades and the endpoint is a clear to light tan liquid in which the dissolution of all the copper iodide is observed. *N*-(Benzyloxycarbonyl)-3-aza-7-oxatricyclo[4.1.0.0^{2,5}]heptane⁹ **22b** (150 mg, 0.65 mmol) under argon and in dry diethyl ether (5 mL) was added dropwise to the cuprate at 0 °C. The reaction was stirred for 3 h while the temperature gradually warmed to 25 °C. The reaction was quenched with saturated NH₄Cl (15 mL), extracted with diethyl ether (3 x 20 mL), dried over MgSO₄, and the solvent was removed in *vacuo*. Column chromatography afforded 88.1 mg (55 %) of the alcohol **24** at R_f = 0.10 (1:1 ether/hexane): ¹H NMR (400 MHz, CDCl₃, 60 °C) δ 7.5 (m, 5H), 5.25 (d, J = 9 Hz, 1H), 5.15 (d, J = 9 Hz, 1H), 4.17 (d, J = 5 Hz, 1H), 3.97

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(d, $J = 5$ Hz, 2H), 3.87 (d, $J = 5$ Hz, 1H), 2.75 (dq, $J = 8, 5$ Hz, 1H), 2.41 (ddd, $J = 8, 7.3, 5$ Hz, 1H), 1.30 (br. s, 1H), 1.11 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 137.1, 128.9, 128.7, 128.2, 80.5 and 79.5, 67.9, 67.1, 50.3 and 49.7, 41.1 and 39.8, 29.8, 14.2; HRMS m/z 270.1091, calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_3\text{Na}$ (MNa^+) 270.1101.

Attempted Reaction of Alcohol 24 with Selectfluor. The alcohol **24** (45 mg, 0.18 mmol) was dissolved in 1:1 water/acetonitrile (8 mL) and Selectfluor (193 mg, 0.55 mmol) was added. The temperature was raised successively after 16 h intervals from 40 °C to 60 °C and then to 80 °C. Monitoring of the mixture by both ^1H NMR and by TLC showed that no reaction of alcohol **24** occurred.

Preparation of *N*-(Benzyloxycarbonyl)-6-*exo*-hydroxy-5-*endo*-phenyl-2-azabicyclo-[2.2.0]hexane (25). Bromobenzene (273 mg, 1.74 mmol) was placed in an oven dried vial under argon and dry diethyl ether (3 mL) was added. The solution was cooled to -78 °C, *n*-butyllithium (1.08 mL, 1.74 mmol) was added dropwise over 3 min, and the reaction was allowed to stir at -78 °C for an additional 10 min. The solution was then added dropwise to an oven dried vial containing copper(I) iodide (165 mg, 0.87 mmol) under argon in dry diethyl ether (3 mL) at 0 °C. After all the phenyllithium was added the resulting solution was allowed to stir for an additional 5 min at 0 °C. The epoxide **22b** (68 mg, 0.29 mmol) under argon and in dry diethyl ether (3 mL) was added dropwise to the cuprate at 0 °C. The reaction was stirred for 3 h and over that time period the temperature gradually warmed to 25 °C. The reaction was quenched with saturated NH_4Cl (15 mL), extracted with diethyl ether (3 x 20 mL), dried over MgSO_4 , and the solvent was removed *in vacuo*. After column chromatography using silica gel, there was

Supplementary: Krow, G. R., et al. "Novel Selectfluor and Deoxo-Fluor Mediated ...S-12 obtained 60.9 mg (68%) of the alcohol **25** at $R_f = 0.10$ (1:1 ether/hexane): ^1H NMR (400 MHz, CDCl_3 , 60 °C) δ 7.5-6.9 (m, 10H), 5.25 (d, $J = 9$ Hz, 1H), 5.15 (d, $J = 9$ Hz, 1H), 4.72 (d, $J = 6$ Hz, 1H), 4.48 (d, $J = 5$ Hz, 1H), 4.15 and 4.08 (d, $J = 9.4$ Hz, 1H), 3.87 (dd, $J = 9.4$, 3 Hz, 1H), 3.80 (br, 1H), 3.26 (ddd, $J = 7$, 5, 3 Hz, 1H), 2.8-2.4 (br, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 156.2, 138.2, 136.7, 128.8, 128.4, 128.1, 127.2, 126.7, 126.3, 67.4, 66.9, 52.5, 51.5, 50.8, 30.1; HRMS m/z 310.1424, calcd for $\text{C}_{19}\text{H}_{20}\text{NO}_3$ 310.1438.

