

diester **18**: mp (C₆H₆-petroleum ether) 181–182°; ir (KBr) 1710 cm⁻¹ (COOMe); nmr (CDCl₃) δ 4.55 (s, 3, CH₃), 4.40 (s, 3, CH₃).

Anal. Calcd for C₁₇H₁₄N₂O₄: C, 65.80; H, 4.55; N, 9.03. Found: C, 65.85; H, 4.76; N, 9.06.

Compound 16b. Under conditions corresponding to those offered for **16a**, equivalent amounts of **6a** and ethyl propiolate provided 0.6 g (25%) of acid **16b**: mp (aqueous EtOH) 233–234°; ir (KBr) 1660 cm⁻¹ (COOH).

Anal. Calcd for C₁₄H₁₀N₂O₂: C, 70.38; H, 4.23; N, 11.76. Found: C, 70.59; H, 4.44; N, 11.84.

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Registry No.—1, 13750-62-4; **2a**, 98-88-4; **2g**, 76-02-8; **2h**, 541-41-3; **3a**, 52083-14-4; **3f**, 52855-65-9; **4a**, 52083-19-9; **4a HCl**, 52855-66-0; **4f**, 52855-67-1; **4g**, 52855-68-2; **4h HCl**, 52855-69-3; **5a**, 52855-70-6; **5b**, 52855-71-7; **5c**, 52855-72-8; **5d**, 52855-73-9; **6a**, 52855-74-0; **6a HCl**, 52855-75-1; **6b HCl**, 52855-76-2; **6c HCl**, 52855-77-3; **6d HCl**, 52855-78-4; **7a**, 52726-21-3; **7b**, 52726-27-9; **7c**, 39269-64-2; **8a**, 52855-81-9; **8b**, 52855-84-2; **9a HCl**, 52855-82-0; **9b**, 52855-85-3; **10**, 52855-83-1; **11a**, 52855-79-5; **11b**, 52855-80-8; **12**, 52083-24-6; **13a**, 52855-86-4; **14**, 52855-87-5; **16a**, 52855-88-6; **16b**, 52855-90-0; **17**, 26192-22-3; **18**, 52855-89-7; 2-methylimidazole, 693-98-1; phenyl isocyanate, 103-71-9; phenyl isothiocyanate, 103-72-0; dimethyl acetylenedicarboxylate, 762-42-5; ethyl propiolate, 623-47-2; *p*-methoxybenzoyl chloride, 100-07-2; *p*-methylbenzoyl chloride, 874-60-2; *p*-nitrobenzoyl chloride, 122-04-3.

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Allylic Rearrangement of 17 α -Vinyl-17 β -hydroxy Steroids

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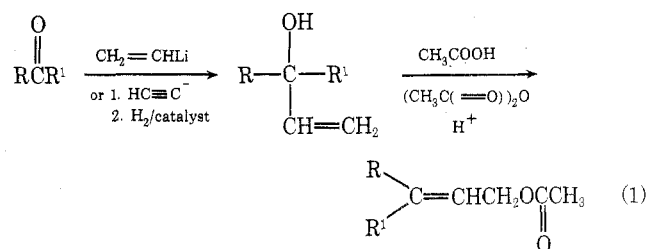
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It is well known that generation of a cationic center at C-17 in steroids can promote the 1,2 shift of the C-18 methyl group (the K \ddot{a} gi-Miescher rearrangement).¹ For example, Morrow, Culbertson, and Hofer reported² 17-methyl-18-nor-17 α -pregna-5,13,20-trien-3 β -ol (**1a**) as a by-product of the acid-catalyzed isomerization of 17 α -pregna-5,20-diene-3 β ,17-diol (**4a**). This same group also reported² that the direct acid-catalyzed conversion of the latter compound (**4a**) to pregna-5,17(20)-diene-3 β ,21-diol (**5a**) proceeded erratically (with generally 8–15% yield). They demonstrated,

however, that allylic rearrangement of 17 α -pregna-5,20-diene-3 β ,17-diol 3-acetate (**4b**) using thionyl chloride in an ether-pyridine mixture, followed by treatment of the rearranged chloride **6b** with potassium acetate (and subsequent saponification) was a good alternative to the direct one-step acid-catalyzed process.

In an effort to facilitate allylic rearrangements of the type cited above and avoid the unnecessary formation of an intermediate allylic halide (e.g., **6** and **11**), we decided to examine the behavior of 17 α -vinyl-17 β -hydroxy steroids in a mixture of acetic acid-acetic anhydride containing a strong acid catalyst. Earlier we had reported³ such reaction conditions as the key step in a method for the bishomologation of simple ketones to functionalized trisubstituted olefins (eq 1).

