JOC*Article*

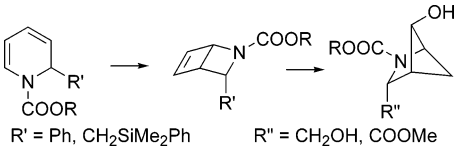
The Rearrangement Route to 3-Carboxy- and 3-Hydroxymethyl-2-azabicyclo[2.1.1]hexanes: 3,5-Methanoprolines

Grant R. Krow,* Guoliang Lin, and Fang Yu

Department of Chemistry, Temple University, Philadelphia, Pennsylvania 19122

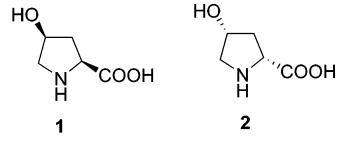
grantkrow@aol.com

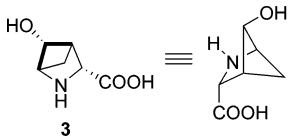
Received September 8, 2004



Improved stereocontrolled syntheses of 5-*anti*-hydroxy-3-*exo*-methoxycarbonyl-2-azabicyclo[2.1.1]-hexanes have been effected from pyridine. The key step in the electrophilic addition−rearrangement of 2-azabicyclo[2.2.0]hex-5-ene precursors incorporates either a 3-*endo*-phenyl group, as an acid precursor, or a 3-*endo*-phenyldimethylsilylmethyl group, as a potential hydroxymethyl and acid precursor.

One strategy in the search for bioactive molecules is to incorporate key pharmacophoric units into inflexible structures, such as fused or bridged small rings.[1] Hydroxyprolines are representative of such units that have proven to be valuable scaffolds for drug discovery.[2−12] Among cis hydroxyprolines, the *allo*-4-hydroxy-L-proline **1** is found in the lipopeptide component of the cytotoxic[13] majusculamide D and the immunosuppressive antileukemic[14] microcolin A, which also has protein kinase C inhibitory properties.[15] The enantiomeric *allo*-4-hydroxy-D-proline **2** has been isolated from the hydrolysate of





etamycin, a broad-spectrum antibiotic.[16] We require methanobridged proline structures related to **3** and its enantiomer as building blocks for projects designed to prepare conformationally constrained analogues of substituted prolines and pyrrolidines.[17] There is a potential for both the 5-hydroxy and 3-methoxycarbonyl groups of **3** to serve as useful functional groups for preparation of

(1) For leading references with bridged pyrrolidines, see: (a) Bunch, L.; Liljefors, T.; Greenwood, J. R.; Frydenvang, K.; Brauner-Osborne, H.; Krogsgaard-Larsen, P.; Madsen U. *J. Org. Chem.* **2003**, *68*, 1489. (b) Hart, B. P.; Rapoport, H. *J. Org. Chem.* **1999**, *64*, 2050. (c) Piotroski, D. W. *Synlett* **1999**, 1091. (d) Esslinger, C. S.; Koch, H. P.; Kavanaugh, M. P.; Philips, D. P.; Chamberlin, A. R.; Thompson, C. M.; Bridges, R. J. *Bioorg. Med. Chem. Lett.* **1988**, *8*, 3101. (e) Koch, H. P.; Kavanaugh, M. P.; Esslinger, C. S.; Zerangue, N.; Humphrey, J. M.; Amara, S. G.; Chamberlain, A. R.; Bridges, R. J. *Mol. Pharmacol.* **1999**, *56*, 1095. (f) Mapelli, C.; van Halbeek, H.; Stammer, C. H. *Biopolymers* **1990**, *29*, 407. (g) Bell, E. A.; Qureshi, M. Y.; Pryce, R. J.; Janzen, D. H.; Lemke, P.; Clardy, J. *J. Am. Chem. Soc.* **1980**, *102*, 1409. (h) Han, W.; Pelletier, J. C.; Mersinger, L.; Ketner, C. A.; Hodge, C. N. *Org. Lett.* **1999**, *1*, 1875. (i) Park, T. H.; Ha, Y. H.; Jeong, D. Y. Patent Application WO 98-KR246 19989898; *Chem. Abstr*. **1999**, *130*, 182388.

(2) For a review of naturally occurring proline analogues, see: Mauger, A. B. *J. Nat. Prod.* **1996**, *59*, 1205.

(3) For a review of 4-hydroxy-L-proline as a building block, see: Remuzon, P. *Tetrahedron* **1996**, *52*, 13803.

(4) For generation of nonproteinogenic amino acids from 4-hydroxyproline, see: (a) Cheng, W.-C.; Liu, Y.; Wong, M.; Olmstead, M. M.; Lam, K. S.; Kurth, M. J. *J. Org. Chem.* **2002**, *67*, 5673. (b) Webb, T. R.; Eigenbrot, C. *J. Org. Chem.* **1991**, *56*, 3009. (c) Tamaki, M.; Han, G.; Hruby, V. J. *J. Org. Chem.* **2001**, *66*, 1038.

(5) For aminonucleotides based on 4-hydroxyprolinol, see: (a) Reed, M. W.; Lukhtanov, E. A.; Gorn, V. V.; Lucas, D. D.; Zhou, J. H.; Pai, S. B.; Cheng, Y.; Meyer, R. B., Jr. *J. Med. Chem.* **1995**, *38*, 4587. (b) Peterson, M. L.; Vince, R. *J. Med. Chem.* **1991**, *34*, 2787.

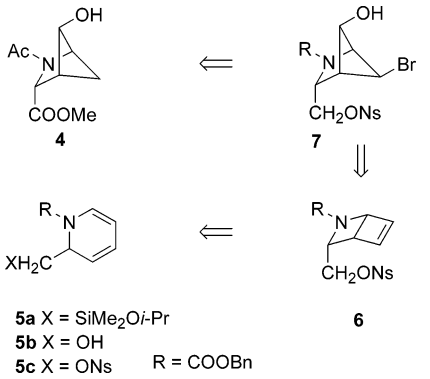
(6) For peptide nucleic acids from 4-hydroxyproline, see: (a) Lowe, G.; Vilaivan, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 547. (b) Lowe, G.; Vilaivan, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 555. (c) Westwood, N. B.; Walker, R. T. *Tetrahedron* **1998**, *54*, 13391. (d) Lowe, G.; Vilaivan, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 539. (e) Jordan, S.; Schwemler, C.; Kosch, W.; Kretschmer, A.; Schwenner, E.; Stropp, U.; Mielke, B. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 681. (f) Jordan, S.; Schwemler, C.; Kosch, W.; Kretschmer, A.; Stropp, U.; Schwenner, E.; Mielke, B. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 687. (g) Puschl, A.; Tedeschi, T.; Nielsen, P. E. *Org. Lett.* **2000**, *2*, 4161.

