IR (Nujol) 2800, 2950, 1480, 1360, 1215, 1210, 910, 830 cm^{-1}; NMR ($CDCl_3$) δ 0.29 (s, 12 H), 1.02 (s, 18 H), 1.34 (s, 18 H), 6.72 (s, 2 H); mass spectrum *m/e* (rel intensity) 452 (7), 451 (20), 450 (49, M^+), 337 (9), 75 (8), 74 (9), 73 (100), 47 (53), 41 (11); calcd for $C_{26}H_{50}O_2Si_2$ 450.3349, measd 450.3313. Anal. Calcd for $C_{26}H_{50}O_2Si_2$: C, 69.27; H, 11.18. Found: C, 69.46; H, 11.31.

Oxidation of 1,4-Bis(trimethylsiloxy)benzene (1b). The disilyl ether **4** was oxidized at a platinum anode (40 cm^2) in a three-compartment H-type cell (anolyte capacity 100 mL) equipped with a magnetic stirrer, an SCE reference electrode, and a stainless-steel cathode. Solvent-supporting electrolyte was acetonitrile–0.05 M Et_4NBF_4. Background current was less than 1 mA at 1.5 V. Addition of 0.30 g (1.2 mmol) of **1b** resulted in a current of 40 mA which decayed to 2 mA after passage of 2.0 F mol^{-1}. The electrolysis was terminated after 2.1 F mol^{-1}. The anolyte was reduced in vacuo to small volume, and 40 g of chopped ice was added followed by 40 mL of ether. The organic layer was separated, the aqueous layer was extracted with 2 × 20 mL of ether, and the combined organic layers were washed with brine and dried over $MgSO_4$. Filtration and removal of solvent in vacuo gave 0.109 g (86%) of benzoquinone, mp 114 °C, identical in all respects with an authentic sample. Compound **1b** was also oxidized in acetonitrile–$LiClO_4$ and methylene chloride–Bu_4NClO_4, in each case producing benzoquinone in nearly quantitative yield.

Oxidation of 1,4-Bis(trimethylsiloxy)-2-chlorobenzene. 1,4-Bis(trimethylsiloxy)-2-chlorobenzene (1.20 g, 4.17 mmol) was oxidized in acetonitrile–0.1 M $LiClO_4$ at an anode potential of 1.3 V vs. SCE using a graphite felt anode (5 × 2.5 × 0.64 cm). Workup of the anolyte in the usual manner after passage of 2.2 F mol^{-1} yielded 0.63 g of crude product. Recrystallization from hexane gave 0.47 g (80%) of chlorobenzoquinone, mp 57 °C, identical in all respects with an authentic sample.

Oxidation of 9,10-Bis(trimethylsiloxy)anthracene. 9,10-Bis(trimethylsiloxy)anthracene was oxidized at a potential of 1.0 V vs. SCE using a graphite felt anode using acetonitrile–0.1 M $LiClO_4$ as solvent supporting electrolyte. Workup after passage of 2.5 F mol^{-1} gave a 92% yield of anthraquinone, mp 283–285 °C, identical in all respects with an authentic sample.

Oxidation of 1,4-Bis(trimethylsiloxy)-2-methoxybenzene (2). 1,4-Bis(trimethylsiloxy)-2-methoxybenzene (1.42 g, 5 mmol) was oxidized at 1.0 V vs. SCE using a platinum anode (40 cm^2) with acetonitrile–0.2 M $LiClO_4$ as solvent–supporting electrolyte. The reaction was terminated after passage of 1.1 F mol^{-1}. The anolyte was reduced in vacuo and partitioned between methylene chloride and water. The organic layer was washed with water and dried over Na_2SO_4. Filtration and removal of solvent in vacuo yielded 0.47 g of tan crystals. Recrystallization from chloroform gave 0.45 g (65%) of 3,6-dihydroxy-2,7-dimethoxydibenzofuran: mp 180–181 °C; IR (Nujol) 3560, 3520, 3400, 2950, 1640, 1500, 1470, 1450, 1380, 1295, 1150, 915, 850, 815 cm^{-1}; NMR (acetone-d_6) δ 3.95 (s, 6 H), 7.15 (s, 2 H), 7.25 (s, 2 H), 7.28 (s, 2 H); mass spectrum *m/e* (rel intensity) 261 (10), 260 (62, M^+), 246 (16), 245 (100), 230 (22), 217 (10), 202 (15), 44 (30), 40 (40). Anal. Calcd for $C_{14}H_{12}O_5$: C, 64.61; H, 4.64. Found: C, 64.58; H, 4.48.

Oxidation of 4-Methoxy-1-(trimethylsiloxy)benzene. 4-Methoxy-1-(trimethylsiloxy)benzene (0.39 g, 2 mmol) was oxidized at 1.2 V vs. SCE using a platinum anode (40 cm^2) in a solvent–electrolyte solution consisting of 40 mL of methanol, 60 mL of acetonitrile, 1 g of lithium carbonate, and 3 g of lithium perchlorate. The background current was 5 mA. This increased to 220 mA upon addition of substrate and decayed to 9 mA after passage of 2.1 F mol^{-1}. The solvent was reduced in vacuo, combined with 50 mL of methylene chloride, washed with 2 × 10 mL of water and 10 mL of brine, and dried over $CaCl_2$. Removal of solvent in vacuo yielded 0.299 g (99%) of 4,4-dimethoxy-2,5-cyclohexadien-1-one: IR (neat) 2825–2300, 1690, 1640, 1150, 1040, 960, 850 cm^{-1}; NMR ($CDCl_3$) δ 3.41 (s, 6 H), 6.30 (d, 2 H), 6.92 (d, 2 H);[21] mass spectrum *m/e* (rel intensity) 154 (41, M^+), 139 (37), 124 (61), 123 (100), 111 (30), 109 (25), 95 (100), 80 (21), 65 (23), 54 (36), 52 (39), 41 (62); calcd for $C_8H_{10}O_3$ 154.0651, measd 154.0604.

Acknowledgments. This work was supported by the National Science Foundation. Discussion with P. Boudjouck is acknowledged.