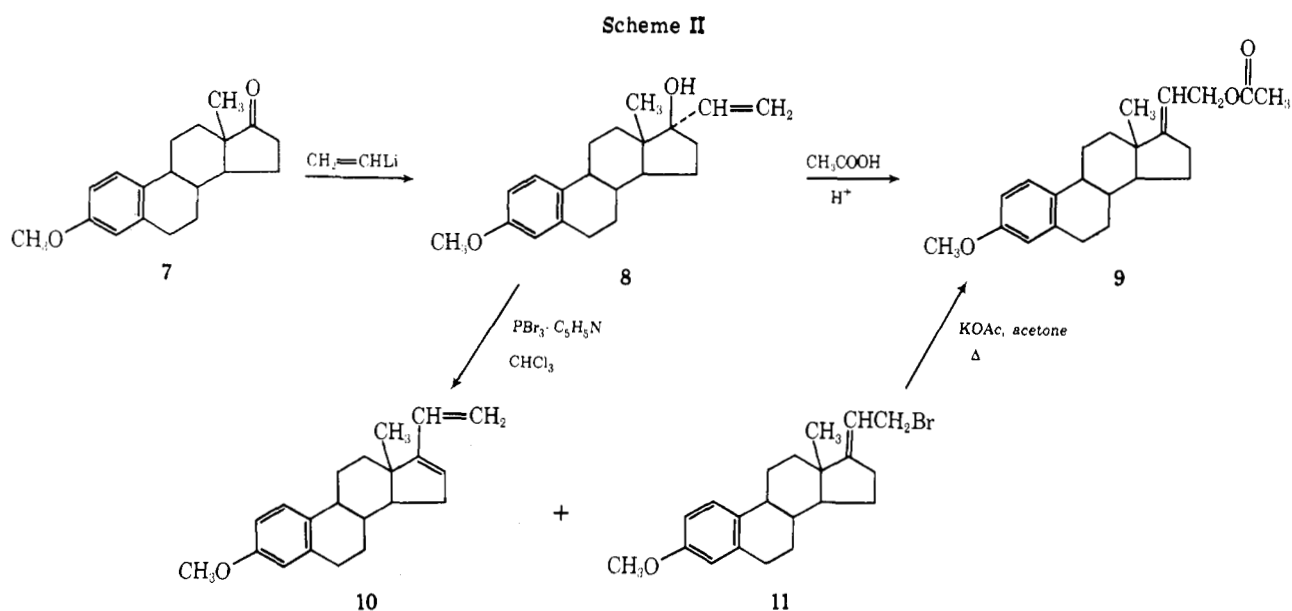
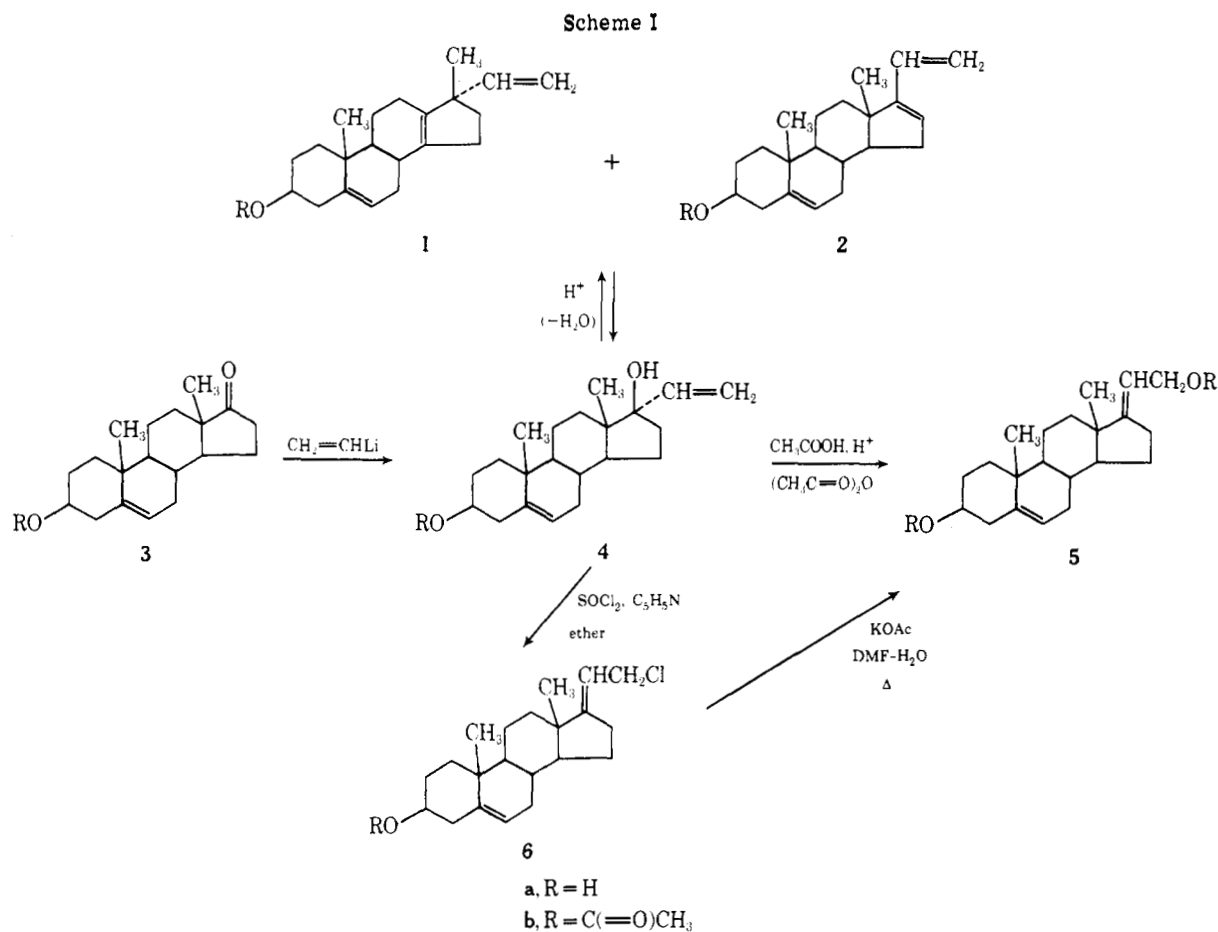


