(24), 109 (40), 108 (31), 107 (29), 105 (32), 95 (30), 93 (25), 82 (30), 81 (100), 69 (46), 43 (95); ^{1}H NMR 5.25–5.20 (m, 2 H), 5.05 (br t, J = 7), 4.99 (br d, J = 12), 1.68 (br s, 3 H), 1.58 (br s, 3 H), 1.53 (br s, 3 H), 1.18 (s, 3 H), 0.83 (d, J = 6.2); ^{13}C NMR 140.1 (d), 132.4 (s), 130.6 (s), 129.1 (d), 126.4 (d), 125.2 (d), 72.9 (s), 52.1 (d), 41.5 (t), 39.8 (t), 38.2 (t), 33.4 (t), 31.0 (q), 25.9 (d), 25.8 (q), 25.5 (t), 23.9 (t), 17.7 (q), 17.2 (q), 16.8 (q).

Microozonolysis of Obscuronatin (23). Ozone in oxygen was bubbled through a solution of compound **23** (10 mg) in ethyl acetate (3 mL) at −70 °C for 4 min. The ozonide was treated with excess of Ph_3P, and the reaction mixture was then warmed up to room temperature and immediately injected into a programmed gas chromatograph.[21] Comparison with fragment **24** obtained from trocheliophorol[22] on a 6 ft × $^1/_4$ in. i.d., 5% Carbowax on GCQ column (60–200 °C and 120–200 °C at 4 °C/min) confirmed the identity of the fragments. (The retention times of fragment **24** were 25.6 min in the first program and 15.9 min in the second one.)

Ph_3P/CCl_4 Dehydration of Alcohol 23 To Give Compounds 25 and 26. A solution of alcohol **23** (112 mg) and Ph_3P (250 mg) in CCl_4 (5 mL) was stirred at room temperature for 88 h. The solvent was then removed and the residue chromatographed on silica gel to give a 1:1 mixture of two isomeric nonpolar compounds (60 mg). This mixture was separated after extensive chromatography on 2% $AgNO_3$ impregenated silica gel columns to give two pure oily olefins **25** and **26**. Compound **25**: IR (CCl_4) 3080, 2960, 2920, 2860, 1645, 1450, 1380, 1280, 1245, 1220, 1165, 890, 720 cm^{-1}; mass spectrum (15 eV), m/e (relative intensity) 272 (M^+, $C_{20}H_{32}$, 86), 257 (4), 201 (8), 187 (100), 161 (54), 159 (24), 119 (38), 105 (60), 93 (36), 91 (42), 81 (50), 69 (76); ^{1}H NMR 5.53 (br s), 5.12 (br t, J = 7), 4.66 (s), 4.55 (s), 1.69 (br s, 6 H), 1.61 (br s, 3 H), 0.74 (d, J = 6.7, 3 H). Compound **26**: IR (CCl_4) 2960, 2920, 2860, 1645, 1450, 1380, 1240, 1180, 1160, 1075, 1010, 940, 910, 720 cm^{-1}; mass spectrum (15 eV), m/e (relative intensity) 272 (M^+, $C_{20}H_{32}$,85), 257 (10), 201 (8), 187 (100), 161 (94), 159 (86), 145 (22), 134 (83), 119 (50), 105 (88), 93 (26), 91 (45), 81 (59), 69 (66); ^{1}H NMR 5.41 (br s), 5.12 (br t, J = 7), 1.68 (br s, 9 H), 1.60 (br s, 3 H), 0.78 (d, J = 6.7, 3 H).

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Registry No. 1, 64504-52-5; 2, 68612-43-1; 3, 74175-94-3; 4, 74175-95-4; 5, 74175-96-5; 6, 70389-63-8; 7a, 70389-64-9; 7b, 74175-97-6; 8, 74175-98-7; 9a, 74175-99-8; 9b, 74176-00-4; 10a, 71117-53-8; 10b, 71093-24-8; 11, 68612-42-0; 12, 68612-41-9; 12 4,5-epoxy stereoisomer, 74219-32-2; 13, 68651-47-8; 14, 74176-01-5; 15a, 74176-02-6; 15b, 74176-03-7; 16, 74176-04-8; 17, 87-44-5; 18, 118-65-0; 19, 1139-30-6; 20, 60362-44-9; 21, 10306-22-6; 22, 74176-05-9; 23, 74176-06-0; 24, 68043-35-6; 25, 74219-33-3; 26, 74176-07-1.

