3-Substituted 4-Azahomoadamantanes and *endo*-7-Aminomethylbicyclo[3.3.1]nonan-3-one from Rearrangement of 1-*N*,*N*-Dichloroaminoadamantane by Aluminum Chloride[1-3]

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Abstract: Treatment of 1-*N*,*N*-dichloroaminoadamantane (**2**) with aluminum chloride in methylene chloride gave rearranged product which was converted to *endo*-7-aminomethylbicyclo[3.3.1]nonan-3-one (**7**) on contact with aqueous acid. A similar end result, after initial amination, occurred with adamantane and 1-bromoadamantane in the presence of trichloramine–aluminum chloride. Exposure of the reaction mixture after rearrangement to other nucleophiles, *e.g.*, methanol, thiophenol, and 1,3-dimethoxybenzene, gave 3-methoxy-4-azahomoadamantane (**6b**), 3-phenylthio-4-azahomoadamantane (**6c**), and 3-(2,4-dimethoxyphenyl)-4-azahomoadamantane (**6d**), respectively. On reduction with lithium aluminum hydride, **7** was converted to 4-azahomoadamantane (**8**). The rearrangement is believed to involve electron-deficient nitrogen.

Recently, the direct synthesis of 1-aminoadamantane from treatment of adamantane with trichloramine and aluminum chloride was described,[2] in which 1-*N*,*N*-dichloroaminoadamantane (**2**) was shown to be an intermediate. This report discusses the aluminum chloride catalyzed rearrangement of **2** as a means of preparing *endo*-7-aminomethylbicyclo[3.3.1]nonan-3-one (**7**), and 3-substituted 4-azahomoadamantanes (**6b–d**).[5] In addition, the mechanistic implications are treated.

The literature contains various examples of rearrangements involving *N*-halamines.[6] These include the Hofmann–Löffler reaction,[7] transformations leading to α-amino ketones,[8] and the rearrangement of *N*-chloroazabicyclic compounds with silver ion.[9]

Results and Discussion

Synthetic Aspects. Treatment of **2** with aluminum chloride (1:2) in methylene chloride solution at 0°, followed by exposure to hydrochloric acid and subsequent neutralization, gave crude **7**. Good purity material is obtained in 70–80% yield by recrystallization. Elemental analyses and the mass spectrum (molecular ion at *m*/*e* 167) indicated the molecular formula to be $C_{10}H_{17}NO$; the proposed structure is consistent with the mass spectral fragmentation pattern. The infrared spectrum shows a broad band in the NH and OH stretching regions and a relatively weak carbonyl band, reflecting intramolecular interaction between the carbonyl and amino functionalities. Particular features of the nmr spectrum which support the assignment are a D_2O exchangeable signal (2 H) and a doublet for the methylene adjacent to the amino group. Chemical confirmation of structure was derived from basicity, benzamide formation, behavior toward carbonyl group reagents,[10] and almost quantitative conversion of **7** to 4-azahomoadamantane (**8**) by treatment with lithium aluminum hydride. Characterization of **8** was carried out by comparison with authentic material.[11]

Various conditions were examined for the rearrangement reaction. Use of either crude or purified **2** gave essentially the same results. The dihalamine is added to a suspension of aluminum chloride in methylene chloride at 0°, or aluminum chloride is introduced into a solution of **2** in methylene chloride at −30°, followed by reaction at 0°. Appropriate work-up conditions are required in order to obtain the amino ketone. When water was used instead of acid, little **7** was isolated. If the rearrangement temperature is permitted to rise above 5–10°, yields of **7** are reduced.

Related substrates gave the same end product. Addition of trichloramine to a mixture of aluminum chloride and adamantane (**1a**) or addition of 1-bromoadamantane (**1b**) to a mixture of trichloramine–aluminum chloride also leads to **7**. In the case of **1a**, the reaction is carried out as previously described,[2] but additional aluminum chloride is added prior to work-up, leading to rearrangement of **2** to **7**. Without augmentation of the catalyst, good yields of 1-aminoadamantane result.[2] At temperatures higher (10°) or lower (−25°) than 0°, the amount of amino ketone decreased appreciably. An enhanced yield of desired product was brought about when the ratio of bromoadamantane–trichloramine–aluminum chloride was increased from 1:1:2 to 1:2:4.