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Silicon in Synthesis. 10. The (Trimethylsilyl)allyl Anion: A β-Acyl Anion Equivalent for the Conversion of Aldehydes and Ketones into γ-Lactones

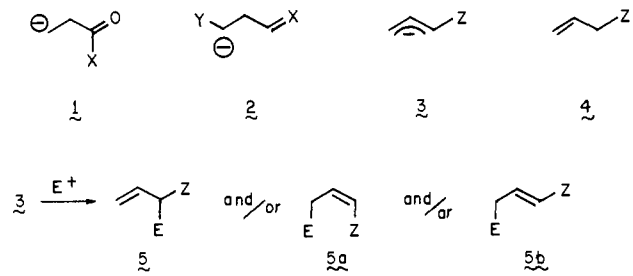
Ed Ehlinger and Philip Magnus*

Contribution from the Evans Chemistry Laboratory, The Ohio State University, Columbus, Ohio 43210. *Received January 1, 1980*

Abstract: The (trimethylsilyl)allyl anion reacts with a number of ketones and aldehydes to give adducts **11–21**, resulting from the γ mode of ambident reactivity. These adducts were epoxidized to provide the corresponding α,β-epoxysilanes **23–31**. Treatment of the epoxysilanes with methanol in the presence of boron trifluoride etherate gave the lactol methyl ethers **32–39**. Jones oxidation of the lactol methyl ethers gave γ lactones **40–45**. Addition of bromine to the 4-hydroxy vinylsilane derivative **19** gave the oxetane **47** which was converted into the compounds **49**, **50**, and **51**. Application of the (trimethylsilyl)allyl anion, as its zinc counterion, to the synthesis of 17-spirosteroidal lactones is described.

Introduction

As an extension of classical enolate anion chemistry, the concept of umpolung[1] or reverse polarity has received much ingenious attention during the past several years. The β-acyl anion **1** or homoenolate is a particularly important synthetic species since it is capable of converting aldehydes or ketones into γ-lactols or γ-lactones, depending upon the nature of X. In most attempts to produce reagents that behave as overall equivalents to **1**, the carbonyl group is masked, although some efforts have been made to have direct access to **1**.[2]



(1) For a review describing methods of reactivity for umpolung, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239 For nucleophilic acylation, see: Lever, O. W., Jr. *Tetrahedron* **1976**, *32*, 1943. Martin, S. F. *Synthesis* **1979**, 633.

0002-7863/80/1502-5004$01.00/0

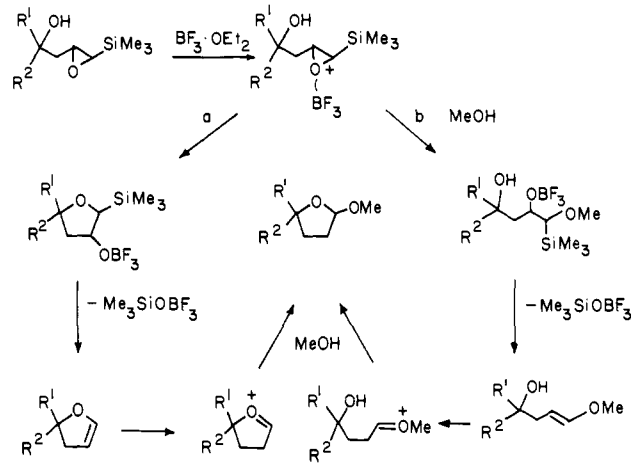
Ideally, a reagent that behaves as a β-acyl anion equivalent should fulfill the following broad criteria. (a) It should be readily available to nonspecialists in methodology; esoteric reagents that require lengthy preparation are too specialized for general use. (b) It should be highly nucleophilic with respect to addition to carbonyl groups; otherwise, its use in synthesis will be severely limited. (c) If the β-acyl anion equivalent is based upon an allylic anion moiety with the usual ambident reactivity associated with such anions, it should exhibit at least greater than 95% regioselectivity; otherwise, mixtures will result, and the utility of the system is considerably reduced. (d) Unmasking of the latent carbonyl group β to the newly formed carbon–carbon bond should be conducted under mild conditions compatible with a reasonable amount of functionality.

The approaches taken to solve this problem of synthetic methodology have been many and varied, but they can be roughly divided into two categories. The first comprises those systems which have a masked carbonyl with an anion-stabilizing group situated β to it (**2**).[3] The second category consists of systems that attempt to take advantage of the ambident reactivity of heteroatomically substituted allylic anions (**3**).[4] Allylic systems such as **4**, where Z is usually OR, SR, NR_2, or $P(O)R_2$, can be deprotonated with an appropriate base to the corresponding anion (**3**). The subsequent reactions of **3** with an electrophile (E^+) can

Table I. Products Formed from Treatment of 6 with Substrates Listed

Substrate	Equiv. of 6	Temp °C	Product	Yield %
a	2.6	-30°	11	84(crude)53(dist)
b	2.5	-30°	12	88(crude)65(dist)
c	2.0	-78°	13	96(crude)
d	2.0	-76°	14	86
e	3.0	-20°	6, M = ZnCl	66 (dist.)
f	2.6	-30° to 0°	15	71 (pure)
g	6.5	0°	6, M = ZnCl	89 (dist. pure)
h	5.5	-20°	17	97 (dist. pure)
i	5.2	0°-5°	18	85(sublimed)
j	1.5	-75° to -26°	19	80 (dist.)
k	2.6	-75°	20	65 (dist.)
			21	5
			22	

Scheme I



produce three adducts, **5**, **5a**, and **5b**. The adducts **5**, **5a**, and **5b** are regioisomers, while **5a** and **5b** differ only in olefin geometry. Generally, the desired mode of ambident reactivity is to produce **5a** and/or **5b**. Provided Z is a functional group that can readily be transformed into a carbonyl group, the vinyl derivatives of Z,

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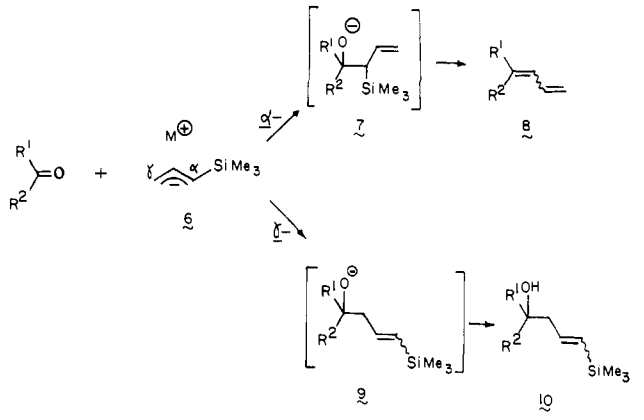
namely **5a** and **5b**, are the masked derivatives of the addition of a β-acyl anion. As part of a general investigation of the use of silicon reagents in synthesis for carbon–carbon bond-forming reactions, we were particularly interested in allyltrimethylsilane (**4**), Z = $SiMe_3$, and its derived ambident anion **3**, Z = $SiMe_3$.[5] The electrophilic chemistry of allylsilanes has attracted much attention during the last few years,[6] whereas the anion chemistry has not been developed to nearly the same degree. In principle, the (trimethylsilyl)allyl anion **6**[7] can react with an aldehyde or ketone in two ways. α attack leads to a β-alkoxysilane (**7**) which