Preparation of *N*-(Benzyloxycarbonyl)-5-*anti*-fluoro-6-*syn*-methyl-2-azabicyclo[2.1.1]hexane (27). To alcohol **24** (90 mg, 0.36 mmol) in CH_2Cl_2 (25 mL) under argon at -78 °C Deoxo-Fluor reagent (300 μL , 0.56 mmol) was added dropwise over a 5 min period. After 4 h the reaction was warmed to 25 °C and allowed to stir for an additional 5 h. The reaction was quenched with H_2O (20 mL), extracted with CH_2Cl_2 (3 x 20 mL), dried over MgSO_4 and the solvent was removed in *vacuo*. Following chromatography 67.5 mg (75%) of the rearranged fluoride **27** was obtained at $R_f = 0.65$ (4:1 ethyl acetate/hexanes): ^1H NMR (400 MHz, CDCl_3 , 60 °C), δ 7.5 (m, 5H), 5.25 (d, $J = 9$ Hz, 1H), 5.15 (d, $J = 9$ Hz, 1H), 4.7 (d, $J = 62$ Hz, 1H), 4.33 (d, $J = 7$ Hz, 1H), 3.52 (d, $J = 9$ Hz, 1H), 3.38 (dd, $J = 9$, 1 Hz, 1H), 3.25 (m, 1H), 2.75 (m, 1H), 0.88 (d, $J = 7$ Hz, 3H); ^{13}C NMR δ 156.2, 137.1, 128.7, 128.4, 128.1, 96.2 ($J_{\text{F,C}} = 250$ Hz), 67.3, 64.5, 46.1, 43.9, 39.9 and 39.6, 9.8; HRMS m/z 250.1224, calcd for $\text{C}_{14}\text{H}_{17}\text{NO}_2\text{F}$ (MH^+) 250.1238.

Preparation of *N*-Benzyloxycarbonyl-5-*anti*-fluoro-6-*syn*-phenyl-azabicyclo[2.1.1]-hexane (28). According to the above procedure, alcohol **25** (60 mg, 0.2 mmol) was dissolved in 5 mL of CH_2Cl_2 under argon and cooled to -78 °C. The Deoxo-Fluor reagent (155 μL , 0.30 mmol) was added dropwise to the solution over 5 min. After 2 h, the

Supplementary: Krow, G. R., et al. "Novel Selectfluor and Deoxo-Fluor Mediated ...S-13
reaction was warmed to 25 °C and allowed to stir for an additional 2 h. The reaction was
quenched with H₂O (5 mL), extracted with CH₂Cl₂ (3 x 20 mL) and worked up as above
to afford after chromatography 46.2 mg (77%) of the rearranged phenylfluoride **28** at R_f
= 0.4 (4:1 hexanes/acetone): ¹H NMR (400 MHz, CDCl₃, 60 °C) δ 7.5-6.9 (m, 10H), 5.15
(d, *J* = 9 Hz, 1H), 5.05 (d, *J* = 9 Hz, 1H), 4.87 (d, *J* = 62 Hz, 1H), 4.86 (br, 1H), 4.28 (br,
1H), 3.30 (d, *J* = 9 Hz, 1H), 3.21 (d, *J* = 9 Hz, 1H), 3.13 (d, *J* = 7 Hz, 1H); ¹³C NMR δ
156.5, 138.7, 137.1, 128.6, 128.3, 128.0, 127.2, 126.8, 126.1, 96.5 (*J*_{F,C} = 255 Hz), 67.4,
53.5, 52.5, 51.8, 39.1; HRMS *m/z* 312.1384, calcd for C₁₉H₁₉NO₂F (MH⁺) 312.1395.

