6-*O*-Acetyl-1-iodocodeine (3). A 1-g sample of 1-iodocodeine was added to a mixture of dry pyridine (1 mL) and acetic anhydride (5 mL). The resulting solution was stirred at room temperature for 20 h then concentrated in vacuo to a residual oil which was treated twice with 5 mL each of benzene which was evaporated under reduced pressure. After the addition of 10 mL of water to the residual oil, solidification occurred after stirring for about 1 h. The product was collected by filtration, washed with water, and dried under high vacuum yielding 670 mg of **3**, mp 177–179 °C. A second crop of 360 mg (total yield is 94%) was obtained from the mother liquors. A sample for x-ray crystallographic analysis, crystallized from ethyl acetate–cyclohexane–hexane, was of mp 180–181 °C: NMR ($CDCl_3$) δ 2.13 (s, 3 H, CH_3CO_2), 2.43 (s, 3 H, NCH_3), 3.82 (s, 3 H, OCH_3), 5.40, 5.62 (dd, 2 H, CH=CH), 7.06 (s, 1 H, aromatic); *m/e* 467 (calcd for $C_{20}H_{22}NO_4I$, 467).

1-Iodomorphine (5). A solution of 2.12 g (5 mmol) of **2** in 12.5 mL of chloroform was added over a 4-min period to a stirred solution of 7.5 g of BBr_3 in 80 mL of chloroform maintained at 15–20 °C. Stirring was continued for an additional 15 min after which time the mixture was poured into 50 g of cracked ice and 10 mL of concentrated ammonium hydroxide solution. After standing 0.5 h at 0 °C, the solid was collected by suction filtration and washed successively with small portions of cold chloroform and water then dried to a constant weight of 1.14 g (54%): mp 215 °C dec; IR (KBr) 3500 (b, phenolic OH), 3350, 3255 (H-bonded OH); UV (methanol) λ_{max} 216 (E 27 070), inflection 245 (6450), inflection 288 (2100), max 293 nm (2160); NMR ($CDCl_3$ + Me_2SO) δ 2.30 (s, 3 H, NCH_3), 4.13 (m, 1 H, CHOH), 5.30, 5.53 (dd, 2 H, –CH=CH–), 7.00 (s, 1 H aromatic); *m/e* 411 (calcd for $C_{17}H_{18}NIO_3$, 411). A sample recrystallized from 0.1 N HCl was of mp 217 °C dec. Anal. Calcd for $C_{17}H_{18}NIO_3 \cdot HCl \cdot \frac{1}{2}H_2O$: C, 44.7; H, 4.3; N, 3.1; Cl, 7.8; I, 27.8. Found: C, 44.7; H, 4.9; N, 3.2; Cl, 7.5; I, 27.5.

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Registry No.—1, 76-57-3; **2**, 64739-74-8; **3**, 64754-11-6; **4**, 64739-75-9; **5**, 64739-76-0; **5**-HCl, 64739-77-1; NaI, 7681-82-5; $Na^{125}I$, 24359-64-6; acetic anhydride, 108-24-7.

Supplementary Material Available: Atomic and anisotropic thermal parameters for **3** (2 page). Ordering information can be found on any current masthead page.

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(10) See supplementary material paragraph.

Rearrangement of *N*-Chloro-*N*-acetyl-1-aminoadamantane by Aluminum Chloride[1]

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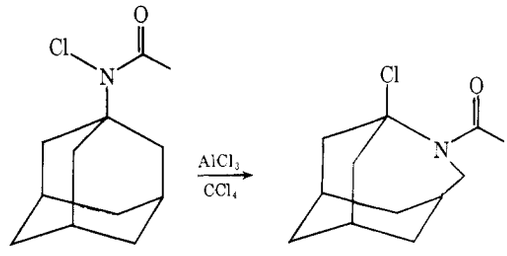
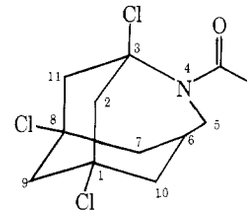
In 1971 it was reported that *N*-chloro-*N*-acetyl-1-aminoadamantane (**1**) rearranges to 3-chloro-*N*-acetyl-4-azahomoadamantane (**2**) in carbon tetrachloride with aluminum chloride catalyst,[2] eq 1. The authors assigned the structure on the basis of elemental analysis, IR, NMR, Beilstein test,



(1)