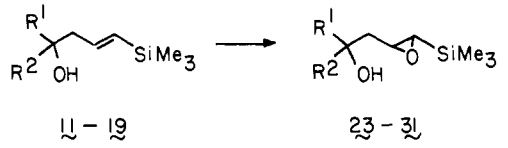
can undergo the Peterson reaction (syn elimination of $^-OSiMe_3$)[8] to give a diene (**8**). This in itself would be useful since the conversion of aldehydes and ketones into dienes (**8**) is not a particularly efficient process with allyl Wittig reagents.[9] γ attack leads to a δ hydroxy vinylsilane (**10**) which can be considered as a masked δ hydroxy aldehyde since vinylsilanes can be oxidized to α,β-epoxysilanes, which are readily hydrolyzed to aldehydes.[10] Furthermore, the adducts **7** and **9** have the potential to interconvert via an alkoxide-accelerated [1.3]sigmatropic shift.[11] With these possibilities in mind, we have examined the formation of the (trimethylsilyl)allyl anion **6** and its subsequent reactions with ketones and aldehydes.

Results

Allyltrimethylsilane[12] (**4**), Z = $SiMe_3$, is conveniently deprotonated by treatment with *sec*-butyllithium (1.0–1.4 M in *n*-hexane or cyclohexane) in tetrahydrofuran at −76 °C containing 1 equiv of tetramethylethylenediamine (TMEDA). The mixture is warmed to −40 °C to ensure complete anion formation (**6**, M = Li), and then may be used at a variety of temperatures (usually between −76 and 0 °C) depending upon the substrate. Treatment of the resulting lithio species **6**, M = Li, with a variety of ketones and aldehydes listed in Table I gave the results shown. In all of the entries listed (a–j), we did not detect any 1,3-dienes resulting from α attack whereas for the acetylcyclohexene case (k) we were able to isolate the diene **22** in 5% yield. The γ adducts **11–21** were isolated in nearly pure (≥95%) form directly from the reaction workup and did not require further purification for subsequent reactions. It should be noted that the yields quoted refer to purified products, either by distillation or, in the case of **19**, by sublimation. The vinylsilane double bond in the adducts **11–21** was exclusively trans in all cases, from ^1H and in certain cases ^{13}C NMR studies (J_{AB} ~ 19 Hz). For the entries e, g, and h, it was found to be advantageous to convert the lithio species **6**, M = Li, into the corresponding zinc chloro **6**, M = ZnCl, counterion by treatment of **6**, M = Li, at −76 °C with freshly dried zinc chloride. This procedure gave higher yields and in particular reduced enolization problems that were noticeable with nopinone (h) (recovered starting material). The adducts of ketones exhibit very characteristic NMR spectra of the newly introduced propenylsilane unit [δ 2.5 (2 H, d, J_{BX} = 6 Hz), 5.8 (1 H, d, J_{AB} = 19 Hz), and 6.3 (1 H, m, J = 19, 6 Hz)], confirming the *E* geometry of the vinylsilane.

The conversion of the masked carbonyl group inherent in the vinylsilane moiety of the adducts **11–21** was accomplished by conversion of the vinylsilane into an α,β-epoxysilane by treatment with *m*-chloroperbenzoic acid in dichloromethane at 0–20 °C for 10–30 min (Table II). Frequently, small amounts of byproducts in the crude adducts **11–21** were removed in this oxidation. In the case of the adduct **21**, where there are contained within the same molecule a homoallylic and an allylic alcohol, we were unable

Table II. Conversion of Vinylsilanes 11–21 to α,β-Epoxysilanes 23–31

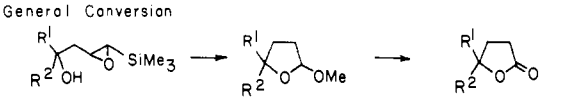


11 – 19 23 – 31

Substrate	Derived α,β-Epoxysilane	Yield %
11	23	89
12	24	94
13	25	90
14	26	88
15	27	94
16	28	90
17	29	89
18	30	88
19	31	92

Table III. Conversion of Epoxysilanes 23–31 to γ-Lactones 40–45

General Conversion



Substrate	Lactol O-methylether	Yield %	Substrate	Lactone	Yield %
23	32	51	32	40	75
24	33	78	33	41	76
25	34	90	34	42	80
26	35	98	35	43	77
27	36	10	–	–	–
29	37	75	37	44	75
30	38	22	–	–	–
31	39	97	38	45	80

(5) For preliminary reports of part of this work, see: Ayalon-Chass, D.; Ehlinger, E.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 772. Ehlinger, E.; Magnus, P. *Ibid.* **1979**, 421. (c) Ehlinger, E.; Magnus, P. *Tetrahedron Lett.* **1980**, 11.

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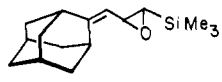
(12) Commercially available from Petrarch Systems, Inc., Box 141, Levittown, PA 19059.

to distinguish between these two systems with either *m*-chloroperbenzoic acid or the Sharpless procedure, $VO(acac)_2/Bu^+$-OOH,[13] and as a result obtained a mixture of epoxides that was not pursued further. The introduction of new stereochemistry at the epoxidation stage poses no problems since it is removed in the next step; it merely inconvenienced NMR interpretation since for the nonsymmetrical cases **13**, **14**, **15**, **17**, and **18** we obtained the epoxides **25**, **26**, **27**, **29**, and **30** as diastereomeric mixtures.