Synthesis of Adamantane Derivatives. 50.[1] Facile Synthesis of 2,4-Oxa-Bridged Protoadamantanes and Their Conversions to 2-Substituted and 2,4-Disubstituted Protoadamantanes and a 2,4-Disubstituted Adamantane

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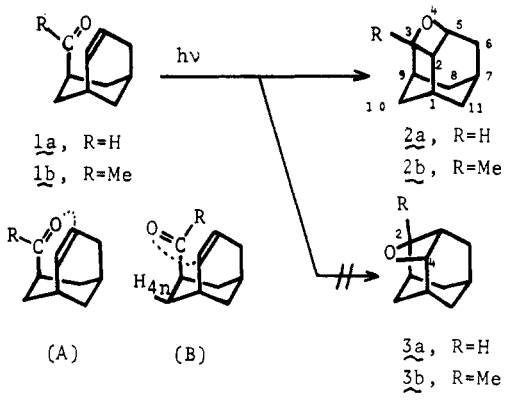
Intramolecular Paterno–Büchi reaction of 3-*endo*-acylbicyclo[3.3.1]non-6-enes **1a,b** proceeded regioselectively to afford exclusively 2,4-oxa-bridged protoadamantanes **2a,b** in good yields. The oxetane rings of **2a** and **2b** were cleaved by addition of hydrogen halides and by reduction with $LiAlH_4$, affording stereospecifically the corresponding 2,4-disubstituted and 2-substituted protoadamantane derivatives **7a, 7b, 9,** and **10**, respectively. Dehydration of 2-*exo*-methyl-2-*endo*-hydroxyprotoadamantane (**10**) with $POCl_3$–pyridine gave 2-methyleneprotoadamantane (**11**), while dehydration of the corresponding 4-*exo*-chloro derivative (**7b**) afforded exclusively 4(*e*)-chloro-2-methyleneadamantane (**14**) as a rearranged product in a high yield.

As an extension of our studies on the synthesis of 2,4-methanoadamantane and 2,4-methanoprotoadamantane,[2] we report in this paper a facile synthesis of 2,4-oxa-bridged protoadamantanes **2a** and **2b** via the intramolecular Paterno–Büchi reaction[3] as well as their conversions to some 2-substituted and 2,4-disubstituted protoadamantanes and a 2,4-disubstituted adamantane.

Results and Discussion

Intramolecular Paterno–Büchi Reaction of 3-*endo*-Acylbicyclo[3.3.1]non-6-enes. Irradiation of a 6.67 mM solution of 3-*endo*-formylbicyclo[3.3.1]non-6-ene (**1a**)[4] in deoxygenated *n*-hexane with a high-pressure mercury lamp (Vycor filter) led to a production of a new single sublimable product. Isolation of this product by chromatography on a silica gel column yielded 4-oxatetracyclo[5.3.1.0.^{2,5}0^{3,9}]undecane (**2a**; trivial 2,4-oxa-bridged

Scheme I



(1) Part 49: Sasaki, T.; Ohno, M.; Usuki, A., *J. Org. Chem.*, in press.
(2) Sasaki, T.; Eguchi, S.; Hirako, Y. *J. Org. Chem.* **1977**, *42*, 2981.
(3) For recent examples of the intramolecular Paterno–Büchi reaction, see: (a) Sauers, R. R.; Schinski, W.; Mason, M. M. *Tetrahedron Lett.* **1969**, 79; (b) Sauers, R. R.; Whittle, J. A. *J. Org. Chem.* **1969**, *34*, 3579; (c) Lange, G. M.; Bosch, M. *Tetrahedron Lett.* **1971**, 315; (d) Adam, G.; Sung, T. C. *Tetrahedron* **1979**, *35*, 557.
(4) Sasaki, T.; Eguchi, S.; Toru, T. *J. Org. Chem.* **1971**, *36*, 3460.

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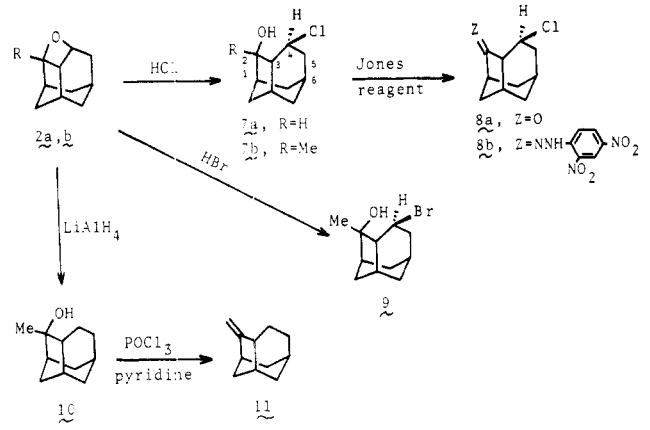
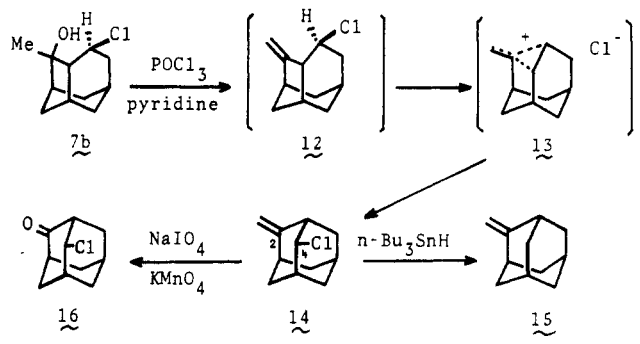
Scheme II