(7) For azasugars from 4-hydroxyprolinal, see: Zhu, Y.-H.; Vogel, P. *J. Org. Chem.* **1999**, *64*, 666.

10.1021/jo0484171 CCC: $30.25
Published on Web 12/29/2004

other 3- and 5-substituted methanopyrrolidines and such methanoproline analogues might be incorporated into native protein sequences.[18]

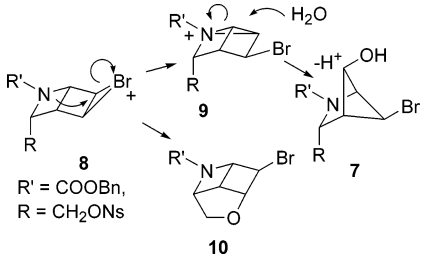
Recently, we showed that *N*-acetyl-3-methoxycarbonyl-5-hydroxy-2-azabicyclo[2.1.1]hexane **4**, in which the pyrrolidine ring of the *allo*-4-hydroxyproline is constrained into a unique envelope conformation, can provide insights into the factors that stabilize collagens.[19a] The synthetic route to **4** required 14 steps from pyridine. Key intermediates in the sequence include the 1,2-dihydropyridines **5**, the photoproduct **6**, and the rearranged bromohydrin **7**. Contributing to the length of the synthesis are five steps associated with introduction and removal of the *p*-nitrobenzenesulfonate (ONs) group and protection of the 5-hydroxyl group of **7** during subsequent oxidation steps leading to ester **4**.[19a,20] Thus, we desired a more efficient route to this type of compound.



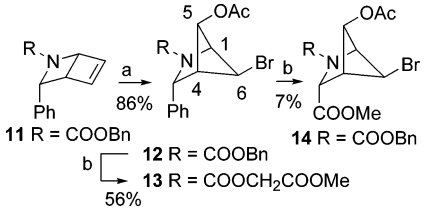
Results and Discussion

Our previous rearrangement approach to the methanoproline **4** shown in Scheme 1 takes advantage of the finding that the bromonium ion **8**, formed by addition of Br^+ to photoproduct **6**, rearranges to the aziridinium ion **9**.[19] This is followed by a regioselective attack of water on ion **9** to give a 2-azabicyclo[2.1.1]hexane system **7**. The *O*-nosylate protecting group is necessary to minimize intramolecular trapping of bromonium ion **8** by oxygen to give the unwanted tricycle **10**.

SCHEME 1. The Rearrangement Route



SCHEME 2. A Nonselective Oxidation[a]



[a] Reagents and conditions: (a) NBS, HOAc, NaOAc, Ac_2O, 25 °C, 1 h; (b) $RuCl_3$, $NaIO_4$, CCl_4, CH_3CN, H_2O, 25 °C, 24 h; then Me_3SiCHN_2, hexane, *i*-PrOH.

A shorter alternative that avoids the problem of neighboring group participation by the 3-endo substituent of a 1,2-dihydropyridine photoadduct is desirable. Two superior alternative routes to structures related to methanoproline **4** are now described. In one approach a phenyl group was chosen as a latent carboxylic acid. In a second approach the dimethylphenylsilylmethyl group was chosen as the precursor of a hydroxymethyl group.

The 2-Phenyl-1,2-dihydropyridine Route. Pyridine previously has been converted to 2-phenyl-1,2-dihydropyridine and then by irradiation to 3-*endo*-phenyl-2-azabicyclo[2.2.0]hex-5-ene **11** in 15% yield.[21] Attempted selected use of the phenyl group as a latent ester is shown in Scheme 2. Reaction of **11** with NBS/Ac_2O/AcOH affords the rearranged bromoacetate **12** (86%) that shows characteristic doublets, $J_{1,4} = 7.2$ Hz and $J_{5,6} = 7.5$ Hz, for this 2-azabicyclo[2.1.1]hexane ring system.[22] Selective oxidation of the 3-phenyl group of **12** with ruthenium tetroxide was not successful;[23] following esterification with trimethylsilyldiazomethane[24] an 8:1 mixture (63%)

(8) For incorporation of 4-hydroxyproline derivatives into antibiotics, see: (a) Kamal, A. *J. Org. Chem.* **1991**, *56*, 2237. (b) Kamal, A.; Reddy, G. S. K.; Reffy, K. L.; Raghavan, S. *Tetrahedron Lett.* **2002**, *43*, 2103. (c) Azami, H.; Barrett, D.; Tanaka, A.; Sasaki, H.; Matsuda, K.; Chiba, T.; Matsumoto, Y.; Matsumoto, S.; Moringa, C.; Ishiguro, K.; Tawara, S.; Sakane, K.; Takasugi, H. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 2199.

(9) For use of 4-hydroxyproline in the synthesis of antihypertensives, see: Krapcho, J.; Turk, C.; Cushman, D. W.; Powell, J. R.; DeForrest, J. M.; Spitzmiller, E. R.; Karanewsky, D. S.; Duggan, M.; Rovnyak, G.; Schwartz, J.; Natarajan, S.; Godfrey, J. D.; Ryono, D. E.; Neubeck, R.; Atwal, K. S.; Petrillo, E. W., Jr. *J. Med. Chem.* **1988**, *31*, 1148.

(10) For generation of polyamines from 4-hydroxyproline, see: Nagamani, D.; Ganesh, K. N. *Org. Lett.* **2001**, *3*, 103.

(11) For incorporation of 4-hydroxyproline derivatives into macrocycles, see: (a) Arasappan, A.; Chen, K. X.; Njoroge, F. G.; Parekh, T. N.; Girijavallabhan, V. *J. Org. Chem.* **2002**, *67*, 3923. (b) Goldberg, M.; Smith, L., II; Tamayo, N.; Kiselyov, A. S. *Tetrahedron* **1999**, *55*, 13887.

(12) For recent synthetic efforts related to the synthesis of 4-substituted-prolines and 2-hydroxymethylpyrrolidines, see: (a) Del Valle, J. R.; Goodman, M. *J. Org. Chem.* **2003**, *68*, 3923. (b) Tamaki, M.; Han, G.; Hruby, V. J. *J. Org. Chem.* **2001**, *66*, 3593.

(13) Moore, R. E.; Entzeroth, M. *Phytochemistry* **1988**, *27*, 3101.

(14) Koehn, F. E.; Longley, R. E.; Reed, J. K. *J. Nat. Prod.* **1992**, *55*, 613.