STANDARD 1H OBSERVE

```

expt stdh
SAMPLE
date Jul 11 2003 DEC. & VT 299.966
solvent CDCl3 dn
f1le ACQUISITION exp dpr 30
sfreq 299.966 dm 0
in HI dam mn
at 3.744 dmf 200
np 29952 dres C
sv 4000.0 1.0
fb 2000 homo n
bs 15 1b PROCESSING -8.60
ss 2 0T 0.240
tpwr 57 0T not used
pv 7.0 0T not used
d1 0 wttle
nt 0 proc ft
ct 16 fn not used
alock 16 math
gain 5 weff
bain not used wexp
11 in n wds
dn y wnt
hs DISPLAY -500.0 nm
sp -500.0
wp 4000.0
vs 200
sc 0
hzam 250
ls 16.00
rfi 500.00
rfp 500.0
th 0
ins 20
nm cdc ph 100.000
  
```

11 10 9 8 7 6 5 4 3 2 1 -0 -1 ppm

@ 25°C

ppm

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F2 - Acquisition Parameters
 Date_ 20030827
 Time 11.37
 INSTRUM spect
 PROBRD 5 mm QNP 1H/13
 PULPROG zgpg60
 TD 65536
 SOLVENT CDCl3
 NS 600
 DS 0
 SMH 25125.629 Hz
 FTRES 0.383187 Hz
 AQ 1.3042164 sec
 RG 2580.3
 DM 19.900 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 d12 0.0002000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 12.00 usec
 PL1 2.00 dB
 SFO1 100.5961334 MHz

===== CHANNEL f2 =====
 CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 0.00 dB
 PL12 20.00 dB
 PL13 25.00 dB
 SFO2 400.0216001 MHz

F2 - Processing parameters
 SI 32768
 SF 100.5850690 MHz
 WDW EM
 SSB 0
 LB 4.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters
 CX 20.00 cm
 CY 12.50 cm
 F1P 215.000 ppm
 F1 21625.79 Hz
 F2P -5.000 ppm
 F2 -502.92 Hz
 PRCH 11.00000 ppm/cm

F2 - Acquisition parameters
 Date_ 20030826
 Time 15.43
 INSTRUM spect
 PROBRD 5 mm QNP 1H/13
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 600
 DS 0
 SM 25125.629 Hz
 FIDRES 0.38387 Hz
 AQ 1.3042164 sec
 RG 5160.6
 IN 19.900 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 d12 0.00002000 sec

===== CHANNEL f1 =====
 NUC1 13C
 P1 12.00 usec
 PL1 2.00 dB
 SFO1 100.5961334 MHz

===== CHANNEL f2 =====
 CDPFRC2 waltz16
 NUC2 1H
 P2 100.00 usec
 PL2 0.00 dB
 PL12 20.00 dB
 PL13 25.00 dB
 SFO2 400.0216001 MHz

F2 - Processing parameters
 SI 32768
 SF 100.5850690 MHz
 NDM EM
 SSB 0
 LB 4.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters
 CX 20.00 cm
 CY 12.50 cm
 F1P 215.000 ppm
 F1 21625.79 Hz
 F2P -5.000 ppm
 F2 -502.92 Hz
 PPMCH 11.00000 ppm/cm

18

19

130	F2: 500.130	SWH: 6006	PD: 1.0 sec	OE1: 2500.6	NA: 16	LB: 0.0	PTSID: 16384	USER: - DATE: Sun Aug 8 14:37:58
S		PW: 8.0 usec						WinNMR - Scholastic

19

20

20

F2 - Acquisition Parameters

Date_ 20030726
 Time 15.16
 INSTRUM spect
 PROBRD 5 mm QNP 1H/13
 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl3
 NS 600
 DS 0
 SWH 25125.629 Hz
 FIDRES 0.383387 Hz
 AQ 1.3042164 sec
 RG 8192
 DW 19.900 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec
 d11 0.03000000 sec
 d12 0.0002000 sec