Scheme III



protoadamantane or 2,5-dehydro-4-oxahomoadamantane[5]) as colorless crystals (50%), mp 255–256 °C. The assigned structure of **2a** was supported by the analysis and spectral data. In the ^1H NMR spectrum, **2a** revealed a characteristic doublet of doublets at δ 4.85 ($J_{3,9}$ = 5.0 Hz, $J_{3,2}$ = 8.0 Hz, 1 H) due to H_3 and an overlapped multiplet at δ 5.0–4.7 (1 H) assignable to H_5. The remaining oxetane ring proton H_2 appeared as a quartet at δ 3.33 (J = 8.0 Hz, 1 H). The given 2,4-oxa-bridged protoadamantane skeleton was furthermore corroborated by appearance of ten lines (four triplets and six doublets) in the ^{13}C NMR spectrum, which was never compatible with 2,4-oxa-bridged adamantane, a regioisomer (**3a**, Scheme I). Irradiation of 3-*endo*-acetylbicyclo[3.3.1]non-6-ene (**1b**)[6] afforded also 2,4-oxa-bridged protoadamantane derivative **2b** in 64% yield but no 2,4-oxa-bridged adamantane **3b**. The selective formation of only **2** in the intramolecular Paterno–Büchi reaction of **1** may be rationalized by a conformational preference of A to B: the interatomic distance between oxygen and C_7 or C_6 on a Dreiding stereomodel is closer in A than in B. Also, steric repulsion between oxygen and H_{4n} in B is unfavorable to formation of **3** as in the intramolecular ketene cycloaddition of this ring system.[2,7]

Conversions of 2,4-Oxa-Bridged Protoadamantanes 2a,b to 2-Substituted and 2,4-Disubstituted Protoadamantanes and a 2,4-Disubstituted Adamantane. Treatment of **2a** and **2b** with dry hydrogen chloride gas under ice cooling produced stereospecifically 2-*endo*-hydroxy-4-*exo*-chloroprotoadamantane derivatives **7a** and **7b**, respectively, in high yields (Scheme II).[8] The chlorohydrin **7a** revealed ^1H NMR signals at δ 4.61 (dt, 1, $J_{4n,5n}$ = 7.5 Hz, $J_{4n,3}$ = $J_{4n,5x}$ = 2.3 Hz, H_{4n})[9] and 4.30 (dd, 1, $J_{2x,3}$ = 9.0 Hz, $J_{2x,1}$ = 4.5 Hz, H_{2x}),[10] supporting the assigned stereochemistry. The regiochemistry of the oxetane ring opening was furthermore supported by conversion of **7a** to **8a** via the Jones oxidation.[11] The cyclopentanone structure of **8a** was supported by appearance of a strong IR (CCl_4) carbonyl absorption in 1740 cm^{-1} which was practically identical with that reported for protoadamantan-2-one[10] but quite different from that reported for protoadamantan-4-one.[12] The stereo- and regiochemistry of **7b** were also supported by appearance of a characteristic broad doublet at δ 4.58 ($J_{4n,5n}$ = 6.0 Hz) due to H_{4n} and by the chemical conversions described below. The reaction of **2b** with hydrogen bromide also yielded bromohydrin **9** regio- and stereospecifically in 77% yield. The above regioselective oxetane ring openings of **2a** and **2b** could be rationalized by assuming the formation of an intermediate oxonium ion which is subsequently attacked by halide anion at the less hindered C_5.[8] An examination on the Dreiding stereomodel indicated that the nucleophilic attack at C_3 is apparently hindered by the $C_{10}H_{syn}$ group.[13]

Reduction of **2b** with lithium aluminum hydride[14] in *N*-methylmorpholine under reflux gave 2-*endo*-hydroxy-2-*exo*-methylprotoadamantane (**10**) in 71.7% yield. Treatment of **10** with phosphorus oxychloride in pyridine afforded 2-methyleneprotoadamantane (**11**) which had ^1H NMR signals at δ 4.78 and 4.60, both as triplets (J = 1.5 Hz), due to vinyl methylene protons (Scheme II).