A convenient stepwise and generally more reliable method of unraveling the epoxysilanes **23–31** into the γ lactones **40–45** is to proceed via the *O*-methyl lactols **32–39**. Treatment of the δ-hydroxyepoxysilanes in dry methanol with boron trifluoride etherate (1–1.5 equiv) at room temperature gave a clean, high-yield conversion into the *O*-methyl lactols (Table III). The adduct **30** rearranged under these conditions to give the ring-opened product **38**. Also, the benzophenone adduct **28** gave a complex mixture of products, presumably because of the extremely acid-labile nature of the tertiary hydroxyl group. The mechanism of this conversion can be envisioned as proceeding via two possible pathways, a and b (Scheme I). The opening of the epoxysilane α to silicon by either intramolecular nucleophilic attack (a) or intermolecular attack (b) is in keeping with current mechanistic proposals concerning the attack of nucleophiles on epoxysilanes.[6] Pathway a involves a 5-endo-tet opening of the epoxide and is disfavored. It should be noted that treatment of the δ-hydroxy epoxysilane **31** with *p*-toluenesulfonic acid in benzene caused no cyclization to dihydrofuran products, implicated in pathway a, but only dehydration to **46** occurred.

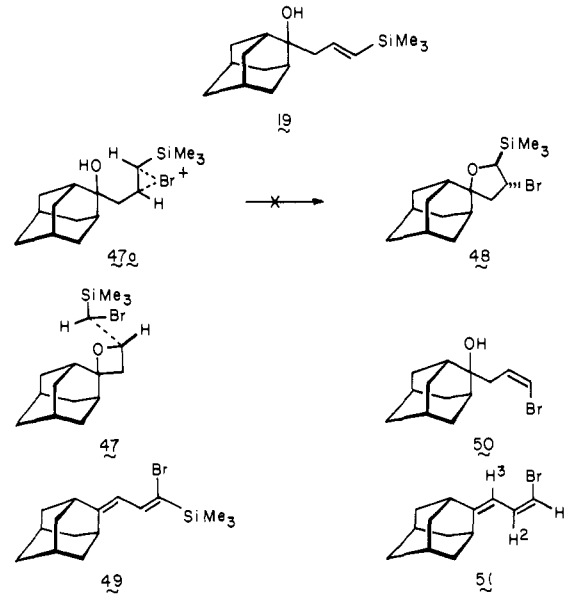


46

The *O*-methyl lactols **32–39** are readily oxidized to the corresponding lactones **40–45** in excellent yield by using the Jones procedure (Table III). Thus, this stepwise oxidative sequence provides a method to convert the δ-hydroxy vinylsilanes into γ-lactones. It seemed reasonable to expect that the δ-hydroxy vinylsilane adducts could be directly oxidized with excess peracid to γ-lactones. Treatment of **11** or its derived epoxide **23** with excess (3.0 equiv) peracetic acid in acetic acid containing a few drops of concentrated sulfuric acid gives the spiro-γ-lactone **40** (50% from **11**; 60% from **23**). In general, the multistep procedure via the *O*-methyl lactols gave purer products, and as shown later, the *O*-methyl lactols are in their own right useful products.

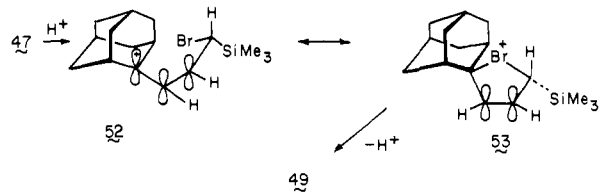
The δ-hydroxy vinylsilane **19**, derived from 2-adamantanone, was treated with a number of electrophiles (Br_2, Cl_2, I_2, PhSeBr, and PhSeCl) only to give complex and synthetically useless mixtures. When **19** was treated with *N*-bromosuccinimide in tetrahydrofuran at 0 °C, the oxetane **47** (92%) was formed rather than the desired tetrahydrofuran derivative **48**. The structure of **47** [δ 4.59 (1 H, q, J = 7.8 Hz), 3.37 (1 H, d, J = 7.8 Hz), 2.37–1.81 (4 H, m), 1.66 (12 H, br s), and 0.14 (9 H, s)] was established by subsequent chemical transformations. If the reaction of **19** with *N*-bromosuccinimide is carried out at 40 °C, or the oxetane **47** is heated in tetrahydrofuran in the presence of a catalytic amount of hydrochloric acid, the bromo trimethylsilyl diene **49** is formed. When the oxetane **47** was treated with potassium fluoride dihydrate in dimethyl sulfoxide at 40–45 °C, the *cis*-vinyl bromide **50** was produced. Dehydration of **50** with thionyl chloride in pyridine gave the *cis*-bromo diene **51**. The configuration of the vinyl bromide **51** was demonstrated by ^1H NMR; $J_{1,2}$ = 10.8, $J_{2,3}$ = 6.96, and $J_{1,3}$ = 1.21 Hz, respectively.[14] Desilylation of **49** with potassium fluoride dihydrate in dimethyl sulfoxide at 40 °C gave **51** in excellent yield.

The unexpected and unprecedented conversion of **47** into **49** required rationalization since conventional thought in organosilicon

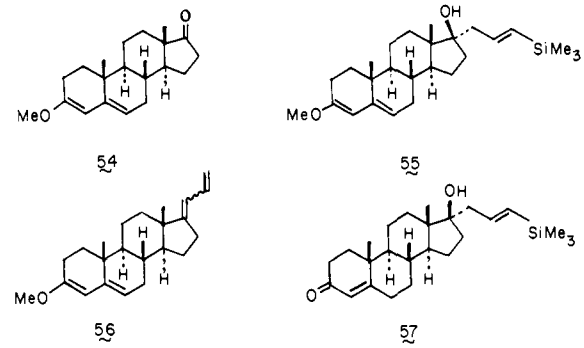


19 **47a** **48** **47** **50** **49** **51**

chemistry would have predicted that buildup of positive charge β to silicon would have resulted in the loss of the trimethylsilyl group to give **51** directly. The initial adduct **47**, from the addition of Br^+ (NBS) to **19**, is the kinetic product (1,2 addition); heating this adduct in the presence of acid can lead to the loss of water to give the allylic cation **52**, which can be stabilized further by 1,4-bromonium ion formation (**53**) (thermodynamic control).



47 **52** **53** **49**



54 **55** **56** **57**

Models show that in the bromonium ion **53**, the trimethylsilyl group is subjected to a marked 1,3 steric interaction with the adamantyl group and as a consequence prefers a quasi-equatorial configuration whereas the proton attached to the same carbon occupies a quasi-axial configuration. This places the proton in the same plane as the π system of the allylic cation whereas the trimethylsilyl group is virtually orthogonal to the π system. Because of these stereoelectronic considerations, the intermediate **53** undergoes proton loss rather than the loss of the trimethylsilyl group. The five-membered-ring bromonium ion **53** also accounts for the exclusive cis stereochemistry of the vinyl bromide **49**.