(15) (a) Koehn, F. E.; McConnell, O. J.; Longley, R. E.; Sennett, S. H.; Reed, J. K. *J. Med. Chem.* **1994**, *37*, 3181. (b) Dicicco, C. P.; Grover, P. *J. Org. Chem.* **1996**, *61*, 3534.

(16) Sheehan, J. C.; Zachau, H. G.; Lawson, W. B. *J. Am. Chem. Soc.* **1958**, *80*, 3349.

(17) For a library based upon 4-hydroxyproline, see: Goldberg, M.; Smith, L., II; Tamayo, N.; Kiselyov, A. S. *Tetrahedron* **1999**, *55*, 13887. For a library based upon amide diols, see: Lee, C. E.; Kick, E. K.; Ellman, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 9735.

(18) Kim, W.; George, A.; Evans, M.; Conticello, V. P. *ChemBioChem* **2004**, *5*, 928.

(19) (a) Jenkins, C. L.; Lin, G.; Duo, J.; Rapolu, D.; Guzei, I. A.; Raines, R. T.; Krow, G. R. *J. Org. Chem.* **2004**, *69*, 8565. (b) Krow, G. R.; Yuan, J.; Lin, G.; Sonnet, P. E. *Org. Lett.* **2002**, *4*, 1259.

(20) Krow, G. R.; Yuan, J.; Fang, Y.; Meyer, M. D.; Anderson, D. J.; Campbell, J. E.; Carroll, R. J. *Tetrahedron* **2000**, *56*, 9227.

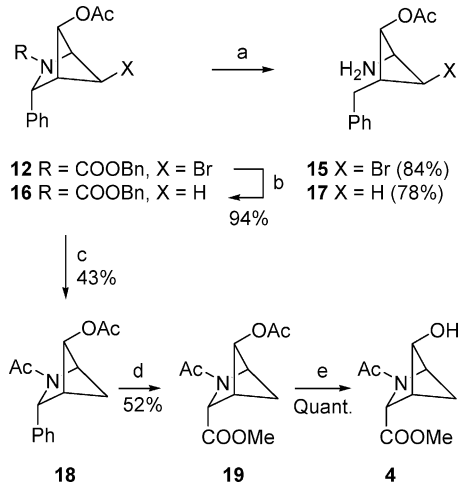
(21) (a) Kurita, J.; Iwata, K.; Sakai, H.; Tsuchiya, T. *Chem. Pharm. Bull.* **1985**, *33*, 4572. (b) The low yield in the photocyclization step can be attributed to competitive aromatization and/or electrocyclic ring opening of the 1,2-dihydropyridine. Kumagai, T.; Saito, S.; Ehara, T. *Tetrahedron Lett.* **1991**, *32*, 6895.

(22) Krow, G. R.; Lin, G.; Rapolu, D.; Fang, Y.; Lester, W. S.; Herzon, S. B.; Sonnet, P. E. *J. Org. Chem.* **2003**, *68*, 5292.

(23) Carlsen, H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

(24) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1981**, *5*, 1475.

SCHEME 3. An *allo*-Hydroxymethanoproline Synthesis[a]

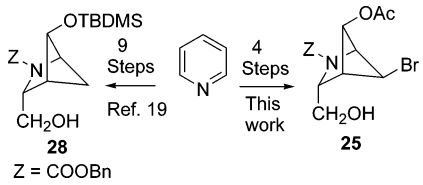


[a] Reagents and conditions: (a) H_2/Pd/C, MeOH, 25 °C, 1 h; (b) Bu_3SnH, AIBN, benzene, reflux, 3 h; (c) *B*-bromocatecholborane, CH_2Cl_2, 25 °C, 2 h; then AcCl, DMAP, CH_2Cl_2, 25 °C, 2 h; (d) $RuCl_3$, $NaIO_4$, CCl_4, CH_3CN, H_2O, 25 °C, 24 h; then Me_3SiCHN_2, hexane, *i*-PrOH; (e) Et_3N, MeOH, 25 °C, 6 h.

of an undesired 3-phenyl isomer **13**, in which the benzyl protecting group was preferentially oxidized, and the desired 3-ester **14** was obtained.

To avoid oxidation of the nitrogen protecting group, we attempted selective removal of the *N*-benzyloxycarbonyl group of bromoacetate **12** by catalytic hydrogenation (Scheme 3). Although reduction of **12** with $Pd(OH)_2/H_2$/MeOH removed the benzyloxycarbonyl group, it also broke the benzylic N−C_3 bond to give the bromocyclobutylamine **15**. To relieve strain the 5-bromo substituent of **12** was removed with tributyltin hydride (94%) to give acetate **16**.[25] Nevertheless, reductive removal of the *N*-benzyloxycarbonyl group of **16** with Pd/C/MeOH again resulted in ring cleavage at the benzylic position to give cyclobutylamine **17**. Finally, the *N*-benzyloxycarbonyl group was selectively removed with *B*-bromocatecholborane[26] in CH_2Cl_2 and the resulting amine was directly acylated with AcCl/pyridine/DMAP to give the amide **18** in 43% yield. The phenyl group of **18** was oxidized with RuO_4 and the resulting acid was immediately esterified with trimethylsilyldiazomethane to give the diester **19** (52%). Selective hydrolysis of the acetate of **19** with Et_3N/MeOH[27] quantitatively afforded the known hydroxyester **4** in seven steps (16%) from the dihydropyridine photoproduct **11** and nine steps (2.4%) from pyridine. While the result is an improvement over the previously described route to ester **4**, an alternative route remained desirable.