Similar treatment of **7b** with phosphorus oxychloride also yielded a dehydration product **14**, however, which was not protoadamantane derivative **12** on the basis of the following spectral and chemical evidence (Scheme III). In the ^1H NMR spectrum, **14** exhibited two singlets at δ 4.63 (2 H) and 4.29 (1 H) assignable to vinyl methylene protons and H_{4a}, respectively. Reduction of **14** with tri-*n*-butyltin hydride gave known methyleneadamantane **15**[15] in 79% yield, and the Lemieux–von Rudloff oxidation[16] led to the formation of known 4(*e*)-chloroadamantan-2-one (**16**)[17] in 14% yield. The isolation of **15** and **16** from **14** confirmed the formation of the adamantane skeleton (**14**) during the

(5) For carbocyclic dehydrohomoadamantane isomers, see: Murray, R. K., Jr.; Ford, T. M. *J. Org. Chem.* **1979**, *44*, 3504.
(6) Goff, D. L.; Murray, R. K., Jr. *J. Org. Chem.* **1978**, *43*, 3179.
(7) For mechanistic studies on intramolecular cycloadditions of $\Delta^{\gamma,\delta}$-unsaturated carbonyl systems, see: (a) Sauers, R. R.; Rousseau, A. D.; Byrne, B. *J. Am. Chem. Soc.* **1975**, *97*, 4947; (b) Dalton, J. C.; Tremont, S. J. *Ibid.* **1975**, *97*, 6916 and references cited therein.
(8) For oxetane ring openings with hydrogen halides, see: Searles, S., Jr.; Pollart, K. A.; Block, F. *J. Am. Chem. Soc.* **1957**, *79*, 952; ref 3d.
(9) (a) The signal pattern was quite different from that (td, J = 9.0, 3.8 Hz) of H_{4x} observed for 2-*endo*-(methylamino)-4-*endo*-hydroxyprotoadamantane (Sasaki, T.; Eguchi, S.; Suzuki, T. *J. Chem. Soc., Chem. Commun.* **1979**, 506). (b) See also: Lenoir, D.; Hall, R. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 2138. (c) For ^1H NMR data of 2-*exo*-chloroprotoadamantan-5-one, see: Murray, R. K., Jr.; Morgan, T. K., Jr. *J. Org. Chem.* **1975**, *40*, 2642.
(10) For IR and ^1H NMR spectral data of protoadamantan-2-one and 2-*endo*-hydroxyprotoadamantane, see: Whitlock, H. W., Jr.; Siefken, M. W. *J. Am. Chem. Soc.* **1968**, *90*, 4929.
(11) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 142.
(12) Protoadamantan-4-one is known to exhibit characteristic splitted carbonyl absorptions at 1719–1729 and 1712–1719 cm^{-1} in CCl_4: (a) ref 9b; (b) Alford, J. R.; McKervey, M. A. *J. Chem. Soc. D* **1970**, 615; (c) Lunn, W. H. W. *J. Chem. Soc. C* **1970**, 2124; (d) Sinnott, M. L.; Storesund, H. J.; Whiting, M. C. *J. Chem. Soc. D* **1969**, 1000.
(13) A referee suggested kindly that 2-*exo*-chloro-4-*endo*-hydroxyprotoadamantane, a product from C_3 attack, instead of the given **7a** may be more likely structure for the product from **2a** and HCl on the basis of mechanistic considerations: cyclopentyl systems undergo S_N2 reactions faster than cyclohexyl systems in general. However, the spectral and chemical evidence clearly supported the given **7a** structure as discussed in the text. The anomalous behavior of **2** is apparently ascribable to the unique cage structure.
(14) For reductive cleavage of oxetanes, see: (a) Searles, S., Jr.; Pollart, K. A.; Lutz, E. F. *J. Am. Chem. Soc.* **1957**, *79*, 948; (b) ref 3a,b.
(15) Schleyer, P. v. R.; Nicholas, R. D. *J. Am. Chem. Soc.* **1961**, *83*, 182.
(16) Reference 11, p 810.
(17) Snatzke, G.; Eckhardt, G. *Chem. Ber.* **1968**, *101*, 2010.

dehydration of **7b**. Considering the normal formation of 2-methyleneprotoadamantane (**11**) from **10** (Scheme II), this rearrangement could be rationalized by a protoadamantyl–adamantyl rearrangement via a homoallyl cation **13** of primary product **12** as shown in Scheme III.[18]

As described above, the relative ease with which **2** and **14** can be obtained by the route presented here demonstrates the feasibility of extending this method to the synthesis of other 2-substituted and 2,4-disubstituted protoadamantane and adamantane derivatives.