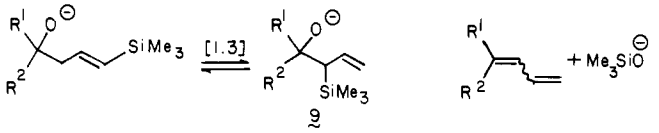
It should also be noted that the oxetane **47** and the tetrahydrofuran **48** correspond to 4-exo-tet and 5-endo-tet openings of the bromonium ion intermediate **47a**, respectively, the former being the favored and observed course.[15] Interestingly, the overall

(13) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. (b) Tanaka, S.; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *Ibid.* **1974**, *96*, 5254.

(14) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(15) Dr. Charles Cottrell of this department is thanked for his expertise in these NMR experiments.

Scheme II

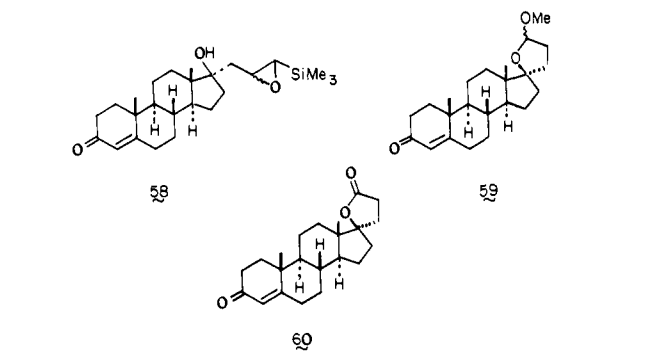


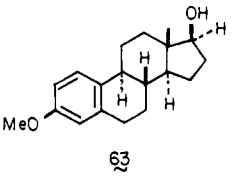
conversion of **19** (*E* geometry) to **50** (*Z* geometry) takes place with inversion.

Steroidal Lactone Synthesis. While the number of β-acyl anion equivalents listed in ref 3 and 4 is almost encyclopedic, their application is very limited. Apart from lithium β-lithiopropionate, which adds to *O*-methylestrone in 26% yield,[2] and Trost's cyclobutanone chemistry,[3] there are no examples of nucleophilic additions to the sterically demanding 17-keto steroids. Additions to 17-keto steroids are particularly interesting in that they provide an excellent test of the nucleophilicity of the β-acyl anion reagent, and if successful, the eventual 17-spirosteroidal lactones are useful aldosterone blockers.[16]

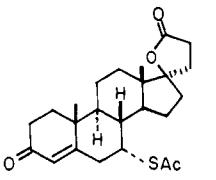
Treatment of 3-methoxyandrosta-3,5-dien-17-one (**54**) with [(trimethylsilyl)allyl]lithium (**6**, M = Li) in tetrahydrofuran containing TMEDA at −40 °C gave the adduct **55** (65%) along with starting material (ca. 30%) and a small amount of the 17-diene **56**. Using 10 equiv of **6**, M = Li, did not change this situation. This unsatisfactory state of affairs was resolved by treating the solution of **6**, M = Li, with freshly dried zinc chloride at −40 °C to give [(trimethylsilyl)allyl]zinc chloride (**6**, M = ZnCl), which when treated with 3-methoxyandrosta-3,5-dien-17-one (**54**) (no TMEDA present) gave clean addition to C-17 with no enolization to give **57** (≥95%, after acid hydrolysis) and traces (ca. 1%) of C-17 reduction to give testosterone. No trace of the 17-diene could be detected by using the zinc procedure. This is in marked contrast to the usual effect of zinc chloride on allyl anion systems.[17]

Initial efforts to epoxidize the C21–C22 double bond of **57** using *m*-chloroperbenzoic acid gave a complex mixture which from the infrared spectrum on the crude reaction contained products resulting from Baeyer–Villiger oxidation of the ring A enone. Other peracids gave similar results. The Sharpless procedure [VO(acac)$_2$/*tert*-BuOOH in benzene][13] solved this problem and gave selective oxidation of the homoallylic vinylsilane in **57**, without any destruction of the ring A enone, yielding the epoxide **58** as a mixture of diastereomers (90–95%). Exposure of the α,β-epoxysilane **58** to methanol and boron trifluoride etherate gave the lactol *O*-methyl ether **59** as a mixture of epimers at C22 (90–95%). Jones oxidation of **59** gave the required lactone **60**, mp 145–148 °C. The overall sequence from **54** to **60** on a 5-g sample proceeds in 35–40% yield. None of the intermediates require purification except the final lactone **60**. An analogous series of reactions starting with estrone *O*-methyl ether (**61**) provided 25% overall yield of the pure lactone **62**. The reason for the reduced yield of lactone **62** in the estrone case is that the initial addition of **6**, M = ZnCl, proceeds in 70% yield; the remaining isolated material is the reduction product **63** (20%).



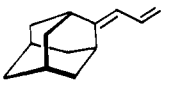


It should be noted that the lactol **59**, which is available in approximately 70% yield from **54**, is a valuable precursor to spironolactone (**65**), an aldosterone blocker.[16]



1,3-Diene Synthesis. The predominant γ attack of the (trimethylsilyl)allyl anion with carbonyl compounds has the implicit mechanistic possibility to be reversed through a [1.3]sigmatropic rearrangement (Scheme II). We were especially interested in this possibility for two reasons. First, Chan[8] has shown that the trimethylsilyl anion in the presence of hexamethylphosphoramide and magnesium bromide reacts with carbonyl compounds to give appreciable amounts of 1,3-dienes (40–50%). Second, the Wittig reaction to produce 1,3-dienes is replete with complications,[9] and as such, it would be useful to have a simple alternative.

Treatment of **19** with potassium hydride in tetrahydrofuran at 60 °C resulted in a clean transformation to the diene **66**. The



rationale of this result is as follows. A [1.3]sigmatropic rearrangement[11] of **19** is reversible, but the α adduct **9** can enter into an irreversible Peterson-type elimination of (trimethylsilyl)potassium oxide to give the observed diene (**66**). Unfortunately, application of this procedure to the other γ adducts **12**, **16**, **17**, **18**, and **21** gave predominantly the starting ketones with little or no diene formation.