===== CHANNEL f1 =====

NUC1 13C
 P1 12.00 usec
 PL1 2.00 dB
 SFO1 100.5961334 MHz

===== CHANNEL f2 =====

CPDPRG2 waltz16
 NUC2 1H
 PCPD2 100.00 usec
 PL2 0.00 dB
 PL12 20.00 dB
 PL13 25.00 dB
 SFO2 400.0216001 MHz

F2 - Processing parameters

SI 32768
 SF 100.5650590 MHz
 WDW EM
 SSB 0
 LB 4.00 Hz
 GB 0
 PC 1.40

1D NMR plot parameters

CX 20.00 cm
 F1P 234.884 ppm
 F1 23625.79 Hz
 F2P -14.911 ppm
 F2 -1499.84 Hz
 DPMVW 17.00074

11

F2 - Acquisition Parameters
 Date_ 20040109
 Time 11.28
 INSTRUM spect
 PROBD 5 mm PABO BB-
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 26
 DS 0
 SMH 4006.410 Hz
 FIDRES 0.061133 Hz
 AQ 8.1789427 sec
 RG 128
 INW 124.800 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.00 usec
 PL1 0.00 dB
 SFO1 400.0220668 MHz

F2 - Processing parameters
 SI 32768
 SF 400.0200667 MHz
 WDW GM
 SSB 0
 LB -0.50 Hz
 GB 0.1
 PC 1.00

1D NMR plot parameters
 CX 20.00 cm
 CY 18.00 cm
 P1P 10.008 ppm
 F1 4003.30 Hz
 F2P -0.008 ppm
 F2 -3.11 Hz
 PPMCH 0.50078 ppm/cm
 HZCH 200.32051 Hz/cm

Pulse Sequence: szpu1
Solvent: CDCl3
Ambient temperature
INOVA-300 "nmr300"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.015 sec
Width 18059.0 Hz
64 repetitions
DSSERVE C13, 75.431129 MHz
DECOUPLE H1, 299.9858744 MHz
Power 34 dB
continuously on
VALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 48 min, 11 sec

21

F2 - Acquisition Parameters
 Date_ 20040113
 Time 10.52
 INSTRUM spect
 PROBD 5 mm PABO BB-
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 0
 SFR 4789.272 Hz
 FTRES 0.073078 Hz
 AQ 6.842086 sec
 RG 1024
 DM 104.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUCL 1H
 P1 15.60 usec
 PL 0.00 dB
 SFO1 400.0220001 MHz

F2 - Processing parameters
 SI 32768
 SF 400.019929 MHz
 WDW EM
 SSB 0
 LB 0.20 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 20.00 cm
 CY 12.50 cm
 FLP 10.000 ppm
 FL 4000.20 Hz
 FZP 0.000 ppm
 F2 0.00 Hz
 PRNCH 0.50000 ppm/cm
 HZCH 200.00999 Hz/cm

Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 INOVA-300 "nmr300"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.015 sec
 Width 15641.6 Hz
 16000 repetitions
 OBSERVE C13, 75.431129 MHz
 DECOUPLE H1, 299.9650744 MHz
 Power 34 dB
 continuously on
 VOLTAGE modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 12 hr, 33 min, 3 sec

26

solvent: CDCl_3
 ambient temperature
 OVA-300 "nmr300"
 relax. delay 1.000 sec
 pulse 45.0 degrees
 eq. time 2.500 sec
 width 3599.9 Hz
 repetitions
 F1, 299.9843744 MHz
 TA PROCESSING
 esol. enhancement 0.4 Hz
 gauss apodization 0.240 sec
 size 32768
 total time 0 min, 35 sec

v1se Sequence: szpu1
 Solvent: CDCl3
 Ambient temperature
 NOVA-300 "nmr300"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.015 sec
 Width 15841.6 Hz
 128 repetitions
 RESERVE C13, 75.431123 MHz
 ECDUPL H1, 299.9658744 MHz
 Power 34 dB
 continuously on
 VALTZ-16 modulated
 ATA PROCESSING
 Line broadening 1.0 Hz
 T size 65536
 Total time 12 min, 2 sec