Experimental Section[19]

4-Oxatetracyclo[5.3.1.0.^{2,5}0^{3,9}]undecane (2a). A stirred solution of 3-*endo*-formylbicyclo[3.3.1]non-6-ene (**1a**;[4] 300 mg, 2.00 mmol) in deoxygenated *n*-hexane (300 mL) under an argon atmosphere was irradiated for 20 h through a Vycor filter with a 100-W high-pressure mercury lamp. Removal of the solvent and purification on a silica gel (Mallinckrodt, 100 mesh) column eluting with *n*-hexane–ether afforded **2a** as colorless crystals: 150 mg (50.0%); mp 255–256 °C; IR (KBr) 2900, 2840, 1440, 1330, 1010, 950, 930, 900, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.85 (dd, 1, $J_{3,2}$ = 8.0 Hz, $J_{3,9}$ = 5.0 Hz, C_3H), 5.0–4.7 (m, 1, C_5H), 3.33 (q, 1, $J_{2,3} = J_{2,1} = J_{2,5}$ = 8.0 Hz, C_2H), 2.60–1.08 (m, 11, other protons); ^{13}C NMR ($CDCl_3$) δ 87.6 (d, 1 C, $J_{C,H}$ = 151.4 Hz), 79.1 (d, 1 C, $J_{C,H}$ = 153.9 Hz), 39.8 (t, 1 C), 39.7 (d, 1 C), 39.1 (t, 1 C), 38.6 (d, 1 C), 34.5 (t, 1 C), 31.9 (t, 1 C), 30.7 (d, 1 C), 27.9 (d, 1 C); mass spectrum, *m/z* (relative intensity) 150 (66.7, M$^+$), 117 (33.3), 81 (51.5), 80 (100).

Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.89; H, 9.47.

3-Methyl-4-oxatetracyclo[5.3.1.0.^{2,5}0^{3,9}]undecane (2b). A stirred solution of 3-*endo*-acetylbicyclo[3.3.1]non-6-ene (**1b**;[6] 1.148 g, 7.00 mmol) in deoxygenated *n*-hexane (500 mL) was irradiated as above for 20 h. Removal of the solvent gave crude products which were purified by Kugelrohr distillation (50–60 °C, 5.0 mm), followed by chromatography on a silica gel column eluting with *n*-hexane–ether to give the oxetane **2b** as a colorless oil: 738 mg (64.3%); $n^{20}$$_D$ 1.5096; IR (neat) 2920, 1440, 1380, 1340, 1220, 1210, 1160, 1130, 970, 910, 860 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.67 (br d, 1, $J_{5,2}$ = 7.8 Hz, C_5H), 2.89 (t, 1, $J_{2,1} = J_{2,5}$ = 7.8 Hz, C_2H), 1.40 (s, 3, CH_3), 2.8–1.0 (m, 11, other protons); ^{13}C NMR ($CDCl_3$) δ 93.2 (s, 1 C), 73.8 (d, 1 C, $J_{C,H}$ = 153.8 Hz), 45.6 (d, 1 C), 43.7 (d, 1 C), 40.7 (t, 1 C), 39.1 (t, 1 C), 34.7 (t, 1 C), 32.2 (t, 1 C), 31.3 (d, 1 C), 27.7 (d, 1 C), 25.7 (q, 1 C); mass spectrum, *m/z* (relative intensity) 164 (100, M$^+$), 131 (54.3), 121 (76.1), 117 (37.0).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.49; H, 9.76. Found: C, 80.44; H, 9.83.

2-*endo*-Hydroxy-4-*exo*-chloroprotoadamantane (7a). Into an ice-cooled solution of oxetane **2a** (120 mg, 0.80 mmol) in anhydrous benzene (6 mL) was bubbled dry hydrogen chloride gas for 5 min, and the mixture was allowed to stand for 0.5 h. The mixture was diluted with benzene (14 mL), washed with 5% aqueous sodium bicarbonate and water successively, and dried ($MgSO_4$). Removal of the solvent gave practically pure chlorohydrin **7a**: 140 mg (93.8%); mp 157–161 °C; IR (KBr) 3350, 1450, 1310, 1260, 1090, 970, 950, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.61 (dt, 1, $J_{4n,5n}$ = 7.5 Hz, $J_{4n,3} = J_{4n,5x}$ = 2.3 Hz, H_{4n}), 4.30 (dd, 1, $J_{2x,3}$ = 9.0 Hz, $J_{2x,1}$ = 4.5 Hz, H_{2x}), 1.80 (s, 1, OH, disappeared on shaking with D_2O), 3.0–1.2 (m, 12, other protons); mass spectrum, *m/z* (relative intensity) 188 (1.3), 186 (3.8, M$^+$), 170 (16.3), 168 (48.8), 150 (100), 133 (75.0).