The 2-Dimethylphenylsilylmethyl-1,2-dihydropyridine Route. An alternative to synthon **11** was sought that would avoid the problems inherent in deprotecting a benzylic amine protected as a benzyl carbamate. In the alternative route shown in Scheme 4, pyridine was reacted with the Grignard reagent prepared from chloromethyldimethylphenylsilane in the presence of benzylchloroformate.[28] The resulting crude 1,2-dihydropyridine **20** was directly subjected to irradiation at 300 nm in acetone for 2−5 days to give 3-*endo*-dimethylphenylsilylmethyl-2-azabicyclo[2.2.0]hex-5-ene **21** in 30% overall yield.[21] Reaction of alkene **21** with NBS/THF/water[25] gave an unstable yellow oil with an ^1H NMR spectrum that showed characteristic doublet patterns $J_{1,4} = 7.5$ Hz and $J_{5,6} = 7.5$ Hz consistent with the rearranged bromo alcohol **22**; however, the color changed to blue in the NMR tube. Chromatography of this new material resulted in isolation of a cyclopentenone **23** (65%). The methyl group of **23** was assigned adjacent to the carbonyl group on the basis of NOESY correlations between the vinyl proton and the two adjacent allylic protons. This surprising molecular rearrangement **21** → **23** can be suppressed by protection of the alcohol,[29] since alkene **21**, when it was reacted with NBS/AcOH/Ac_2O,[22] affords the stable bromoacetate **24** (89% yield). Oxidation of the alkylsilane of bromoacetate **24** with bromine/peracetic acid/acetic acid gives the 3-hydroxymethyl bromoacetate **25** (80%).[30] Oxidation of the 3-hydroxymethyl group with NaOCl/TEMPO[31] and esterification with trimethylsilyldiazomethane[24] gives the desired 3-ester **14** (80%). This is converted to the known hydroxymethanoproline analogue **4** in several steps. The *N*-benzyloxycarbonyl group is removed with H_2/Pd/C/MeOH to give the amine **26** (85%) and acylation gives amide **27** (93%). Debromination of **27** with tributyltin hydride in benzene affords diester **19** (93%), which was earlier converted to **4** as described in Scheme 3. The overall yield of **4** as described in Scheme 2 from silyl photoproduct **21** is 42%; from pyridine the yield is 13%. The four-step yield from pyridine to the selectively protected multifunctional 3-hydroxymethylbromoacetate **25** is 21%. This route is a 5-fold improvement over the previous nine-step (4.4% yield) route[19a] from pyridine to the TBDMS-protected alcohol **28**.



Experimental Section

Preparation of *N*-(Benzyloxycarbonyl)-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-phenyl-2-azabicyclo[2.1.1]-hexane (12). Alkene **11** (292 mg, 1 mmol)[21] and NBS (445 mg, 2.5 mmol) in a solution of acetic acid (8 mL), sodium acetate (205 mg, 2.5 mmol), and acetic anhydride (0.2 mL, 2

(25) (a) Krow, G. R.; Lee, Y. B.; Lester, W. S.; Christian, H.; Shaw, D. A.; Yuan, J. *J. Org. Chem.* **1998**, *63*, 8558. (b) Krow, G. R.; Lester, W. S.; Liu, N.; Yuan, J.; Hiller, A.; Duo, J.; Herzon, S. B.; Nguyen, Y.; Cannon, K. *J. Org. Chem.* **2001**, *66*, 1811.

(26) Boeckman, R. K., Jr.; Potenza, J. C. *Tetrahedron Lett.* **1985**, *26*, 1411.

(27) Tsuzuki, K.; Nakajima, Y.; Watanabe, T.; Yanagiya, M.; Matsumoto, T. *Tetrahedron Lett.* **1978**, *19*, 989.

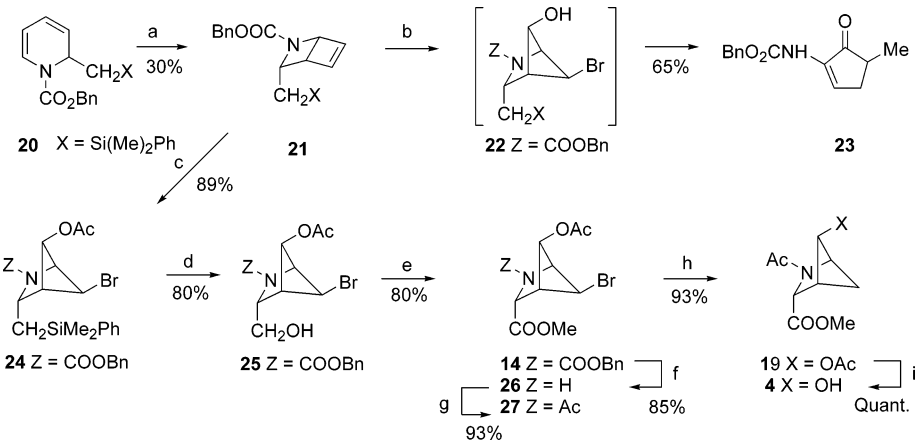
(28) Comins, D. L.; Libby, A. H.; Al-awar, R. S.; Foti, C. J. *J. Org. Chem.* **1999**, *64*, 2184.

(29) The rearrangement of alcohol **22** might be envisioned as occurring through a series of steps shown in Scheme 5. An alcohol proton catalyzed ring opening could give a β-silyl cation **i**. A subsequent 1,2-alkyl shift gives a ring-enlarged cation **ii**. Proton loss generates an allylic silane **iii**. Desilylation accompanied by bromide elimination gives diene **iv** and a series of acid-catalyzed proton transfers affords ketone **23**.

(30) Fleming, I.; Henning, R.; Parker, D. C.; Plaut, H. E.; Sanderson, P. E. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317.

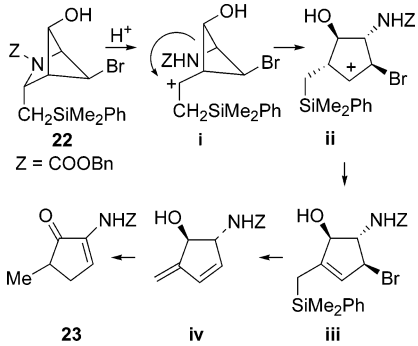
(31) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559.

SCHEME 4. An Improved Route to *allo*-Hydroxymethanoproline[a]



[a] Reagents and conditions: (a) $h\nu$, 300 nm, Rayonet reactor, acetone, 25 °C, 2−5 d; (b) NBS, THF, H_2O, 25 °C, 2.5 h; (c) NBS, HOAc, NaOAc, Ac_2O, 25 °C, 1 h; (d) Br_2, PAA, HOAc, 25 °C, 5 h; (e) NaOCl, TEMPO, KBr, Bu_4NCl, CH_2Cl_2, $NaHCO_3$, H_2O, 0 °C, 45 min; then $TMSCHN_2$, hexane, *i*-PrOH; (f) H_2/Pd/C, MeOH, 25 °C, 2 h; (g) AcCl, DMAP, CH_2Cl_2, 25 °C, 2 h; (h) Bu_3SnH, AIBN, benzene, reflux, 3 h; (i) Et_3N, MeOH, 25 °C, 6 h.