Conclusions

The results reported here show that the readily available (trimethylsilyl)allyl carbanion is a reagent that is a highly nucleophilic β-acyl anion (homoenolate) equilvalent whose ambident reactivity is almost exclusively γ in its reactions with carbonyl compounds. Thus, the resulting δ-hydroxy vinylsilane adducts **11**–**21** can be converted into γ-lactol *O*-methyl ethers and γ-lactones, and for the adamantyl system (**19**) the derivatives **47**, **49**, **50**, **51**, and **66** are easily prepared.

It should be noted that apart from aldehydes and ketones which react with **6** in the γ position, treatment of **6** with methyl iodide or chlorotrimethylsilane also gave γ products.[7] The ambident

(16) (a) Cella, J. A.; Kagawa, C. M. *J. Am. Chem. Soc.* **1957**, *79*, 4808. (b) Dodson, R. M.; Tweit, R. C. *Ibid.* **1959**, *81*, 1224. (c) Cella, J. A.; Brown, E. A.; Burtner, R. R. *J. Org. Chem.* **1959**, *24*, 743. (d) Cella, J. A.; Tweit, R. C. *Ibid.* **1959**, *24*, 1109. (e) Brown, E. A.; Muir, R. D.; Cella, J. H. *Ibid.* **1960**, *25*, 96. (f) Atwater, N. W.; Bible, R. H.; Brown, E. A.; Burtner, R. R.; Minina, J. H.; Nysted, L. N.; Sollman, P. B. *Ibid.* **1961**, *26*, 3077. (g) Lenz, G. R.; Schulz, J. A. *Ibid.* **1978**, *43*, 2334. (h) Heusler, K. *Helv. Chim. Acta* **1962**, *45*, 1939. (i) Neef, G.; Eder, U.; Wiechert, R. *J. Org. Chem.* **1978**, *43*, 4679.

(17) (a) Evans, D. H.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560. (b) Evans, D. A.; Barllargeon, D. J.; Nelson, J. V. *Ibid.* **1978**, *100*, 2242. (c) Martin, S. F.; DuPriest, M. T. *Tetrahedron Lett.* **1977**, 3925.

reactivity of allylic anions can vary with solvent, electrophile, temperature, and counterion, and as such, a unifying explanation of their positional reactivity is not readily forthcoming. In any event, we have shown that the (trimethylsilyl)allyl anion reacts predictably to provide a viable β-acyl anion equivalent based upon organosilicon chemistry.

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer grating spectrometer. ^{1}H NMR spectra were recorded on either a Varian A-60A or a Varian EM-360 spectrometer. For compounds containing a trimethylsilyl group, spectra were recorded in deuteriochloroform containing approximately 2% benzene as an internal standard. Mass spectra were recorded on a Consolidated Electronic MS-9 double-focusing mass spectrometer. Elemental analyses were performed by M-H-W Laboratories. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected.

All solvents were dried and purified by standard techniques prior to use. Reactions involving alkyllithiums were run under argon or nitrogen unless stated otherwise. For experimental procedures of a general nature (Tables I, II, and III), a complete procedure is given for a specified example, and subsequent details for other examples include quantities of substrate and reagents, yield, and characterization details. Thin-layer chromatography (TLC) for monitoring the progress of reactions was conducted with Merck GF_{254} silica gel, aluminum-backed plates. High petroleum refers to the fraction with bp 65–110 °C. Rotations were taken for solutions in chloroform (1.5 g/100 mL) at the D line. Spectral information is given for illustrative examples; for other compounds where the changes are unexceptional, the data are available in the microfilm version (Supplementary Material).

(*E*)-1-[3-(Trimethylsilyl)allyl]-1-cyclopentanol (11). To a stirred solution of *sec*-butyllithium (107 mL of a 1.4 M solution in cyclohexane, 0.15 mol) and TMEDA (17.4 g, 22.6 mL, 0.15 mol) in freshly dried THF (50 mL) at −75 °C was added dropwise trimethylallylsilane (18.2 g, 25.3 mL, 0.16 mol). The resulting solution was warmed to −30 °C and held there for 0.5 h. Cyclopentanone (5.0 g, 60 mmol) was added dropwise to the above mixture. The reaction was complete upon addition, as judged by TLC (4:1 high petroleum ether/EtOAc). The above mixture was poured into saturated aqueous ammonium chloride solution (100 mL) layered with dichloromethane (100 mL). The aqueous phase was extracted with dichloromethane (2 × 50 mL), and the combined organic extracts were washed with water (200 mL). Evaporation in vacuo of the dried ($MgSO_4$) extract gave the adduct **11** (9.98 g, 84% crude) purified by vacuum distillation: bp 66–70 °C (0.025 mmHg); yield 6.25 g, 53%; ν_{max} (thin film) 3400, 2950, 1615, 1247, 864, 840 cm^{-1}; ^{1}H NMR δ 0.18 (9 H, s), 1.5–2.0 (8 H, m), 2.21 (1 H, s, OH), 2.48 (1 H, d, J_{BX} = 6 Hz), 5.81 (1 H, d, J_{AB} = 18.0 Hz), 6.23 (1 H, m, J_{AB} = 18.0 Hz, J_{BX} = 6 Hz, ABX_2 system). Mass spectral analysis gave only *m/e* 183 (100, $M^+ - H_2O$), 180 (79, $M^+ - H_2O$), 169 (69). Anal. ($C_{11}H_{22}OSi$) C, 66.70; H, 11.13.

(*E*)-1-[3-(Trimethylsilyl)allyl]-1-cyclohexanol (12). *sec*-Butyllithium (92.8 mL of a 1.4 M solution in cyclohexane, 0.13 mol), TMEDA (15.1 g, 19.6 mL, 0.13 mol), trimethylallylsilane (14.8 g, 20.6 mL, 0.13 mol), and cyclohexanone (5.0 g, 51 mmol) in THF (40 mL) gave the adduct **12** (9.49 g, 88% crude). Vacuum distillation, bp 66–70 °C (0.025 mmHg), gave 7.00 g (65%) of **12**; exact mass found; *m/e* 194.150. Anal. ($C_{12}H_{24}OSi$) C, 68.14; H, 11.50.