The literature describes other methods for preparation of substituted bicyclo[3.3.1]nonanes from adamantanes, *e.g.*, from 1,3-[12] and 2,4-[13]disubstituted

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precursors and the 1-adamantyloxy radical.[14] In the present case, a simple, high-yield pathway provides a versatile, bifunctional member.

The rearranged product was also exposed to other nucleophiles. Quenching with dry methanol containing hydrogen chloride afforded 3-methoxy-4-azahomoadamantane (**6b**) in about 50% yield. The structural formulation is supported by elemental analyses and mass, infrared, and nmr spectral data. In particular, the molecular ion at *m/e* 181 in the mass spectrum, and a D_2O exchangeable, one-proton signal, a methoxy singlet, and a doublet for the methylene protons adjacent to nitrogen in the nmr spectrum provide important information. The compound was also prepared in 75% yield by treatment of **7** with dry methanol and sulfuric acid. Exposure of **6b** to aqueous acid in the work-up stage is to be avoided; otherwise **7** is generated at the expense of **6b**. Hydrolysis of **6b** in aqueous acid gave **7**. Hydrolytic breakdown occurs even under mild conditions, namely, at room temperature for 2 hr with a 1:1 ratio of acid:**6b**. When rearranged material is mixed with nonacidified methanol, **6b** is not produced.

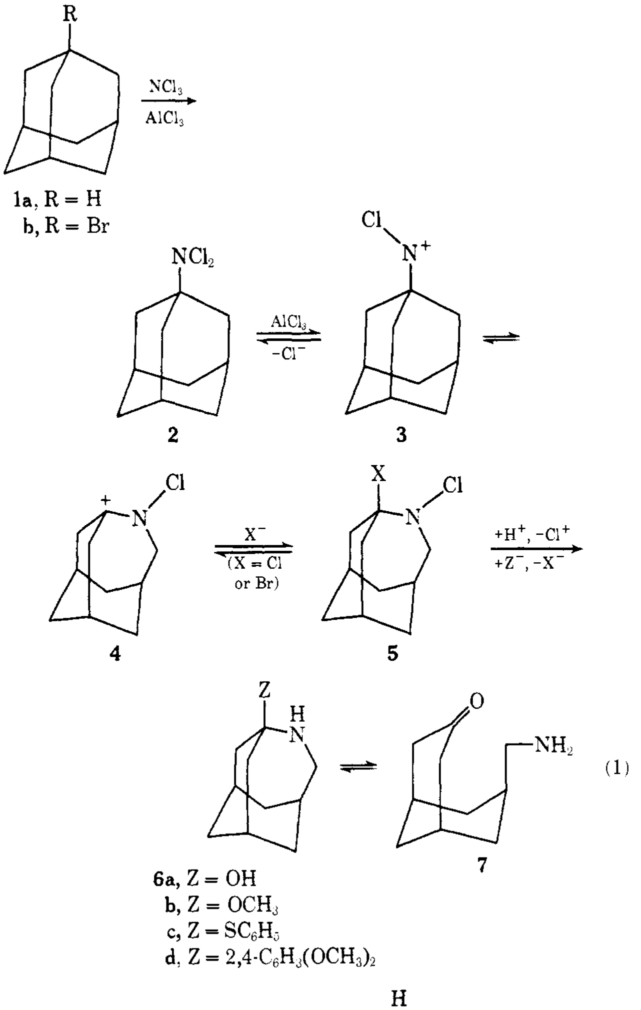
3-(Phenylthio)-4-azahomoadamantane (**6c**) was prepared in a manner similar to that of **6b** with thiophenol as the nucleophile. The assignment is consistent with microanalytical, nmr, and infrared spectral data. The mass spectrum does not show the molecular ion; however, the base peak at *m/e* 150 is contributing evidence since one would expect facile loss of $C_6H_5S\cdot$ (mass 109) from the parent molecule (mass 259). The phenylthio derivative **6c** is more stable to acid than its methoxy counterpart. Under conditions which suffice for hydrolysis of **6b**, there was recovery of **6c** with little decomposition. At reflux in concentrated hydrochloric acid, **6c** could be converted to **7**. An attempt at reversal of the process, *i.e.*, conversion of **7** to **6c** through the agency of thiophenol and sulfuric acid, was unsuccessful.