SCHEME 5. A Proposed Ring-Cleavage Mechanism



mmol) were stirred at 25 °C for 1 h.[22] The solution was diluted with CH_2Cl_2 (20 mL), washed with 10% $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried over $MgSO_4$, and filtered and solvent was removed in vacuo to provide an oil that was chromatographed on silica gel (1:2 ether/hexane) to afford 432 mg (86%) of rearranged bromoacetate **12** at R_f 0.36 (2:1 hexane/ether): ^{1}H NMR δ 7.34 (m, 10H), 5.23 (s and br, 3H), 4.81 (d, J = 7.5 Hz, 1H), 4.74 (d, J = 7.5 Hz, 1H), 4.26 (d, J = 7.2 Hz, 1H), 3.30 (d, J = 7.2 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR δ 170.5, 156.0, 137.6, 136.0, 128.8, 128.5, 127.7, 127.4, 127.0, 126.3, 83.6, 67.6, 65.3, 62.8, 53.8, 46.5, 21.1; HRMS *m/z* 452.0468 and 454.0451, calcd for $C_{21}H_{21}NO_4{}^{79}BrNa$ (MNa^+) 452.0473 and $C_{21}H_{21}NO_4{}^{81}BrNa$ (MNa^+) 454.0452.

Oxidation of Bromoacetate 12: Preparation of *N*-[(Carbomethoxymethyl)methoxycarbonyl]-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-phenyl-2-azabicyclo[2.1.1]hexane (13) and *N*-(Benzyloxycarbonyl)-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-methoxycarbonyl-2-azabicyclo[2.1.1]hexane (14). To a solution of bromoacetate **12** (600 mg, 1.45 mmol) in carbon tetrachloride (3 mL), acetonitrile (3 mL), and water (5 mL) was added sodium metaperiodate (4.64 g, 5.95 mmol). To this biphasic solution was added 8.43 mg (2.2 mol %) of ruthenium trichloride and the entire mixture was stirred for 24 h at room temperature. Then CH_2Cl_2 (15 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated. Hexane (15 mL) and 2-propanol (15 mL) were added followed by a 2 M solution of trimethylsilyldiazomethane in hexane (700 μL).[24] The resulting mixture was stirred under argon for 0.5 h. The solvent was removed in vacuo to give an oil that was chromatographed on silica gel (1:2 ether/hexane) to afford 322 mg (56%) of *N*-$COOCH_2$-COOMe product **13** at R_f 0.29 (2:1 hexane/ether): ^{1}H NMR δ 7.29 (m, 5H), 5.21 (br, 1H), 4.81 (d, J = 8.0 Hz, 1H), 4.60 (m, 3H), 4.11 (d, J = 7.2 Hz, 1H), 3.67 (br, 3H), 3.20 (d, J = 7.2 Hz, 1H), 2.06 (s, 3H); ^{13}C NMR δ 170.4, 168.4, 155.5, 137.2, 130.0, 128.6, 127.7, 126.2, 83.5, 65.1, 62.8, 61.6, 54.0, 52.5, 46.3, 21.1; HRMS *m/z* 434.0209 and 436.0185, calcd for $C_{17}H_{18}NO_6{}^{79}$-BrNa (MNa^+) 434.0215 and $C_{17}H_{18}NO_6{}^{81}BrNa$ (MNa^+) 436.0195. Also obtained was 31.3 mg (7%) of *N*-COOBn product **14** at R_f 0.31 (2:1 hexane/ether): ^{1}H NMR δ 7.39 (br, 5H), 5.22 (s, 2H), 4.66 (d, J = 7.2 Hz, 1H), 4.55 (m, 2H), 3.82 (br, 3H), 3.33 (d, J = 7.2 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR δ 170.2, 169.0, 154.3, 153.3, 135.7, 128.4, 128.2, 127.9, 83.6, 67.7, 64.3, 59.3, 52.7, 51.7, 46.2, 21.0; HRMS *m/z* 434.0213 and 436.0197, calcd for $C_{17}H_{18}NO_6{}^{79}BrNa$ (MNa^+) 434.0215 and $C_{17}H_{18}NO_6{}^{81}BrNa$ (MNa^+) 436.0195.

Hydrogenative Cleavage of Acetate 12: *c*-3-Acetoxy-*t*-2-amino-1-*r*-*bromo*-*t*-4-benzylcyclobutane (15). To a solution of acetate **12** (415 mg, 0.97 mmol) in methanol (40 mL) was added 10% $Pd(OH)_2$/C (150 mg). The solution was stirred at 25 °C under a hydrogen balloon for 2 h and filtered through Celite, and solvent was removed in vacuo to give an oil. Purification by flash chromatography (EtOAc) afforded 241 mg (84%) of amine **15** at R_f 0.20 (ethyl acetate): ^{1}H NMR δ 7.2−7.1 (m, 5H), 4.31 (t, J = 7.1 Hz, 1H), 3.44 (t, J = 7.1 Hz, 1H), 3.23 (t, J = 7.7 Hz, 1H), 2.92 (m, 2H), 2.56 (m, 1H), 1.99 (s, 3H), 1.73 (br, 2H); ^{13}C NMR δ 171.3, 138.2, 130.0, 129.2, 127.2, 76.4, 64.3, 48.8, 45.3, 36.7, 21.4; HRMS *m/z* 298.0443 and 300.0422, calcd for $C_{13}H_{17}NO_2{}^{79}Br$ (MH) 298.0443. and $C_{13}H_{17}$-$NO_2{}^{81}Br$ (MH) 300.0422.

Debromination of Acetate 12: Preparation of *N*-(Benzyloxycarbonyl)-5-*anti*-acetoxy-3-*exo*-phenyl-2-azabicyclo-[2.1.1]hexane (16). To a solution of acetate **12** (415 mg, 0.97 mmol) in benzene (50 mL) was added tributyltin hydride (0.59 g, 2.05 mmol) and AIBN (22 mg, 0.13 mmol).[25] The resulting mixture was refluxed for 3 h. The solvent was removed in vacuo and the crude product was purified by column chromatography to give 220 mg (94%) of halide free acetate **16** as a colorless oil at R_f 0.53 (1:1 ether:/hexane): ^{1}H NMR (400 MHz) δ 7.40 (m, 10H), 5.20 (d, J = 10.3 Hz, 2H), 5.12 (s,1H), 4.75 (d, J = 7.0 Hz, 1H), 4.59 (m, 1H), 3.00 (br, 1H), 2.53 (br, 1H), 2.17 (s, 3H), 1.87 (m, 1H); ^{13}C NMR δ 170.6, 156.6, 138.9, 136.4, 128.3, 127.7, 127.4, 127.1, 126.4, 82.6, 66.9, 62.2, 61.3, 49.3 and 48.7, 32.5 and 31.7, 13.6; HRMS *m/z* 374.1382, calcd for $C_{21}H_{21}NO_4Na$ (MNa) 374.1368.