Anal. Calcd for $C_{10}H_{15}OCl$: C, 64.34; H, 8.10. Found: C, 64.61; H, 7.82.

4-*exo*-Chloroprotoadamantan-2-one (8a). To a stirred solution of **7a** (30 mg, 0.15 mmol) in acetone (2 mL) was added the standard Jones reagent (2.67 M solution, 0.06 mL, 0.16 mmol)[11] at 20 °C. After the stirring was continued for 2 h, the acetone layer was decanted, and the residual green layer was washed with acetone (2 × 1 mL). The combined acetone layer and washings were evaporated to dryness, and the residue was sublimed (120–125 °C, 20 mm) to afford the chloro ketone **8a** as a camphoraceous solid: 27 mg (96.8%); mp 150–151 °C; IR (CCl_4) 1740, 1450, 1270, 1175, 1083, 900 cm^{-1}; ^{1}H NMR (CCl_4) δ 4.38 (dd, 1, $J_{4n,5n}$ = 7.2 Hz, $J_{4n,3}$ = 3.0 Hz, $J_{4n,5x}$ = 0 Hz, H_{4n}), 2.9–1.1 (m, 12, other protons); mass spectrum, *m/z* (relative intensity) 186 (6.8), 184 (18.1, M$^+$), 149 (61.5), 121 (75.0), 79 (100), 77 (51.0), 42 (96.5), 39 (54.5).

Anal. Calcd for $C_{10}H_{13}OCl$: C, 65.04; H, 7.10. Found: C, 64.96; H, 7.21.

Compound **8a** gave 2,4-dinitrophenylhydrazone **8b** as orange needles after recrystallization from CH_2Cl_2–EtOH: mp 164–165 °C; IR (KBr) 3310, 2920, 1615, 1590, 1510, 1430, 1336, 1300, 1270, 1135, 1095, 1070, 830, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 11.3–10.7 (m, 1, NH, disappeared on shaking with D_2O), 9.2–7.7 (ABX m, 3, aromatic protons), 5.4–3.9 (m, 1, H_{4n}),[20] 3.7–3.1 (m, ca. 2, H_1 and H_3), 3.1–1.2 (m, 10, other protons).

Anal. Calcd for $C_{16}H_{17}N_4O_4Cl$: C, 52.68; H, 4.70; N, 15.36. Found: C, 52.69; H, 4.72; N, 15.33.

2-*endo*-Hydroxy-2-*exo*-methyl-4-*exo*-chloroprotoadamantane (7b). Into an ice-cooled solution of **2b** (164 mg, 1.00 mmol) in anhydrous benzene (7 mL) was bubbled dry hydrogen chloride gas for 5 min. After being allowed to stand for 0.5 h, the mixture was diluted with benzene (13 mL), washed with 5% aqueous sodium bicarbonate and water successively, and dried ($MgSO_4$). Removal of the solvent gave analytically pure **7b** as colorless crystals: 185 mg (92.2%); mp 77–78 °C; IR (KBr) 3440, 1430, 1370, 1300, 1240, 1140, 1100, 950, 900 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.58 (br d, 1, $J_{4n,5n}$ = 6.0 Hz, C_4H_n), 1.36 (s, 3, CH_3), and 2.5–1.1 (m, 13, OH and other protons, decreased to 12 H on shaking with D_2O); mass spectrum, *m/z* (relative intensity) 200 (3.0, M$^+$), 187 (16.0), 185 (49.0), 184 (10.0), 182 (30.0), 147 (100).

Anal. Calcd for $C_{11}H_{17}OCl$: C, 65.83; H, 8.54. Found: C, 66.00; H, 8.36.

2-*endo*-Hydroxy-2-*exo*-methyl-4-*exo*-bromoprotoadamantane (9). A solution of **2b** (164 mg, 1.00 mmol) in benzene (7 mL) was treated with dry hydrogen bromide gas as above. The usual workup gave **9** as crystals: 197 mg (77.3%); mp 93–94 °C; IR (KBr) 3320, 1450, 1350, 1290, 1200, 1120, 900, 740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.75 (br d, 1, $J_{4n,5n}$ = 6.0 Hz, C_4H_n), 1.38 (s, 3, CH_3), 2.6–1.2 (m, 13, OH and other remaining protons, decreased to 12 H on shaking with D_2O); mass spectrum, *m/z* (relative intensity) 245 (1.6), 244 (1.3), 243 (1.7, M – 1), 165 (100), 148 (73.0), 147 (99.0), 119 (58.0), 105 (95.0).

Anal. Calcd for $C_{11}H_{17}OBr$: C, 53.89; H, 6.99. Found: C, 53.96; H, 6.92.