25

INSTRUM spect
PROCED 5 mm PABO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SME 4006.410 Hz
PULPROS 0.061133 Hz
AQ 8.1789427 sec
RG 2896.3
TM 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

----- CHANNEL F1 -----
NUC1 1H
P1 9.80 usec
PL1 0.00 dB
SFO1 400.0220201 MHz

F2 - Processing parameters
SI 32768
SF 400.0200200 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

ID NMR plot parameters
CX 20.00 cm
CY 12.50 cm
PLP 8.000 ppm
PL 3200.16 Hz
F2P 1.000 ppm
F2 400.02 Hz
FPCN 0.35000 ppm/cm
HZCM 140.00700 Hz/cm

ACQUISITION
 sw 15841.6
 at 1.615
 np 57500
 fb 5000
 bs 64
 dl 1.000
 nt 1000
 ct 1800

TRANSMITTER
 tn C13
 srfq 75.438
 tot -394.6
 tpvr 56
 pw 3.900

DECOUPLER
 dn H1
 dot 0
 dm yyy
 dnm w
 dpr 34
 dmr 7605

SPECIAL
 temp not used
 gain not used
 spin 20
 hst 9.000
 pw90 7.000
 alfa 20.000

FLAGS
 n
 n
 y
 nm

PROCESSING
 lb 1.00
 fn not used
 display -754.6
 sp 15841.6
 wp 754.6
 rfi 0
 rfp 63.3
 lp -126.6

PLOT
 wc 250
 sc 0
 vs 6355
 th 2
 at no ph

Pulse Sequence: s2pul
 Solvent: CCl₃
 Ambient temperature
 INOVA-300 "nuc300"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.815 sec
 Width 15841.6 Hz
 448 repetitions
 OBSERVE C13, 75.431129 MHz
 DECOUPLE H1, 299.3858744 MHz
 Power 34 dB
 continuously on
 VOLTAGE modulated
 DATA PROCESSING
 Line broadening 1.0 Hz
 FT size 65536
 Total time 35 min, 48 sec

27

28

3.31728
3.29470
3.22387
3.21553
3.14780
3.12829

5.09408
5.06420
4.94622
4.87562
4.85205
4.79184
4.28213

7.36669
7.34100
7.30006
7.27835
7.26329
7.26164
7.24584
7.20809
7.19187
7.15789
7.12375
7.07576
7.06496

INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 0
SMH 4006.410 Hz
FIDRES 0.061133 Hz
AQ 8.1789427 sec
RG 2896.3
IN 124.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.80 usec
PL1 0.00 dB
SFO1 400.0220201 MHz

F2 - Processing parameters
SI 32768
SF 400.0200200 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 12.50 cm
FIP 8.000 ppm
F1 3200.16 Hz
F2 1.000 ppm
F2 400.02 Hz
PPMCH 0.35000 ppm
HZCM 140.00700 Hz/1

28

ACQUISITION
 sw 15041.6
 at 1.015
 np 57500
 qb 5000
 hs 84
 di 1.000
 nt 1.000
 ct 1.000

TRANSMITTER
 tn C13
 frq 75.420
 tot -304.6
 tpr 56
 pw 3.000
 deCOUPLER
 dn H1
 cor 0
 dm 0
 dnm 24
 dpr 7000
 der

SPECIAL
 temp not used
 gain not used
 spin 20
 hst 0.000
 mode 7.000
 a17a 20.000
 FLAG

PROCESSING
 lb 1.00
 fn not used
 display -754.6
 sp 15041.6
 wp 754.6
 rfp 0
 rp 82.2
 ip -120.6
 plot 250
 wc 0
 sc 0
 vs 0
 th 0
 a1 no ph 2