The first system we examined was 3-methoxy-19-nor-17 α -pregna-1,3,5(10), 20-tetraen-17-ol (**8**), obtained in 97% yield by the addition of vinyl lithium to estrone methyl ether (**7**). Subsequent acid-catalyzed rearrangement of alcohol **8** in a mixture of acetic acid and acetic anhydride proceeded smoothly, affording 3-methoxy-19-norpregna-1,3,5(10),17(20)-tetraen-21-ol acetate (**9**) in approximately 65% yield after purification via column chromatography. The identity of this rearranged allylic acetate (**9**) was confirmed by nmr analysis as well as comparison of its melting point and infrared spectrum with the corresponding physical properties previously reported⁴ for this same compound, which had been synthesized from the corresponding bromide (**11**) as outlined in Scheme II. The only other component in our crude rearrangement product was a relatively nonpolar substance, subsequently shown by nmr analysis to be a mixture of aromatic ethers.

To further demonstrate the utility of our rearrangement conditions, we used as our next substrate 17 α -pregna-5,20-diene-3 β ,17-diol (**4a**), prepared in approximately 80% yield by the addition of vinyl lithium to dehydroisoandrosterone acetate (**3b**). As expected, the rearrangement afforded pregna-5,17(20)-diene-3 β ,21-diol diacetate (**5b**) in >60% yield after purification via column chromatography. As in the previous system examined, a mixture of at least two unsaturated compounds (determined by the vinyl patterns observed on its nmr spectrum) was formed during the reaction. Since the rearrangement we report proceeded in high yield to afford the desired allylic acetates (**5b** and **9**) and the elimination by-products failed to separate on silica gel tlc, we made no further effort to characterize them.

Experimental Section⁵

3-Methoxy-19-nor-17 α -pregna-1,3,5(10),20-tetraen-17-ol (8). Treatment of a solution of 702 mg (2.47 mmol) of 3-methoxy-estra-1,3,5(10)-trien-17-one (**7**) in 15 ml of anhydrous tetrahydrofuran with 3.0 ml of 2.5 M vinyl lithium-tetrahydrofuran solution⁶ at room temperature for 30 min, using experimental conditions similar to those described for the preparation of diol **4a**, afforded crude alcohol **8** contaminated by hydrocarbon impurities evidently present in the vinyl lithium reagent. The product was purified via chromatography on 50 ml of Florisil (60–100 mesh). Elution with hexane-25% ether afforded 746 mg (97%) of crystalline alcohol **8**: mp 110–112° (lit.⁴ mp 114–115°); λ_{max} (KBr) 3560, 3495, 1617, 1508, 1255, 1142, 1025, 930 and 910 cm⁻¹; δ_{TMS} (CDCl₃) 6.42–5.07



(complex pattern, three vinyl H's, peaks at 6.42, 6.26, 6.13, 5.97, 5.39, 5.37, 5.28, 5.26, 5.11, 5.07), 3.81 (OCH₃), 3.52 (OH), 0.95 ppm (18-CH₃).