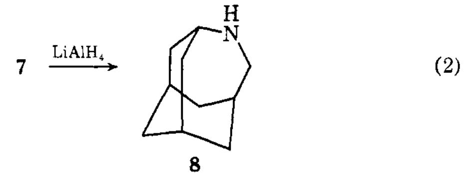
We also were able to realize the preparation of a 3-aryl-4-azahomoadamantane. After rearrangement, contact with 1,3-dimethoxybenzene, followed by aqueous acid, gave a white solid. Elemental analyses and spectral information indicated that the compound is 3-(2,4-dimethoxyphenyl)-4-azahomoadamantane (**6d**) hydrochloride. In particular, the nmr spectrum shows two D_2O exchangeable protons at low field, three aromatic protons in two groups (1:2), two methoxy singlets, and the doublet (2 H) associated with the methylene group adjacent to nitrogen. The pattern and positions of the signals for the aromatic protons are almost identical with those of 1-bromo-2,4-dimethoxybenzene. The free base **6d** was isolated by treatment of the hydrochloride with caustic. The nmr spectrum of **6d** is similar to that of the hydrochloride except that only one D_2O exchangeable proton signal is present, shifted to higher field. There are also minor changes in position of some of the other bands. The mass spectrum shows the molecular ion as the base peak at *m/e* 287. Identical material was obtained by an alternate route—reaction of **7** with 1,3-dimethoxybenzene in the presence of aluminum chloride.

In the synthesis of 3-substituted 4-azahomoadamantanes from **7** and Lewis acid catalyst, it is uncertain as to which process occurs initially, attack on the nucleophile or ring closure. Compounds of type **6** comprise a novel category. A related substance, 5-methoxy-4-azahomoadamant-4-ene, was recently described.[15]

Mechanistic Considerations. We propose that reaction proceeds according to the indicated pathway, eq 1.

The 1,2 shift leading to **4** may be concerted. Evidence for the intermediacy of **4** or **5** rests on the successful trapping by nucleophiles such as water, methanol, thiophenol, and 1,3-dimethoxybenzene. The ready hydrolysis of **6b** and **6c** to **7** suggests a ring-opening route from **4** or **5** to **7**. The transformation of **7** to **6b** with acidified methanol demonstrates the equilibrium nature of the interconversion (except for **6d**). The spectral data point to some degree of interaction between the amino and keto groups. The effect of environment on the equilibrium, **6a** $\rightleftharpoons$ **7**, is under investigation. A recent report claims that the open chain is favored when the ring is larger than five atoms.[16]





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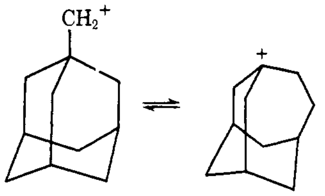
Changing **2** into **4** *via* electron-deficient nitrogen bears analogy to the work of Gassman and collaborators,[9] *e.g.*, the skeletal rearrangement of 4,7,7-trimethyl-2-chloro-2-azabicyclo[2.2.1]heptane to 2-chloro-3,3,4-trimethyl-1-azabicyclo[2.2.1]heptane promoted by silver salt. Although it was elegantly demonstrated in the previous work[9] that *N*-chloramines can rearrange by alkyl migration, the investigated compounds contained nitrogen in, or adjacent to, a strained ring system whose carbon analogs are known to undergo carbonium ion rearrangements quite readily. In contrast, the nitrogen in our case is outside the tricyclic structure and attached to a relatively unstrained[17] ring system. Since the process entails expansion of a carbocyclic ring adjacent to a positive nitrogen, analogy can be made to several earlier reports involving cyclopropyl-[9] and norbornylnitrenium[18] ions.

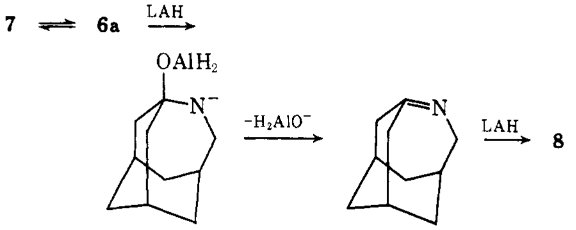
Also, there is similarity to ring enlargement of the 1-adamantylcarbinyl cation **9** to the 3-homoadamantyl cation **10**, eq 3. The relationship of kinetic and thermodynamic aspects for **3** *vs.* **4** merits attention in comparison[19] with **9** *vs.* **10**. The *tertiary* cation **10** can be obtained by kinetic control, whereas under thermodynamic conditions, the form, **9**, with the less strained adamantane nucleus is preferred. We suspect that the energy differences are smaller, or perhaps the situation may even be reversed, for **3** *vs.* **4**. Electron-deficient nitrogen should be a higher energy species than a carbonium ion, and the nitrogen in **4** may participate to some extent in delocalization of the bridgehead carbonium ion. Also, in rearrangements of this type, C–C cleavage (**3** → **4**) usually occurs more readily than C–N rupture (**4** → **3**).[20]