Hydrogenative Cleavage of Acetate 16: *r*-1-Acetoxy-*t*-2-amino-*t*-4-benzylcyclobutane (17). To a solution of acetate **16** (168 mg, 0.48 mmol) in methanol (20 mL) was added

Pd/C (100 mg). The solution was stirred at 25 °C under a hydrogen balloon for 2 h and filtered through Celite, and solvent was removed in vacuo to give an oil. Purification by flash chromatography (EtOAc) afforded 82 mg (78%) of amine **17** at R_f 0.18 (ethyl acetate): ^{1}H NMR δ 7.13 (m, 5H), 4.50 (t, J = 7.20 Hz, 1H), 3.82 (br, 2H), 3.20 (m, 1H), 2.87 (dd, J = 14.0, 7.3 Hz, 1H), 2.66 (dd, J = 14.0, 8.0 Hz, 1H), 2.22 (m, 2H), 1.94 (s, 3H), 1.19 (m, 1H); ^{13}C NMR δ 171.3, 139.5, 128.6, 128.3, 126.1, 80.0, 51.9, 39.5, 36.8, 28.5, 20.9; HRMS *m/z* 220.1334, calcd for $C_{13}H_{18}NO_2$ (MH) 220.1334.

Preparation of *N*-Acetyl-5-*anti*-acetoxy-3-*exo*-phenyl-2-azabicyclo[2.1.1]hexane (18). To a solution of acetate **16** (200 mg, 0.57 mmol) in dry CH_2Cl_2 (4 mL) was added *B*-bromocatecholborane (240 mg, 1.20 mmol) dropwise at room temperature. The solution was stirred at 25 °C for 2 h, treated with water (3 mL), and stirred for 20 min, then diluted with additional CH_2Cl_2 (30 mL) and washed with 10% NaOH solution (2 × 10 mL) and brine (5 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed in vacuo to give an oil (143 mg). To the crude amine in dry CH_2Cl_2 (10 mL) at 0 °C was added (dimethylamino)pyridine (244 mg, 2.0 mmol); acetyl chloride (124 mg, 1.2 mmol) was added dropwise and the mixture was stirred another 30 min at 0 °C, then slowly warmed to 25 °C and stirred for another 2 h. Water (5 mL) was added to form two layers. The water layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered, solvent was removed in vacuo, and the residue was purified by flash chromatography to afford 59 mg (43%) of amide **18** at R_f 0.15 (1:1 hexane/ethyl acetate): ^{1}H NMR δ 7.23 (m, 5H), 5.23 and 4.95 (two s, 1H), 4.85 and 4.33 (two d, J = 7.3, 7.2 Hz, 1H), 4.58 and 4.54 (two d, J = 7.5, 7.4 Hz, 1H), 2.86 (dd, J = 7.5, 2.0 Hz, 1H), 2.07 (m, 1H), 2.04−1.99 (m, 7H); ^{13}C NMR δ 171.2 and 170.7, 138.4, 128.7, 128.3, 127.8, 127.1, 82.4, 64.0 and 62.1, 60.9 and 60.6, 50.2 and 48.1, 33.1 and 30.7, 22.2 and 20.92; HRMS *m/z* 264.0847, calcd for $C_{11}H_{15}NO_5Na$ (MNa) 264.0848.

Preparation from Acetate 18 of *N*-Acetyl-5-*anti*-acetoxy-3-*exo*-methoxycarbonyl-2-azabicyclo[2.1.1]-hexane (19). To a solution of acetate **18** (120 mg, 0.46 mmol) in carbon tetrachloride (2 mL), acetonitrile (2 mL), and water (4 mL) was added sodium metaperiodate (1.9 g, 2.0 mmol). To this biphasic solution ruthenium trichloride (2.8 mg, 2.2 mol %) was added and the entire mixture was stirred for 24 h at room temperature. Then CH_2Cl_2 (10 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated to afford crude acid. To the solution of the crude acid in hexane (10 mL) and 2-propanol (10 mL) was added a 2 M solution of trimethylsilyldiazomethane in hexane (233 μL).[24] The resulting mixture was stirred under argon for 0.5 h. The solvent was removed in vacuo to give an oil that was chromatographed on silica gel (1:2 ether/hexane) to afford 58 mg (52%) of amide **19** at R_f 0.40 (ethyl acetate): ^{1}H NMR (CD_3COCD_3, 400 MHz) δ 4.63 and 4.30 (two s, 1H), 4.57 and 4.36 (two d, J = 7.2, 7.2 Hz, 1H), 4.43 (d, J = 7.2, 1H), 3.70 and 3.60 (two s, 3H), 3.00 and 2.90 (two d, J = 7.2, 7.2 Hz, 1H), 2.59 (m, 1H, H_6), 2.04∼1.66 (m, 7H and acetone); ^{13}C NMR (CD_3COCD_3, 100 MHz) δ 205.2 (solvent), 170.0, 169.6, 168.7, 167.4, 82.4 and 81.7, 63.4 and 60.0, 58.9 and 57.2, 52.1 and 51.5, 47.1, 46.0, 35.7 and 32.6, 20.9, 20.5 and 19.9; HRMS *m*/z 281.1095, calcd for $C_{15}H_{17}NO_3Na$ (MNa) 282.1106.

Preparation of *N*-Acetyl-5-*anti*-hydroxy-3-*exo*-methoxycarbonyl-2-azabicyclo[2.1.1]hexane (4). To a solution of acetate **19** (241 mg, 1.0 mmol) in methanol (10 mL) was added triethylamine (505 mg, 5.0 mmol).[27] The resulting mixture was stirred at room temperature for 6 h. The solvent was removed in vacuo and the resulting mixture was purified by flash chromatography to provide 199 mg (100%) of alcohol **4** as a colorless liquid at R_f 0.30 (1:15 MeOH/ethyl acetate): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.35−3.79 (m, 4H), 3.56 and 3.51 (two s, 3H), 2.69−2.61 (m, 2H), 1.93−1.63 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.1 and 168.5, 81.9 and 81.4, 65.4 and 62.6, 60.0 and 58.0, 52.4, 48.5 and 47.9, 34.2 and 32.9, 21.7 and 21.4; HRMS *m/z* 222.0747, calcd for $C_9H_{13}NO_4Na$ (MNa) 222.0742.