3-Methoxy-19-norpregna-1,3,5(10),17(20)-tetraen-21-ol Acetate (9). To a solution of 190 mg (0.61 mmol) of tertiary vinylcarbinol 8 in 15.0 ml of glacial acetic acid and 3.0 ml of acetic anhydride was added 189 mg of *p*-toluenesulfonic acid monohydrate. After stirring this mixture at room temperature for 3 hr, the reaction was quenched by pouring it into 300 ml of saturated aqueous sodium bicarbonate solution and shaking this mixture vigorously until carbon dioxide evolution had ceased. Extraction with ether afforded 220 mg of crude product, which was subsequently chromatographed on 25 ml of silica gel. Elution with hexane-5% ether afforded 70 mg of an oil, homogeneous on silica gel tlc. The nmr

spectrum indicated the presence of two aromatic methyl ethers in a ratio of 2.5:1, both of which exhibited a vinyl pattern: δ_{TMS} (CCl₄) 1.13 (18-CH₃, major component), 0.93 ppm (18-CH₃, minor component).

Elution with hexane-10% ether afforded 136 mg (63%) of allylic acetate 9 as a viscous oil, homogeneous on silica gel tlc and pure by nmr analysis: δ_{TMS} (CDCl₃) 4.51 (d, $J = 7.0$ Hz, CH₂O-C(=O)CH₃), 3.73 (OCH₃), 1.99 (OCOCH₃), 0.82 ppm (18-CH₃). Crystalline acetate 9 was obtained by dissolving the chromatographed material in warm methanol and chilling this mixture: mp 59-60° (lit.⁴ mp 67-68°).

17 α -Pregna-5,20-diene-3 β ,17-diol (4a). Vinylolithium-tetrahydrofuran solution⁶ (6.0 ml, 2.5 M) was added dropwise rapidly to a solution of 912 mg (2.76 mmol) of 3 β -acetoxyandrost-5-en-17-one

(3b) in 20 ml of 1:1 anhydrous tetrahydrofuran–ethyl ether cooled to 10° in a water bath. After stirring this mixture at room temperature for 4 hr, the reaction was quenched by slow dropwise addition of water. The mixture was subsequently diluted with 200 ml of water, and the product was isolated by extraction with ether. Recrystallization from benzene, which effected removal of hydrocarbon polymers evidently present in the vinyl lithium reagent, afforded 690 mg (78%) of crystalline diol **4a**: mp 181–183° (lit.⁷ mp 184.5–186°); λ_{\max} (KBr) 3280, 1053, 1028, 917 cm^{-1} ; δ_{TMS} (CD_3COOD) 6.36–5.03 (complex pattern, 4 vinyl H's, peaks at 6.36, 6.19, 6.06, 5.90, 5.43, 5.33, 5.23, 5.06, and 5.03), 1.04 (19- CH_3), 0.94 ppm (18- CH_3).

Pregna-5,17(20)-diene-3 β ,21-diol Diacetate (5b). Treatment of 329 mg (1.04 mmol) of tertiary vinylcarbinol **4a** under the same conditions as described above for the preparation of allylic acetate **9** afforded 376 mg of crude product, which was subsequently chromatographed on 50 ml of silica gel. Elution with hexane–5% ether afforded 84 mg of a viscous oil, homogeneous on silica gel tlc. Recrystallization of this fraction from methanol afforded 60 mg of white crystals: mp 72–78°. The nmr spectrum indicated the presence of at least two unsaturated compounds. In addition to more than one vinyl pattern, peaks were observed at δ_{TMS} (CDCl_3) 2.05 (OCOCH_3), 1.10, 1.07, 1.02, 0.94 ppm.

Elution with hexane–10% ether afforded 254 mg (61%) of crystalline diacetate **5b**: mp 132–133° (lit.⁸ mp 134–135°); δ_{TMS} (CDCl_3) 4.60 (d, $J = 7.0$ Hz, $\text{CH}_2\text{OC}(=\text{O})\text{CH}_3$), 2.06 (6 H's, $\text{OC}(=\text{O})\text{CH}_3$), 1.06 (19- CH_3), 0.81 ppm (18- CH_3).

Acknowledgment. The authors wish to thank Dr. Kurt Rorig of Searle Laboratories, a division of G. D. Searle & Co., for a generous gift of both 3-methoxyestra-1,3,5(10)-trien-17-one and 3 β -acetoxyandrost-5-en-17-one. We also wish to acknowledge Dr. Harvey W. Posvic of Loyola University of Chicago for his helpful suggestions during the course of this project.