9 **10** (3)

As mentioned earlier, success with certain of the nucleophiles in the postrearrangement treatment was dependent on the presence of acid. This is understandable since acid is known[2,21] to bring about metathesis of the N–Cl bond with formation of the parent amine (salt form). The effectiveness of thiophenol alone apparently results from its ability to assume the role of acid in relation to the overall result. Recently it was revealed[22] that mercaptans are oxidized to disulfides under the influence of *N*-halamine, accompanied by conversion of N–Cl to N–H. In our case, diphenyl disulfide was isolated from the reaction mixture.

The mechanism of the reductive cyclodehydration, **7** to **8** (eq 2), merits attention. In addition to theoretical considerations, evidence indicates that the bicyclic amino alcohol is not an intermediate since it is not converted to **8** when subjected to excess lithium aluminum hydride. Fundamental driving forces[23a] which may be operating are sketched in eq 4. Since lithium aluminum hydride is known to attack primary amino groups,[23b] cyclization is probably promoted by the more nucleophilic amide-type anion. The imino functionality (highly conjectural, bridgehead unsaturate) would be susceptible to reduction by hydride. Other reductive cyclizations involving related compounds have been noted by prior investigators, *e.g.*, with 7-*exo*-methylenebicyclo[3.3.1]nonan-3-one and sodium-moist ether,[24] and with bicyclo[3.3.1]nonan-3,7-dione in the presence of benzylamine and sodium borohydride.[12d]



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Our principal findings are particularly significant from several aspects. New, convenient synthetic routes are made available for preparation of azahomoadamantane, 3-substituted 4-azahomoadamantanes, and bicyclo[3.3.1]nonanes. Also, additional advances have been made in the mechanistic area of nitrenium rearrangements involving *N*-halamines.

Experimental Section

Trichloramine solution was prepared and analyzed by published procedures.[25] Methylene chloride, methanol, and ether were dried at reflux over calcium hydride, magnesium, and lithium aluminum hydride, respectively, and distilled prior to use. Drying of product solutions was accomplished over anhydrous sodium sulfate. Infrared spectra were obtained with a Beckman IR-8 spectrophotometer (calibrated with the 1601.8-cm^{-1} band of polystyrene). Varian T-60 and HA-100 instruments were used to obtain nmr data which are reported in parts per million relative to tetramethylsilane as internal standard. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by Mr. A. Gasiecki.

7 from 2. Anhydrous aluminum chloride (85 g, 0.636 mol) was quickly added to a solution of **2**[2] (70 g, 0.318 mol) in methylene chloride (*ca.* 500 ml) which had been precooled to below −30°. The temperature quickly rose to 0°, and stirring was maintained at that temperature with a nitrogen sweep for 1.5 hr. After concentrated hydrochloric acid (600 ml) was added at 0°, the mixture was stirred for 2 hr at room temperature. The organic layer from separation was extracted with three additional portions of concentrated hydrochloric acid (each 150 ml). The solid obtained from addition of the acidic solution at about 0° to 1.4 l. of 50% sodium hydroxide was filtered and washed with water. The crude product was crystallized from methanol (or ethanol) to give *endo*-7-aminomethylbicyclo[3.3.1]nonan-3-one (**7**), mp 163.5–165° (42 g, 79%). Concentration of the mother liquor provided an additional crop, mp 159–162° (3 g). Analytically pure **7** was obtained as a white solid by vacuum sublimation: mp 166.5–167.5°; ir ($CHCl_3$), 3600–3200 (OH, NH), 2900, 1700 (C=O), 1450, and 1085 cm^{-1}; nmr δ ($CDCl_3$), 3.26 (b, 2 H, exchangeable with D_2O, NH_2), 2.84 (d, J = 3 Hz, 2 H, CH_2N), 2.00–1.55 (m, 13 H); mass spectrum, *m/e* (rel intensity), 167 (15), 138 (29), 110 (26), 95 (88), and 30 (100).