1 2



3

and chemical behavior (dehalogenation). On repeating this work, the product that we have obtained from the rearrangement is 1,3,8-trichloro-*N*-acetyl-4-azahomoadamantane (**3**). Determination of the structure was accomplished by means of elemental analysis, IR, ^1H and ^{13}C NMR, and mass spectrometry. The ^{13}C NMR spectrum contained nine peaks (as expected based on symmetry of the molecule); however, the downfield position and off-resonance decoupling splitting pattern suggested that both bridgehead carbons, 1 and 8, are quaternary. In our investigations[3] involving the ^{13}C NMR spectra of 3-substituted 4-azahomoadamantanes, a typical range for chemical shift of bridgeheads 1 and 8 is δ 26 to 28. Off-resonance decoupling shows a doublet which is characteristic of tertiary carbon atoms. In work with related models, the chemical shift for C–Cl carbon in 1-chloroadamantane is δ 67.25, for 1,3-dichloroadamantane it is δ 66.57, and for 1,3,5-trichloroadamantane it is δ 64.5[4] which is very close to the value of δ 64.97 for **3**. Mass spectrometry revealed molecular ions at *m/e* 295, 297, and 299 in about 3:3:1 ratio, as expected for the trichloro compound. The difference in melting points of the two preparations, in addition to other data,[5] suggests that the prior preparation may be a mixture derived from varying degrees of chlorination.

Investigation of reaction variables revealed (TLC and NMR) that either lowering the temperature or shortening the time below 24 h produced a complex mixture containing some starting material together with unidentified products (possibly containing a lower degree of chlorination). If the reaction is carried out for less than 4 h, most of the starting material is recovered. Reaction times of over 40 h produced good yields of product which could be easily purified by column chromatography on silica and recrystallization. The same product was obtained at 40 and 68 h but at lower yield for the shorter time.

The formation of compound **3** can be rationalized mechanistically on the basis of two known reactions: (1) the rearrangement of *N,N*-dichloro-1-aminoadamantane to the azahomoadamantyl system,[6] apparently via electron-deficient nitrogen, and (2) chlorination of C–H bonds by the alkyl halide–aluminum chloride combination. The CCl_4–$AlCl_3$ system has been used for 1,3-dichlorination of adamantane.[7] The specificity of chlorination (carbons 1 and 8, but not 6) can be rationalized by the inductive effect of amide nitrogen and by the "cage effect" (cation stabilization by unshared electrons on nitrogen).[8]

Experimental Section

Infrared spectra were obtained on a Beckman IR-8 instrument (KBr disks); ^1H NMR spectra on a Varian T60-A spectrometer and ^{13}C NMR on a Varian CFT-20 spectrometer ($CDCl_3$ as solvent and

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Me_4Si as reference); and mass spectra on a Hitachi Perkin-Elmer RMU-6E instrument (70 eV and 170 °C). Elemental analyses were performed by Baron Consulting Co., Orange, Conn. and Micro-Tech Laboratories, Skokie, Ill. Carbon tetrachloride was dried with calcium chloride. Skelly B was extracted with concentrated H_2SO_4, washed with 10% Na_2CO_3 and water, dried with $CaCl_2$, and distilled from sodium. Other materials were used without purification.

***N*-Chloro-*N*-acetyl-1-aminoadamantane (1).** The method of Sasaki et al. was used:[2] yield 99.8%;[9] mp 69–71 °C (lit.[2] mp 69–71 °C). IR and ^1H NMR spectra were similar to those reported: IR 1660, 1450, 1370, 1250, 1065, 815, 755, 675 cm^{-1} (lit.[2] 1657, 680); ^1H NMR δ 2.20 (12 H), 1.67 (6 H) (lit.[2] 2.13 (12 H), 1.65 (6 H)). Anal. Calcd for $C_{12}H_{18}ClNO$: C, 63.24: H, 7.97; N, 6.15. Found: C, 62.90; H, 7.66; N, 6.07.

Rearrangement of *N*-Chloro-*N*-acetyl-1-aminoadamantane (1). The procedure of Sasaki et al.[2] was used except for a change in reaction time (68 h instead of 40 h). Chromatography on silica with chloroform as eluent produced **3**, mp 74–76 °C dec (lit.[2] 69.5–71.5 °C). Recrystallization from dry Skelly B afforded off-white plates, mp 85–86 °C. IR and ^1H NMR were similar to those reported: IR 1670, 1370, 1320, 1270, 1120, 1015, 850, 780, 735 cm^{-1} (lit.[2] 1671, 853, 743, 713 cm^{-1}); ^1H NMR δ 2.55 (s, NCH_2), 2.22 (s, CH_3), 2.60–1.90 (m) (lit.[2,5] δ 2.55 (d, NCH_2), 2.23 (s, CH_3), 2.50–1.45 (m)); ^{13}C NMR δ 173.92 (C=O), 66.92 (3), 64.97 (1, 8), 55.20 (5), 48.17 and 44.44 (2, 11) and (7, 10), 37.53 (9), 32.50 (6), 25.67 (CH_3); mass spectrum *m/e* (relative intensity) 91 (36), 127 (28), 128 (32), 130 (20), 148 (45), 170 (30), 186 (100), 187 (23), 188 (54), 190 (21), 210 (23), 226 (100), 227 (36), 228 (59), 261 (41), 263 (27), $M^{+\cdot}$ 295 (1), $(M^{+\cdot}+2)$ 297 (1), $(M^{+\cdot}+4)$ 299 (0.3); $(M^{+\cdot}):(M^{+\cdot}+2):(M^{+\cdot}+4)$ = 3:3:1. Anal. Calcd for $C_{12}H_{16}Cl_3NO$: C, 48.59; H, 5.44; Cl, 35.86; N, 4.72. Found: C, 48.40; H, 5.31; Cl, 35.18;[10] N, 4.92.