(*E*)-1-[3-(Trimethylsilyl)allyl]-1-cyclohexylcarbinol (13). *sec*-Butyllithium (36 mL of a 1.0 M solution in cyclohexane), TMEDA (4.2 g, 5.5 mL), trimethylallylsilane (4.1 g), and cyclohexanecarboxaldehyde (2.0 g) in THF (10 mL) at −78 °C gave the adduct **13** (4.07 g, 96%) pure enough for subsequent reactions; exact mass calcd for $C_{13}H_{26}OSi$, *m/e* 226.175; found, 226.176.

(*E*)-[3-(Trimethylsilyl)allyl]-*p*-tolylcarbinol (14). *sec*-Butyllithium (34 mL of a 1.2 M solution in cyclohexane), TMEDA (7.0 mL), trimethylallylsilane (4.65 mL), and *p*-tolualdehyde (2.45 mL) at −76 °C gave the adduct **14** (86%). Anal. ($C_{14}H_{22}OSi$) C, 71.61; H, 9.59.

(*E*)-2-[3-(Trimethylsilyl)allyl]-4,4-dimethoxybutan-2-ol (15). *sec*-Butyllithium (23 mL of a 1.4 M solution in cyclohexane) and trimethylallylsilane (5.12 mL, 32 mmol) were added to the solution of 6, M = Li, which was made in the usual way, cooled to −65 °C, and freshly dried zinc chloride (5.23 g, 38 mmol) was added. The heterogeneous mixture was warmed to −20 °C to give a homogeneous pale yellow solution of **6**, M = ZnCl. To this mixture was added acetylacetaldehyde dimethyl acetal (2.0 mL, 11 mmol). After 15 min, the reaction was worked up as before to give the adduct **15** (2.61 g, 66%), bp 74–77 °C (0.1 mmHg). Mass spectroscopy or analysis could not be obtained because of decomposition (loss of MeOH), although the derived epoxide **27** gave analytical data.

(*E*)-[3-(Trimethylsilyl)allyl]diphenylcarbinol (16). *sec*-Butyllithium (20 mL of a 1.4 M solution in cyclohexane), TMEDA (4.2 mL), trimethylallylsilane (4.6 mL), benzophenone [2.0 g in THF (10 mL)], and THF (20 mL) at −30 to 0 °C gave the adduct **16** (71% after preparative layer chromatography, 30:70 EtOAc/petroleum ether, bp 40–65 °C); exact mass calcd for $C_{19}H_{22}Si$ ($M^+ - H_2O$), *m/e* 278.149; found, 278.150.

(*E*)-1-[3-(Trimethylsilyl)allyl]-1-*exo*-borneol (17). To a stirred solution of *sec*-butyllithium (154 mL of a 1.3 M solution in cyclohexane) in THF (50 mL) at −78 °C was added trimethylallylsilane (24.0 g, 33.3 mL). After 10 min at −78 °C, anhydrous zinc chloride (27.2 g) and 2-norbornanone (7 g) were added, and the mixture was warmed to −20 °C for 30 min. Saturated aqueous ammonium chloride (120 mL) was added to the above reaction mixture, and the precipitate was filtered and washed with THF/H_2O. The filtrate was extracted with THF, washed with saturated aqueous ammonium chloride, dried ($MgSO_4$), and evaporated to give **17** (8.76 g, 99%). Vacuum distillation, bp 108–110 °C (0.025 mmHg), gave pure **17**: yield 7.83 g, 89%; $[\alpha]^{25}_D$ +8.8°; exact mass calcd for $C_{16}H_{30}OSi$; *m/e* 266.206; found, 266.207.

(*E*)-1-[3-(Trimethylsilyl)allyl]-1-pinan-1β-ol (18). *sec*-Butyllithium (128.6 mL of a 1.4 M solution in cyclohexane), trimethylallylsilane (22.8 g, 31.7 mL), anhydrous zinc chloride (24.5 g), THF (50 mL), and nopinone (5.0 g) were used as in the synthesis of **17**, except the reaction was run at −20 °C to give the adduct **18** (8.85 g, 97%), purified by vacuum distillation: bp 105–108 °C (0.15 mmHg); $[\alpha]^{25}_D$ +4.3°; exact mass calcd for $C_{15}H_{26}Si$ ($M^+ - H_2O$), *m/e* 234.180; found, 234.181.

(*E*)-2-[3-(Trimethylsillyl)allyl]-2-adamantanol (19). *sec*-Butyllithium (12.3 mL of a 1.3 M solution in cyclohexane), TMEDA (1.8 g), trimethylallylsilane (1.9 g, 2.6 mL), adamantanone (1.0 g), and THF (8 mL) at −40 to 0 °C (15 min) gave the adduct **19** (0.86 g, 99%). Sublimation, 43 °C (0.025 mmHg), gave pure **19** (0.74 g, 85%), mp 70–75 °C. Anal. ($C_{16}H_{28}OSi$) C, 73.00; H, 10.79; mol wt, 246.181.

(*E*)-1-[3-(Trimethylsilyl)allyl]cyclohex-2-en-1-ol (20). *sec*-Butyllithium (15 mL of a 1.0 M solution in cyclohexane), TMEDA (1.7 g), trimethylallylsilane (1.7 g), cyclohexenone (1.0 g), and the solvent diethyl ether (15 mL) at −75 to −26 °C (30 min) gave the adduct **20** (1.75 g, 80%): bp 68–70 °C (0.2 mmHg); exact mass calcd for $C_{12}H_{22}OSi$, *m/e* 210.144.

(*E*)-[3-(Trimethylsilyl)allyl]methylcyclohex-1-enylcarbinol (21). *sec*-Butyllithium (71.4 mL of a 1.4 M solution in cyclohexane), TMEDA (11.6 g, 15.1 mL), trimethylallylsilane (11.4 g, 15.8 mL), 1-acetyl-1-cyclohexene (5.0 g), and THF (25 mol) were reacted at −75 °C. After workup in the usual way, vacuum distillation gave the adduct **21** (6.18 g, 65%): bp 105–113 °C (0.05 mmHg); exact mass calcd for $C_{14}H_{24}Si$ ($M^+ - H_2O$), *m/e* 220.165; found, 220.165.