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Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37; O, 9.57. Found: C, 71.68; H, 10 31; N, 8.24; O, 9.23.

The benzamide derivative was prepared by means of benzoyl chloride in pyridine-benzene:[26] mp 113.5–114.5° from ether-methanol; ir ($CHCl_3$) 3500 (NH), 3020, 2940, 1700 (C=O), 1650 (NC=O), 1600, 1580, 1510, 1475, 1350, 1200, and 1100 cm^{-1}; nmr δ ($CDCl_3$, CH_2Br_2 standard) 7.8 (m, 2 H), 7.45 (m, 3 H), 6.8 (b, 1 H, NH), 3.17 (indistinct t, 2 H), 2.8–0.7 (m, 13 H); mass spectrum, *m/e* (rel intensity), 271 (0.7), 135 (19), 134 (17), 122 (27), 105 (100), 31 (27), 28 (11).

Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80; N, 5.16. Found: C, 75.16; H, 7.95; N, 5.07.

7 from 1b. Trichloramine in methylene chloride solution (300 ml of 0.67 *M* solution, 0.2 mol) was placed in a 1-l., three-necked flask, equipped with stirrer, addition funnel, thermometer, and nitrogen inlet, and cooled to −20°. After anhydrous aluminum chloride (53.2 g, 0.4 mol) was added, the temperature rose to −2°. 1-Bromoadamantane (**1b**) (21.5 g, 0.1 mol) in methylene chloride (100 ml) was introduced dropwise to the stirred slurry at −2 to 1° over a period of 1 hr. Following an additional 1 hr at the same temperature, 18% aqueous hydrochloric acid (total volume 240 ml) was added (initially dropwise) at 0°. After the mixture was stirred for 6 hr, the layers were separated. The organic layer was extracted three times with 18% aqueous hydrochloric acid (total volume 240 ml). The combined acid solution was added dropwise to 25% sodium hydroxide (550 ml) with vigorous stirring at 0° The white solid in suspension was collected and dried to give **7** (13 g) Vacuum sublimation gave product melting at 166.5–167.5°. The infrared spectrum was indistinguishable from that of material obtained from **2**.

7 from 1a. Adamantane (**1a**) (13.6 g, 0.1 mol), methylene chloride (325 ml), and aluminum chloride (17.8 g, 0.113 mol) were placed in a 1-l., three-necked flask and cooled to 10–15°. Trichloramine in methylene chloride (176 ml, 0.66 *M*, 0.11 mol) was added to the stirred mixture over a period of 1 hr. After an additional 1 hr at 10–15°, the mixture was cooled to 0° and more aluminum chloride (26.6 g, 0.2 mol) was added. After the reaction mixture had been stirred at 0° for 2 hr, the same work-up procedure was used as in the preceding section. Following the isolation of crude **7** (11 g), recrystallization from methanol gave material of mp 166–167.5° (3.1 g).

7 to 8. *endo*-7-Aminomethylbicyclo[3.3.1]nonan-3-one (**7**) (5 g, 0.03 mol) was placed in the thimble of a Soxhlet apparatus and continuously extracted into a stirred mixture of lithium aluminum hydride (4.53 g, 0.12 mol) in dry ether (400 ml) overnight. After water (55 ml) was carefully added, the ether solution was decanted. The gumlike residue was extracted twice with ether (50-ml portions), and the combined ethereal solution was washed with small portions of distilled water. The organic solution was dried and evaporated to give 4-azahomoadamantane (**8**) (4.35 g, 96%). The infrared and nmr spectra of sublimed material and the infrared spectrum of the hydrochloride were indistinguishable from those of authentic materials prepared by known methods.[11]

7-Aminomethylbicyclo[3.3.1]nonan-3-ol and Lithium Aluminum Hydride. An endo-exo mixture of the alcohol[27] (0.6 g, 0.0036 mol) was extracted in a Soxhlet apparatus into a stirred mixture of lithium aluminum hydride (1.5 g, 0.0394 mol) in 150 ml of dry ether. After reflux was continued for 48 hr, distilled water (30 ml) was added dropwise. The ether layer was decanted, and the residue was extracted with several portions of ether. The combined organic solution was washed with water, dried, and freed of solvent to give 0.35 g of white solid whose ir spectrum was identical with that of the original alcohol. Tlc involving silica gel G plates, development by mixed solvent ($CHCl_3$, 50 ml; C_2H_5OH, 50 ml; 30% NH_4OH, 10 ml), and staining with iodine showed only starting material with no indication of 4-azahomoadamantane. Control tlc experiments demonstrated that 4-azahomoadamantane and the isomeric alcohols were separated under these conditions.