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Registry No.—**1**, 64741-22-6; **3**, 64741-23-7; $AlCl_3$, 7446-70-0.

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Thermal Rearrangement of Halocineole to Halopinol Derivatives

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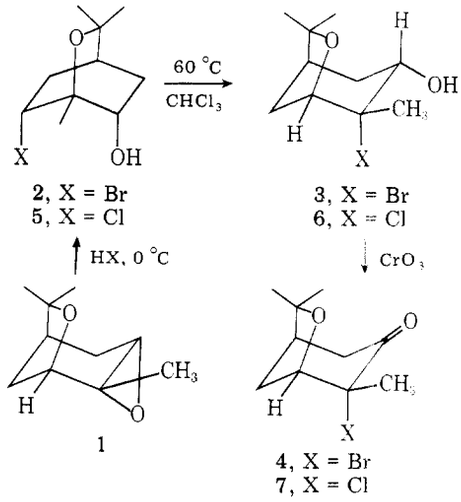
During an investigation of pinol oxide[2] (**1**) it was noted that its conversion to *endo*-6-hydroxy-*endo*-7-bromocineole (**2**) by fuming hydrobromic acid was complete after 1 h at 0 °C. Bromohydrin **2** was stable in chloroform at room temperature; however, at 60 °C it was largely transformed into pinol bromohydrin (**3**). The conversion of **2** into **3** at 60 °C was essentially complete after 20 h, at which time a mixture of 80% **3** and 20% **2** was on hand.



The structure of **3** was suggested by its NMR spectrum which showed, in part, a methyl singlet at 1.87 ppm attributed to a CH_3CBr group and a doublet at 4.22 ppm characteristic of the bridgehead proton of a pinol ring.[2] An axial C-3 proton was indicated by a broad multiplet at 3.73 ppm with a half-width of 30 Hz. Chromic acid oxidation of **3** gave the bromoketone **4**. The NMR chemical shift (1.82 ppm) of the α-methyl group in **4** was not noticeably altered on changing solvent from deuteriochloroform to benzene, while its ultraviolet spectrum showed a maximum at 307 nm requiring the presence of an equatorial methyl and axial bromine atom at C-2.

endo-6-Hydroxy-*endo*-7-chlorocineole (**5**) was recovered unchanged after refluxing in chloroform or benzene for 24 h. In refluxing toluene (110 °C) chlorohydrin **5** slowly rearranged to *cis*-pinol chlorohydrin **6**. Further change was not noted after 120 h and NMR analysis of the resulting mixture indicated the presence of 78% of **6** and 22% of **5**. In refluxing xylene (140 °C) an apparent stationary state was reached in 24 h, and severe darkening was observed on more prolonged heating. Essentially the same mixture of **6** and **5** was obtained from pure **5** when it was heated in xylene for 24 h.

The structures of *cis*-pinol chlorohydrin (**6**) and the ketone **7** obtained by chromic acid oxidation were demonstrated by spectral analysis (see the Experimental Section).

endo,endo-6,7-Dibromocineole (**8**) rearranged to pinol dibromide **9** at about the same rate that chlorohydrin **5** rearranged to **6**. Refluxing in bromobenzene (154 °C) was required for completion in 5 h and despite the formation of appreciable black tar, pinol dibromide **9** could still be isolated by column chromatography. The rearrangement of **8** to **9** was also noted on passing **8** through a GLC column at 190 °C. The structural assignment to **9** is based on its NMR spectrum and the stereochemistry is suggested by analogy with that of bromohydrin **3**.

endo,endo-6,7-Dichlorocineole (**10**) similarly rearranged to pinol dichloride **11** on refluxing in bromobenzene but much more slowly than the corresponding dibromide. A 33% conversion to **11** was noted after 18 h. Heating dichloride **10** at 280 °C for 1 h furnished **11** in good yield. The methoxy chloride **13** rearranged to **14** at a rate comparable with that of dichloride **10**.

By contrast, *endo,endo*-6,7-dihydroxycineole (**12**) and its diacetate derivative **12a**[2,3] were stable at 200 °C in refluxing tetralin.

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