***N*-Benzyloxycarbonyl-2-(phenyldimethylsilylmethyl)-1,2-dihydropyridine (20).** A few milliliters of a solution of chloromethyldimethylphenylsilane (18.47 g, 100 mmol) in dry THF (120 mL) was added to a flask containing Mg turnings (2.43 g, 100 mmol) under argon, a small crystal of iodine was added, and the mixture was heated until an exothermic reaction occurred.[28] The remaining THF solution of chloride was added over 20 min so that gentle reflux was maintained. The tan-gray mixture was then heated to reflux for 0.5 h and cooled to 0 to −5 °C, and a solution of dry pyridine (6.33 g, 80 mmol) was added dropwise with stirring over 20 min. After an additional 20 min, a solution of benzyl chloroformate (13.70 g, 80 mmol) in THF (100 mL) was added dropwise at such a rate as to maintain the temperature below −5 °C. After an additional 2 h, the mixture was allowed to stir at room temperature for 1 h and water (50 mL) was added. The organic layer was separated; if there was too much undissolved solid, dilute HCl was added to dissolve the residue while keeping the pH no less than 7. The aqueous layer was extracted with diethyl ether (4 × 50 mL) and the combined organic layers were washed with brine (50 mL), dried over sodium sulfate, and filtered and solvent was removed in vacuo to give 28.60 g (95%, crude) of 1,2-dihydropyridine **20** as a light yellow oil. The crude product is pure enough for the next reaction. A portion (200 mg) of crude **20** was purified by flash chromatography (10:1 hexane/ether) to give 110 mg (56%) of pure **20** at R_f 0.58 (6:1 hexane/ether): ^{1}H NMR δ 7.31 (m, 10H), 6.74 and 6.58 (two d, J = 7.5 Hz, 1H), 5.79 (m, 1H), 5.51−4.95 (m, 5H), 1.46−1.20 (m, 2H), 0.35 (m, 6H); ^{13}C NMR δ 154.2 and 153.3, 139.2, 136.4, 129.4, 129.0, 128.2, 127.7, 127.5, 133.9, 124.4 and 124.3, 121.3 and 120.7, 106.3, 68.0, 50.67 and 50.22, 23.2 and 22.2, 0.2 and 0.0; HRMS *m/z* 364.1736, calcd for $C_{22}H_{26}NO_2Si$ (MH) 364.1733.

***N*-Benzyloxycarbonyl-3-(phenyldimethylsilylmethyl)-2-azabicyclo[2.2.0]hex-5-ene (21).** Photoirradiation of the crude 2-silylmethyl-1,2-dihydropyridine **20** (28.6 g) in acetone (5wt %) at 300 nm with a Rayonet photoreactor for 2−5 days and removal of solvent gave a crude oil, which was purified by silica gel column chromatography (1:9 ether/hexane) to give 8.7 g (30%) of photoproduct **21** as a yellow oil at R_f 0.33 (6:1 hexane/ether): ^{1}H NMR δ 7.41 (m, 10H), 6.55, 6.48, 6.08, 5.98 (four s, 2H), 5.12 (br, 2H), 4.73 (br, 1H), 4.28 (br, 1H), 3.36 (m, 1H), 1.85 and 1.65 (two br, 1H), 1.16 br, 1H), 0.40 (m, 6H); ^{13}C NMR δ 155.1 and 153.4, 142.4 and 140.7, 138.3 and 137.1, 133.4 and 133.0, 129.2, 128.4, 127.9, 127.7, 66.0, 62.9 and 62.2, 58.3, 43.8, 19.2 and 18.2, −0.0 and −2.7; HRMS *m/z* 386.1557, calcd for $C_{22}H_{25}NO_2NaSi$ (MNa) 386.1552.

Attempted Preparation of Bromohydrin 22: *N*-Benzyloxycarbonyl-2-amino-5-methyl-2-cyclopentenone (23). To silane **21** (0.55 g, 1.51 mmol) in THF (10 mL) and H_2O (5 mL) at 0 °C was added *N*-bromosuccinimide (0.67 g, 3.76 mmol) in small portions so that the temperature never exceeded 0 °C.[25] Upon completion of addition the solution was warmed to room temperature and stirred for 2.5 h, then diluted with water (5 mL) and extracted with chloroform (5 × 10 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4, and the solvent was removed to give a yellow oil that changed to blue. Purification by flash chromatography (1:3 ether/ hexane) provided 0.32 g (65%) of rearranged product **23** at R_f 0.60 (1:1 ether/ hexane): ^{1}H NMR δ 7.41 (m, 6H), 6.98 (br, 1H), 5.23 (s, 2H), 2.91 (ddd, J = 18.6, 6.4, 3.0 Hz, 1H), 2.46 (m, 1H), 2.23 (d, J = 18.6 Hz, 1H), 1.23 (d, J = 8.4 Hz, 3H); ^{13}C NMR δ 206.2, 153.8, 136.6, 136.1, 129.1, 128.8, 128.6, 67.7, 38.6, 34.3, 16.6; HRMS *m*/z 268.0957, calcd for $C_{14}H_{15}NO_3Na$ (MNa) 268.0950. The protons at δ 2.91 and 2.23 have NOESY correlation with the vinyl proton at δ 7.41.

***N*-Benzyloxycarbonyl-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-(phenyldimethylsilylmethyl)-2-azabicyclo[2.1.1]-hexane (24).** Alkene **21** (363 mg, 1 mmol) and NBS (445 mg, 2.5 mmol) in a solution of acetic acid (8 mL), sodium acetate (205 mg, 2.5 mmol), and acetic anhydride (0.2 mL, 2 mmol) were stirred at 25 °C for 1 h,[22] diluted with CH_2Cl_2 (20 mL), washed with 10% $NaHCO_3$ (3 × 10 mL) and brine (10 mL), dried over $MgSO_4$, and filtered and solvent was removed in vacuo to provide an oil, which was chromatographed on silica gel (1:2 ether/hexane) to afford 432 mg (89%) of bromoacetate **24** at R_f 0.50 (1:1 hexane/ether): ^{1}H NMR δ 7.40 (m, 10H), 5.18 (s, 2H), 4.60 (d, J = 7.4 Hz, 1H), 4.56 (d, J = 7.2 Hz, 1H), 4.33 (d, J = 7.4 Hz, 1H), 4.04 (br, 1H), 2.73 (d, J = 7.2 Hz, 1H), 2.14 (s, 3H), 1.95 and 1.04 (m, 2H), 0.42 (m, 6H); ^{13}C NMR δ 170.3, 154.9, 136.1, 133.3, 128.5, 128.3, 128.2, 128.0, 127.7, 83.7, 67.1, 65.0, 58.1, 52.7, 47.9, 21.1, 20.0, −2.4, −2.8; HRMS *m/z* 524.0856 and 526.0848, calcd for $C_{24}H_{28}NO_4NaSi^{79}Br$ (MNa) 524.0869 and $C_{24}H_{28}NO_4NaSi^{81}Br$ (MNa) 526.0839.