6b from 2. A solution of **2** (4.4 g, 0.02 mol) in methylene chloride (50 ml) was added to a cold (ice bath) suspension of aluminum chloride (5.88 g, 0.044 mol) in methylene chloride (100 ml) over a period of 20 min. After the reaction mixture was stirred at 0° for 2 hr, anhydrous methanol (100 ml) containing dry hydrogen chloride was slowly added. The resulting yellow solution was stirred for 45 min at 0°, concentrated to *ca.* 20 ml, and added to ice-cold aqueous sodium hydroxide with efficient agitation. Extraction of the basic solution with methylene chloride (three 100-ml portions), followed by drying, afforded 3.46 g of product. Two sublimations at 25° (0.05 mm) provided crude **6b**, mp 69–73° (2.17 g). Two crystallizations from petroleum ether (30–60°), followed by sublimation, gave the analytical sample (1 g): mp 77–78°; ir (CCl_4) 1440, 1360, 1160, 1130, 1090, 1070, and 1050 cm^{-1}; nmr δ (CCl_4), 1.23 (b, 1 H, exchangeable with D_2O, NH), 1.35–2.07 (m, 13 H), 2.88 (d, J = 4 Hz, 2 H, NCH_2), 3.08 (s, 3 H, OCH_3); mass spectrum *m/e* (rel intensity), 181 (80), 166 (43), 150 (32), 138 (29), 124 (100), 110 (13), 109 (23), 98 (46), 93 (14), 87 (31), 79 (17), 77 (11), 74 (12), 67 (15), 41 (22), 39 (13), and 30 (15).

Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.93; H, 10.44; N, 7.58.

Hydrolysis of 6b. **6b** (0.58 g, 3.2 mmol) was stirred at room temperature with 20% aqueous hydrochloric acid (20 ml) for 2 hr. After the reaction mixture was poured into iced aqueous sodium hydroxide, the cold basic solution was extracted with methylene chloride (three 75-ml portions). The combined extract was dried and evaporated to give crude **7** (0.46 g). Crystallization from methanol gave **7**, mp and mmp 163–164° dec. The infrared spectrum was indistinguishable from that of authentic material.

6b from 7. The amino ketone **7** (6.68 g, 0.04 mol) and concentrated sulfuric acid (1.96 g, 0.02 mol) were stirred at room temperature in dry methanol (*ca.* 400 ml) for 10 days. The solution was concentrated to 200 ml under reduced pressure and poured into cold aqueous sodium hydroxide. After the resulting suspension was extracted with methylene chloride (three 125-ml portions), the extract was dried and evaporated. The solid residue was sublimed at 45° (0.15 mm) to give **6b** (5.52 g, 76%), mp 76–78° (mixture melting point undepressed). The ir spectrum was indistinguishable from that of material prepared from **2**.

2 to 6c. A solution of thiophenol (33 g, 0.33 mol) in methylene chloride (50 ml) was added to the reaction mixture from **2** (2.2 g, 0.01 mol) and aluminum chloride (2.94 g, 0.022 mol). The resulting dark colored solution was stirred at 0° for 2 hr and poured into iced aqueous sodium hydroxide. After the aqueous solution was extracted with additional methylene chloride (two 100-ml portions), the combined organic solution was extracted with ice-cold hydrochloric acid (three portions). The acidic portion was immediately poured into iced aqueous sodium hydroxide, the cold basic solution was extracted with methylene chloride (three 100-ml portions), and the combined extract was dried and evaporated to give an off-white solid, mp 80–100° (1.74 g). Four crystallizations from absolute ethanol gave 3-phenylthio-4-azahomoadamantane (**6c**): mp 105–106° (0.29 g); ir (CCl_4) 3450 (NH), 3130, 2970, 2850, 1580, 1470, 1440, 1360, 1300, 1240, 1160, 1070, 1020, and 990 cm^{-1}; nmr δ ($CDCl_3$) 1.3–2.4 (m, 14 H, after exchange with D_2O, 13 H), 2.98 (d, J = 4 Hz, 2 H, CH_2N), 7.18–7.40 (m, 3 H), 7.45–7.65 (m, 2 H); mass spectrum, *m/e* (rel intensity), 150 (100), 138 (23), 110 (44), 109 (11), 95 (56), and 30 (52).