Registry No.—**3b**, 853-23-6; **4a**, 10291-86-8; **5b**, 53210-12-1; **7**, 1624-62-0; **8**, 6885-48-9; **9**, 34965-79-2.

Reference and Notes

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- Reactions were carried out under a nitrogen atmosphere. The isolation of reaction products was accomplished by extracting the aqueous layer thoroughly with the specified solvent. Anhydrous magnesium sulfate was used to dry the combined extracts, and the solvent was removed on a rotary evaporator under reduced pressure. Melting points were determined on a Fisher-Johns block and are corrected. The nmr spectra were recorded with a Varian A-60 nmr spectrometer and infrared spectra were obtained using a Beckman Acculab 1 spectrophotometer.
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Ion Cyclotron Resonance Studies of Allene Mercurinium Ions

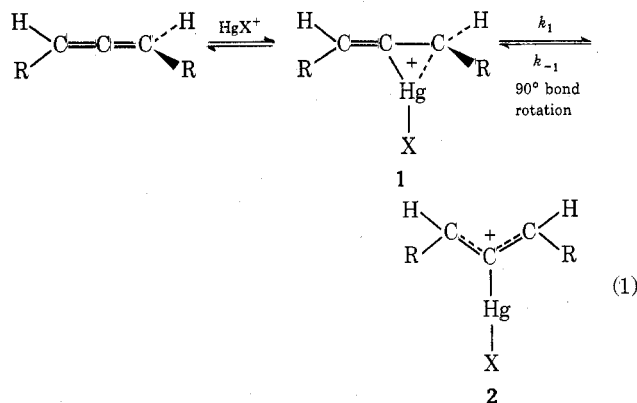
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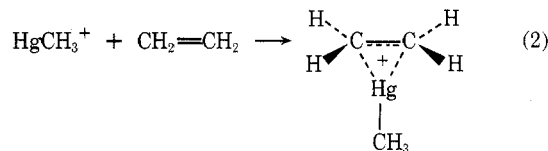
The generally accepted mechanism for the oxymercuration of alkenes in protic solvents involves a bridged or π -complexed mercurinium ion intermediate.¹ Several investi-

gators have also suggested that mercurinium ions are involved in the alkoxymercuration of allenes.² The oxymercuration of optically active allenes² has provided convincing evidence for π bridging since a considerably driving force exists for **1** to form a planar resonance stabilized allylic carbonium ion **2** (eq 1). The formation of optically ac-



tive products in these reactions² precluded exclusive product formation from the planar cation **2** providing evidence for either a mercurinium ion intermediate or a π -bridged transition state. Recently, additional experimental³ and theoretical⁴ evidence has been reported in support of this mechanism. Despite the extensive research on this reaction, unequivocal evidence for mercurinium ions under oxymercuration reaction conditions has not been reported. However, long-lived mercurinium ions derived from alkenes have been observed in solution by nmr spectroscopy.⁵

We have recently provided the first evidence for the existence of π -bridged cyclic mercurinium ions in the gas phase by using ion cyclotron resonance (icr) mass spectrometry.⁶ In this previous study we established that the ion molecule reaction of HgCH_3^+ with ethylene resulted in the formation of a new ion that corresponded to the mass $\text{C}_2\text{H}_4\text{HgCH}_3^+$ as in eq 2. This was a significant finding



since there are few known examples of ion cyclotron resonance (icr) studies on volatile organometallic compounds. Foster and Beauchamp⁷ have reported that ion molecule reactions of $\text{Fe}(\text{CO})_5$ afford ions containing two iron atoms.

We now report the observation of a mercurinium ion derived from the reaction of HgCH_3^+ and allene in the gas phase employing icr mass spectrometry and find that the rate of formation of this ion is the same order of magnitude as the theoretical collision rate constant. We have also examined the relative energies of the various ions formed with extended Hückel molecular orbital calculations to aid in identification of the most probable structures of the product ions.

Experimental Section

A Varian V-5900 ion cyclotron resonance mass spectrometer was used for the observations. A flat cell with the drift plates separated by 1.1 cm was used. Some cell modifications and our operating techniques were described previously.^{8,9} Additional modifications are as follows. A Veeco Model RG-830 ionization gauge together with a Model 523H Barocel are now used in place of a cold cathode gauge to monitor cell pressure. The cell was modified for pulsed electron beam modulation by adding a control grid and appropriate pulsing electronics.⁹ A new emission current control amplifier based on a Burr-Brown Model 3013/15 according to a design of J.