2-*endo*-Hydroxy-2-*exo*-methylprotoadamantane (10). A mixture of $LiAlH_4$ (400 mg, 10.5 mmol) and **2b** (164 mg, 1.00 mmol) in anhydrous *N*-methylmorpholine (15 mL) was heated under reflux under an argon atmosphere for 48 h. The cooled mixture was carefully diluted with 10% hydrochloric acid (50 mL) and extracted with ether (5 × 10 mL). The combined extracts were dried ($MgSO_4$) and evaporated to dryness to give crude product which was purified on a silica gel column eluting with *n*-hexane–ether to afford the alcohol **10** as crystals: mp 97–99 °C; IR (KBr) 3360, 1450, 1360, 1320, 1120, 940, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3, CH_3), 2.4–1.0 (m, 15, OH and other protons, decreased to 14 H on shaking with D_2O); mass spectrum, *m/z* (relative intensity) 166 (6.3, M$^+$), 151 (100), 148 (31.3).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.77; H, 10.61.

2-Methyleneprotoadamantane (11). To an ice-cooled and stirred solution of **10** (70 mg, 0.42 mmol) in anhydrous pyridine

(18) (a) For protoadamantyl–adamantyl rearrangement, see: Kovačević, D.; Goričnik, B.; Majerski, Z. *J. Org. Chem.* **1978**, *43*, 4008 and references cited therein. (b) For the homoallyl–cyclopropylcarbinyl cation system, see: Richey, H. G., Jr.; Wiberg, K. B.; Hess, B. A., Jr.; Ashe, A. J., III In "Carbonium Ions"; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1972; Vol. III, Chapters 25 and 26.

(19) Microanalyses were performed with a Perkin-Elmer 240B elemental analyzer. Melting points were determined in a sealed tube with a Yanagimoto micro melting point apparatus (hot-stage type) and are uncorrected. IR spectra were obtained with a JASCO IRA-I spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM-C-60HL instrument at 60 MHz, while ^{13}C NMR spectra were recorded on a JEOL JNM-FX 60 FT NMR spectrometer at 15.04 MHz in $CDCl_3$. All NMR spectral peak positions are given in parts per million (δ) downfield from tetramethylsilane as an internal standard. Mass spectra were obtained with a Hitachi RMS-4 mass spectrometer at 70 eV.

(20) The hydrazone **8b** may be a mixture of syn and anti isomers.

(5 mL) was added phosphorus oxychloride (1.01 mL, 11.0 mmol). After the stirring was continued for 24 h at room temperature, the mixture was carefully diluted with water (30 mL) and extracted with ether (3 × 15 mL). The combined extracts were washed successively with 10% hydrochloric acid, water, and aqueous saturated sodium chloride solution and dried ($MgSO_4$). Removal of the solvent gave crude olefin which was purified on a silica gel column eluting with *n*-pentane to give pure olefin **11** as a very sublimable colorless solid: 44 mg (70.5%); mp 140–142 °C; IR (KBr) 3080, 2910, 2870, 1650, 1440, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.78, 4.60 (both t, 2, J = 1.5 Hz, C=CH_2), 2.85–2.40 (m, 2, C_1H, C_3H), 2.4–1.0 (m, 12, other protons); ^{13}C NMR ($CDCl_3$) δ 160.5 (s, 1 C), 101.5 (t, 1 C), 43.3 (d, 1 C), 40.9 (t, 1 C), 40.7 (d, 1 C), 39.9 (t, 1 C), 34.0 (d, 1 C), 30.8 (t, 1 C), 27.8 (d, 1 C), 27.7 (t, 1 C), 23.2 (t, 1 C).

Anal. Calcd for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 89.02; H, 10.98.

4(*e*)-Chloro-2-methyleneadamantane (14). To an ice-cooled and stirred solution of **7b** (402 mg, 2.00 mmol) in anhydrous pyridine (20 mL) was added phosphorus oxychloride (4.8 mL, 52 mmol) portionwise during 10 min. After the stirring was continued for 24 h at room temperature, the mixture was diluted with water (50 mL) and extracted with ether (3 × 20 mL). The combined extracts were washed successively with 10% hydrochloric acid, water, and aqueous saturated sodium chloride solution and dried ($MgSO_4$). Removal of the solvent gave crude olefin which was purified on a silica gel column eluting with *n*-hexane to afford the chloro olefin **14** as crystals: 275 mg (75.3%); mp 57–61 °C; IR (KBr) 3080, 1645, 1450, 1360, 1310, 1280, 1230, 1090, 1080, 880, 800, 780, 760, 680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.63 (s, 2, C=CH_2), 4.29 (br s, 1, C_4H_{ax}), 2.76–1.33 (m, 12, other protons); ^{13}C NMR ($CDCl_3$) δ 155.0 (s, 1 C), 104.3 (t, 1 C), 67.2 (d, 1 C), 46.3 (d, 1 C), 39.3 (t, 1 C), 38.6 (t, 1 C), 37.5 (d, 1 C), 35.5 (d, 1 C), 32.7 (t, 1 C), 30.6 (t, 1 C), 27.5 (d, 1 C); mass spectrum, m/z (relative intensity) 184 (32.8, M + 2), 182 (100, cm^+), 147 (50.7), 146 (26.9), 131 (73.1), 105 (46.3), 91 (41.8).