Anal. Calcd for $C_{16}H_{21}NS$: C, 74.08; H, 8.16; N, 5.40; S, 12.35. Found: C, 73.91; H, 8.26; N, 5.34; S, 12.20.

The methylene chloride solution remaining after extraction with acid was freed of solvent. Two crystallizations from ethanol gave material melting at 57–59°, lit.[28] for diphenyl disulfide, mp 60–61°. The nmr spectrum displayed only aromatic protons.

6c to 7. A solution of **6c** (0.5 g) in concentrated hydrochloric acid (25 ml) was heated at reflux for 3 hr, cooled, and poured into ice and aqueous sodium hydroxide. After the suspension was extracted with methylene chloride (three 50-ml portions), the organic solution was dried and evaporated to give crude **7** (0.27 g). Crystallization from ethanol-water gave purified **7** (0.23 g), mp 163–165° dec, mmp 163–165° dec. The infrared spectrum was indistinguishable from that of authentic **7**.

6d from 2. A solution of 1,3-dimethoxybenzene (10 ml) in methylene chloride (25 ml) was added to the reaction mixture obtained from **2** (2.2 g, 0.01 mol) and aluminum chloride (2.94 g, 0.023 mol) in methylene chloride (75 ml). After 1.5 hr at room temperature, aqueous hydrochloric acid (18%, 50 ml) was added, and the mixture was stirred for 2 hr. The aqueous layer was separated and washed with methylene chloride. The combined organic portion was dried and evaporated to give a black solution from which a white solid crystallized on addition of carbon tetrachloride to give crude **6d** hydrochloride (0.42 g, 15%), mp 246–

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[26] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 260.

[27] Prepared by sodium borohydride reduction of 7 (T. A. Wnuk, J. Tonnis, and P. Kovacic, unpublished work).

[28] R. C. Weast, Ed., "Handbook of Chemistry and Physics," 49th ed, The Chemical Rubber Publishing Co., Cleveland, Ohio, 1968–1969, p C-292.

247°. Recrystallization from ethanol gave the analytical sample: mp 246–247°; ir ($CHCl_3$) 3450–2380, 1610, 1580, 1510, 1460, 1440, 1360, 1310, 1260, 1160, 1140, 1040, 1025, 833, and 823 cm^{-1}; nmr δ ($CDCl_3$) 1.57–2.2 (m, 10 H), 2.7–3.4 [m, 5 H, after the N^+H_2 protons are exchanged with D_2O, the multiplet resolved into 2.7–3.2 (m, 3 H), 3.32 (d, J = 3 Hz, 2 H)], 3.77 (s, 3 H), 3.88 (s, 3 H), 6.3–6.5 (m, 2 H), 7.35 (d, J = 8 Hz, 1 H), and 8.67–8.92 (b, 2 H, N^+H_2, absent after exchange with D_2O).

Anal. Calcd for $C_{18}H_{26}ClNO_2$: C, 66.74; H, 8.09; Cl, 10.94; N, 4.34. Found: C, 66.55; H, 8.06; Cl, 11.09; N, 4.24.

The free base was isolated by treatment of the hydrochloride with aqueous ethanolic sodium hydroxide, extraction with ether, drying, solvent evaporation, and crystallization from ethanol, mp 136–138°. The analytical sample resulted from two crystallizations from ethanol–water: mp 136–137°; ir($CHCl_3$) 3390, 1600, 1580, 1490, 1460, 1450, 1150, 1130, 1070, 1030, and 990 cm^{-1}; nmr δ ($CDCl_3$) 1.4–2.7 (m, 14 H, after exchange with D_2O, 13 H), 3.12 (d, J = 3 Hz, CH_2N, 2H), 3.75 (s, 3 H, $ArOCH_3$), 3.80 (s, 3 H, $ArOCH_3$), 6.35–6.55 (m, 2 H), 7.55 (d, J = 8 Hz, 1 H); mass spectrum, *m/e* (rel intensity), 287 (100), 272 (28), 258 (43), 257 (3), 256 (10), 244 (42), 230 (96), 216 (27), 215 (14), 204 (80), 203 (17), 193 (24), 192 (23), 178 (20), 164 (24), 163 (27), 151 (14), 91 (13), 79 (13), 77 (12), 32 (20), and 30 (13).

Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.25; H, 8.67; N, 4.91.

6d from 7. A mixture of **7** (0.5 g, 3 mmol), aluminum chloride (1 g, 7.5 mmol), and 1,3-dimethoxybenzene (6 g, 43.5 mmol) in methylene chloride (10 ml) was refluxed for 17 hr. Then 18% hydrochloric acid (25 ml) was added at 0–5°. The organic layer was separated and extracted with three small portions of 18% hydrochloric acid. The combined acidic solution was washed with three small portions of Skelly C, and then slowly added to 50 ml of 25% sodium hydroxide at 0° with good stirring. The fine white precipitate was collected and washed with water, giving 29% of crude **6d** (0.25 g). Two recrystallizations from ethanol-water gave an 81% recovery of pure product; the melting point, mixture melting point, and ir spectrum (Nujol) demonstrated identity with the material prepared from **2**.

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Rearrangements of 2,5-Dimethyl-2-vinyl-2,3-dihydrofuran and Related Isomers[1,2]

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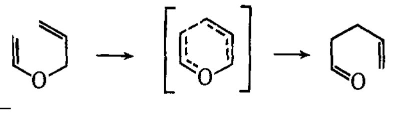
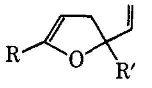
Abstract: The rearrangement of 2,5-dimethyl-2-vinyl-2,3-dihydrofuran (I) to 4-methyl-4-cycloheptenone (III) in the temperature range 140–200° has been demonstrated to occur through the intermediacy of 2-methyl-2-vinyl-5-methylenetetrahydrofuran (VII). Interconversion of I and VII occurs rapidly at active sites on a glass surface but may be arrested in sodium hydroxide coated tubes. At higher temperatures and lower pressures, I rearranges to produce a mixture of III, 1-methyl-4-acetylcyclopentene (IV), and 5-methylene-6-hepten-2-one (X). The isomeric cyclopropane derivatives *cis-* and *trans*-1-acetyl-2-vinyl-2-methylcyclopropane (V and VI) and *cis-* and *trans*-1-acetyl-2-isopropenylcyclopropane (VIII and IX) have been prepared and their thermal behaviors studied. Rearrangement of V and of VIII produces III as well as I, IV, and X, in relative amounts which depend on the rearrangement conditions imposed. A facile enolene rearrangement of VI leads to the formation of X. *trans*-1-Acetyl-2-isopropenylcyclopropane (IX) survives heating at 215°. The results are explained in terms of wall reactions of I and V giving rise to III, and the intermediacy of a common bisallylic diradical which can partition to I, IV, V, and VI (X).

Thermal lability in unconstrained vinyl allyl ethers (Claisen rearrangement) is a familiar phenomenon, attributable to the concerted nature of the electron reorganization leading to the thermodynamically favored homallylic carbonyl isomer.[4] It has been of interest to us to explore the consequences of geometric restraint in such systems and, to this end, we have examined vinyl derivatives of dihydrofurans in which the first and fourth atoms of the vinyl allyl ether are bridged by a methylene group,[5] *i.e.*





I, R = R′ = CH$_3$

Models suggested that in such systems achievement of the orientations required for a concerted rearrangement[4] would be difficult, if not impossible, and that alternative isomerization pathways might be observed.[6]

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(1) A preliminary account of a portion of this work has appeared: S. J. Rhoads and C. F. Brandenburg, *J. Amer. Chem. Soc.*, **88**, 4294 (1966).

(2) Taken from the Ph.D. Dissertation of C. F. B., University of Wyoming, 1969.

(3) U. S. Bureau of Mines Fellow of the Laramie Petroleum Research Center, 1967–1969.

(4) See A. Jefferson and F. Scheinmann, *Quart. Rev., Chem. Soc.*, 22, 391 (1968), for a recent and excellent review of Claisen and related rearrangements.

(5) That bridging of these atoms by two methylene groups does not impede the normal Claisen rearrangement recently has been demonstrated in vinyl dihydropyran systems by G. Büchi and J. E. Powell, Jr., *J. Amer. Chem. Soc.*, **89**, 4559 (1967); **92**, 3126 (1970).

(6) Under a variety of conditions, 2-vinylic-2,3-dihydrofuran systems have been reported to rearrange to acyl cyclopentenes, acyl vinylic