***N*-Benzyloxycarbonyl-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-(hydroxymethyl)-2-azabicyclo[2.1.1]hexane (25).** Bromine (80.0 mg, 0.50 mmol) was added dropwise to a stirred solution of bromoacetate **24** (502 mg, 1.0 mmol) in peracetic acid (1 mL) and acetic acid (1.5 mL) at 0 °C.[30] The disappearance of the starting material was monitored by TLC, and more bromine (160 mg, 1.0 mmol) was added until none remained. The resulting mixture was stirred for 5 h at room temperature. Ether (10 mL) was added to the solution that was then washed with aqueous sodium thiosulfate solution (5 mL), aqueous sodium bicarbonate (3 × 5 mL), and brine (5 mL), dried over $MgSO_4$, and evaporated under reduced pressure. The residue was chromatographed to give 342 mg (80%) of alcohol **25** at R_f 0.24 (2:1 ether/hexane): ^{1}H NMR δ 7.41 (m, 5H), 5.22 (s, 2H), 4.68 (d, J = 7.2 Hz, 1H), 4.63 (d, J = 7.2 Hz, 1H), 4.13 (d, J = 7.2 Hz, 1H), 3.87 (br, 3H), 3.14 (d, J = 7.2 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR δ 170.4, 156.4, 135.6, 128.4, 128.4, 128.1, 84.0, 68.0, 64.9, 64.1, 62.8, 50.7, 47.4, 21.1; HRMS *m/z* 406.0252 and 408.0241, calcd for $C_{16}H_{18}NO_5Na$ ^{79}Br (MNa) 406.0266 and $C_{16}H_{18}NO_5Na$ ^{81}Br (MNa) 408.0246.

***N*-Benzyloxycarbonyl-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-(methoxycarbonyl)-2-azabicyclo[2.1.1]hexane (14).** To a solution of alcohol **25** (384 mg, 1.0 mmol) in dichloromethane (6.0 mL) containing TEMPO (1.2 mg) was added saturated $NaHCO_3$ (aq) (3 mL) containing KBr (11 mg) and tetrabutylammonium chloride (14.2 mg). The mixture was cooled to 0 °C and a solution of NaOCl (2.5 mL), saturated $NaHCO_3$ (aq) (2.0 mL), and brine (2.2 mL) was added dropwise over 45 min. The two layers were separated and the organic layer was extracted with water (4 × 5 mL). The aqueous layers were combined and acidified with 10% HCl. The resulting solution was extracted with EtOAc (4 × 15 mL). The combined organic solution was dried over Na_2SO_4. The solvent was removed to give a crude acid to which was added hexane (15 mL) and 2-propanol (15 mL). A 2 M solution of trimethylsilyldiazomethane in hexane (465 μL) was added and the resulting mixture was stirred under argon for 0.5 h.[24] The solvent was removed in vacuo to give 330 mg (80% from alcohol) of ester **14** (see above).

***N*-H-5-*anti*-Bromo-6-*anti*-acetoxy-3-*endo*-(methoxycarbonyl)-2-azabicyclo[2.1.1hexane (26).** To a solution of ester **14** (814 mg, 2.0 mmol) in methanol (40 mL) was added 10% Pd/C (200 mg). The solution was stirred at 25 °C under a hydrogen balloon for 2 h and filtered through Celite, and solvent was removed in vacuo to give an oil. Purification by flash chromatography (1:1 hexane/EtOAc) afforded 487 mg (85%) of amine **26** at R_f 0.19 (ethyl acetate): ^{1}H NMR (400 MHz) δ 4.71 (d, J = 7.2 Hz, 1H), 4.00 (d, J = 7.3 Hz, 1H), 3.98 (br, 1H), 3.81 (d, J = 7.3 Hz), 3.72 (s, 3H), 3.20 (d, J = 7.2 Hz, 1H), 3.09 (br, 1H), 2.04 (s, 3H); ^{13}C NMR δ 172.4, 171.0, 84.1, 63.9, 57.7, 53.4, 52.6, 48.6, 21.6; HRMS *m*/z 278.0027 and 280.0009, calcd for $C_9H_{13}NO_4{}^{79}Br$ (MH) 278.0028 and $C_9H_{13}NO_4{}^{81}Br$ (MH) 280.0007.

***N*-Acetyl-5-*anti*-bromo-6-*anti*-acetoxy-3-*endo*-(methoxycarbonyl)-2-azabicyclo[2.1.1-hexane (27).** To a solution of the amine **26** (487 mg, 1.6 mmol) in dry methylene chloride (20 mL) at 0 °C was added (dimethylamino)pyridine (0.66 g, 4.8 mmol); CH_3COCl (373 mg, 4.8 mmol) was added dropwise and the mixture was stirred another 30 min at 0 °C, then slowly warmed to 25 °C and stirred for another 2 h. Water (5 mL) was added to form two layers. The water layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over sodium sulfate and filtered, solvent was removed in vacuo, and the residue was purified by flash chromatography to afford 488 mg (93%) of amide **27** at R_f 0.20 (1:1 hexane/EtOAc): ^{1}H NMR (400 MHz) δ 4.50 (d, J = 7.5 Hz, 1H), 4.46 (d, J = 7.2 Hz, 1H), 4.43 (d, J = 7.5 Hz, 1H), 4.42 (s, 1H), 3.74 (m, 3H), 3.23 (d, J = 7.2 Hz, 1H), 1.97 (m, 6H); ^{13}C NMR δ 171.1, 170.4, 168.9, 168.2, 83.7 and 83.2, 65.7 and 62.8, 60.9 and 60.5, 53.2 and 52.9, 52.3 and 51.0, 46.1, 21.3 and 21.1; HRMS *m*/z 341.9951 and 343.9937, calcd for $C_{11}H_{14}NO_5$ Na ^{79}Br (MNa) 341.9953 and $C_{11}H_{14}NO_5$ Na ^{81}Br (MNa) 343.9933.

Preparation from Acetate 27 of *N*-Acetyl-5-*anti*-acetoxy-3-*exo*-methoxycarbonyl-2-azabicyclo[2.1.1]hexane (19). To a solution of acetate **27** (412 mg, 1.3 mmol) in benzene (50 mL) was added tributyltin hydride (0.59 g, 2.05 mmol) and AIBN (22 mg, 0.13 mmol).[25] The resulting mixture was refluxed for 3 h. Then the solvent was removed in vacuo and the crude product was purified by chromatography to give 220 mg (93%) of halide free acetate **19** (see above).

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (CHE 0111208). We thank Professor Hans Reich for helpful insights.

Supporting Information Available: All experimental procedures, spectroscopic data, as well as copies of ^{1}H NMR and ^{13}C NMR for compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0484171