Anal. Calcd for $C_{11}H_{15}Cl$: C, 72.32; H, 8.28. Found: C, 72.57; H, 8.03.

Reduction of 14 with Tri-*n*-butyltin Hydride. A mixture of **14** (78 mg, 0.43 mmol), tri-*n*-butyltin hydride (125 mg, 0.43 mmol), and azobis(isobutyronitrile) (1 mg) in cyclohexane (2 mL) was heated under reflux for 20 h. Removal of the solvent and chromatography on a silica gel column (*n*-pentane) afforded methyleneadamantane **15** (50 mg, 79.1%) which was identical with an authentic sample[15] by comparison of the IR and ^1H NMR spectra and GLC retention times.

Oxidation of 14 with Sodium Periodate–Potassium Permanganate. To an ice-cooled and stirred solution of **14** (91 mg, 0.50 mmol) and sodium periodate (429 mg, 1.80 mmol) in acetone (1.5 mL) and water (1.9 mL) was added a solution of potassium permanganate (14 mg, 0.09 mmol) in water (0.5 mL).[16] After the stirring was continued for 14 h at room temperature, the mixture was diluted with water (10 mL) and extracted with ether (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and evaporated to give crude ketone which was purified by preparative TLC (silica gel, CH_2Cl_2) to afford the chloro ketone **16** as colorless crystals [13 mg (14.0%), mp 192–195 °C] whose IR and ^1H NMR spectra were consistent with those reported.[17]

Registry No. 1a, 31603-46-0; **1b**, 66483-55-4; **2a**, 74381-06-9; **2b**, 74381-07-0; **7a**, 74381-08-1; **7b**, 74381-09-2; **8a**, 74381-10-5; **8b**, 74381-11-6; **9**, 74381-12-7; **10**, 74381-13-8; **11**, 74381-14-9; **14**, 74381-15-0; **15**, 875-72-9; **16**, 56781-81-8.

Synthesis of Pyrrolo[3,2-*d*]pyrimidines from Furazano[3,4-*d*]pyrimidines via Enolate and Ene Adducts[1a,b]

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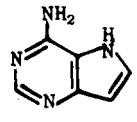
The reaction of 7-(acylamido)furazano[3,4-*d*]pyrimidines **2** (FZP's) with certain enamines and enolate anions provides intermediates suitable for unequivocal transformation into pyrrolo[3,2-*d*]pyrimidines **11** and **12**. The reaction of **2** with enolate anions appears to proceed via an addition–elimination mechanism. The structures of the FZP–enamine adducts (**7a–h**) and their unusual chemical reactivity are explained in terms of an ene–retroene equilibrium. The proposed ene reaction involves the 6,7 nitrogen–carbon double bond of the FZP as the enophile and the 2-aminopropene fragment present in a limited class of ketone enamines as the ene. The amphoteric nature of the ene adducts was used to advantage in their conversion to derivatives **8**, **9**, and **10**, all of which are incapable of decomposition via the retroene pathway followed by **7a–h**. Intermediates **3–5**, **9**, and **10** were subsequently converted into 11 different pyrrolo[3,2-*d*]pyrimidines without complication by using either zinc in acetic acid or catalytic reduction with a palladium-on-carbon catalyst in acetic acid. In five of the cases where a 2-(CH_3S)FZP was the substrate for reduction, the recently uncovered desulfurizing capability of palladium-on-carbon in hot acetic acid permitted direct isolation of 2-unsubstituted pyrrolo[3,2-*d*]pyrimidines in good yield.

Although there is only one antibiotic of limited use known to contain the pyrrolo[3,2-*d*]pyrimidine ring system (**1**),[2] a substantial number of reports concerning the synthesis of variously substituted examples of this purine isoster have been recently reviewed.[3] At least three reports of new synthetic approaches to this ring system have ap-



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(1) (a) This report is based in part on the Ph.D. Thesis of G.P.B., Princeton University, 1971. (b) This report is based in part on the Ph.D. Thesis of L.E.C., Princeton University, 1976. (c) To whom correspondence should be addressed at the Department of Chemistry, New York University, 4 Washington Place, Room 514, New York, NY 10003.

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