The low boiling fraction (1.29 g), bp 50–55 °C (0.03 mmHg), was further purified by chromatography over silica gel, eluting with light petroleum ether to give the triene **22** (310 mg, 5%); exact mass calcd for $C_{11}H_{16}$, *m/e* 148.125; found, 148.126.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]cyclopentanol (23). The adduct **11** (2.0 g, 10 mmol) in dichloromethane (10 mL) at 0 °C was treated with *m*-chloroperbenzoic acid (1.9 g, 11 mmol), and the mixture was warmed to 20 °C. When the reaction was complete (TLC, 20:80 EtOAc/high petroleum ether), it was poured into saturated aqueous sodium bisulfite solution (10 mL) layered with dichloromethane (10 mL). The dichloromethane layer was washed with saturated aqueous sodium bicarbonate solution, dried with $MgSO_4$, and evaporated to give **23** (1.90 g, 89%, ≥95% pure by TLC and NMR); exact mass calcd for $C_{11}H_{20}OSi$ ($M^+ - H_2O$), *m/e* 196.128; found, 196.129.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]cyclohexanol (24). Treatment of the adduct **12** (0.17 g, 0.8 mmol) with *m*-chloroperbenzoic acid (0.21 g, 1.2 mmol) in dichloromethane (3 mL) and workup as before gave the epoxide **24** (0.17 g, 94%); exact mass calcd for $C_{12}H_{22}OSi$ ($M^+ - H_2O$), *m/e* 210.144; found, 210.144.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]cyclohexylcarbinol (25). Treatment of the adduct **13** (0.5 g, 1.9 mmol) with *m*-chloroperbenzoic acid (0.48 g, 2.9 mmol) in dichloromethane (5 mL) at 0 °C and workup as before gave the epoxide **25** (90%); exact mass calcd for $C_{13}H_{26}O_2Si$, *m/e* 244.251; found, 244.252.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]-*p*-tolylcarbinol (26). Treatment of **14** (1.2 g) with *m*-chloroperbenzoic acid (1.32 g) in dichloromethane (20 mL) at 0 °C gave after workup the epoxide **26** (88%); exact mass calcd for $C_{14}H_{22}O_2Si$, *m/e* 250.146; found, 250.145.

2-[2,3-Epoxy-3-(trimethylsilyl)propyl]-4,4-dimethoxybutan-2-ol (27). Treatment of the adduct **15** (0.5 g) with *m*-chloroperbenzoic acid (1.7 g) in dichloromethane (5 mL) followed by the usual workup gave the epoxide **27** (0.49 g 94%). Anal. ($C_{12}H_{26}O_4Si$) C, 54.64; H, 9.87.

[2,3-Epoxy-3-(trimethylsilyl)propyl]diphenylcarbinol (28). Treatment of the adduct **16** (0.5 g, 1.7 mmol) with *m*-chloroperbenzoic acid (0.41 g) in dichloromethane (5.0 mL) for 1 h at 0 °C gave after workup the

epoxide **28** (0.48 g, 90%): mp 97.5–99 °C (from EtOAc); exact mass calcd for $C_{19}H_{22}OSi$ ($M^+ - H_2O$), *m/e* 294.144; found, 294.145.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]-1-*exo*-borneol (29). The adduct **17** (5.0 g) in dichloromethane (6 mL) at 0 °C was treated with *m*-chloroperbenzoic acid (5.3 g). Workup as before gave **29** (4.79 g, 89%) which was purified by TLC (20:80 EtOAc/high petroleum ether); exact mass calcd for $C_{16}H_{30}OSi$, *m/e* 282.201; found, 282.202.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]-1-pinan-1β-ol (30). The adduct **18** (6.0 g) in dichloromethane (18 mL) at 0 °C was treated with *m*-chloroperbenzoic acid (7.8 g). Workup as before gave **30** (5.67 g, 88%); exact mass calcd for $C_{15}H_{26}OSi$ ($M^+ - H_2O$), *m/e* 250.175; found, 250.176.

1-[2,3-Epoxy-3-(trimethylsilyl)propyl]-2-adamantanol (31). The adduct **19** (0.5 g) in dichloromethane (3 mL) at 0 °C was treated with *m*-chloroperbenzoic acid (0.45 g). Workup as before gave **31** (0.49 g, 92%): mp 78.5–82 °C; exact mass calcd for $C_{16}H_{26}OSi$ ($M^+ - H_2O$), *m/e* 262.176; found, 262.176.

2-Methoxyspiro[4.4]-1-oxanonane (32). The epoxysilane **23** (1.5 g, 7.0 mmol) in dry methanol (5 mL) at 0 °C was treated with $BF_3 \cdot Et_2O$ (2.0 g, 14 mmol), and the stirred mixture was warmed to 20 °C. When the starting material no longer remained (TLC, 20:80 EtOAc/high petroleum ether), the mixture was poured into saturated aqueous sodium bicarbonate solution (10 mL) layered with dichloromethane (10 mL). The aqueous phase was extracted with dichloromethane, and the combined organic extracts were washed with water (20 mL) and dried with ($MgSO_4$). Evaporation of the solvent gave **32** (0.56 g, 51%); exact mass calcd for $C_9H_{16}O_2$, *m/e* 156.115; found, 156.115.

2-Methoxyspiro[4.5]-1-oxadecane (33). Treatment of the epoxysilane **24** (1.5 g, 6.6 mmol) as above gave **33** (0.80 g, 78%). Anal. ($C_{10}H_{18}O_2$) C, 70.55; H, 10.35.

2-Methoxy-5-cyclohexyltetrahydrofuran (34). Treatment of the epoxysilane **25** (0.50 g) in dry methanol (10 mL) at 0 °C with $BF_3 \cdot OEt_2$ (0.4 mL, 12% in ether) gave after workup **34** (90%, pure enough for subsequent Jones oxidation); exact mass calcd for $C_{11}H_{20}O_2$, *m/e* 184.134; found, 184.134.

2-Methoxy-5-*p*-tolyltetrahydrofuran (35). Treatment of the epoxysilane **26** (0.40 g, 1.6 mmol) in dry methanol (10 mL) at 0 °C with $BF_3 \cdot OEt_2$ (0.4 mL, 12% in ether) gave after workup **35** (98%, pure enough for subsequent Jones oxidation); exact mass calcd for $C_{12}H_{16}O_2$, *m/e* 192.110; found, 192.110.

4′,5′-Dihydro-5′-methoxyspiro[4,4-dimethoxybutane-2,2′(3′*H*)]furan (36). The epoxysilane **27** (0.1 g, 0.38 mmol) in methanol (2.0 mL) at 0 °C was treated with $BF_3 \cdot OEt_2$ (0.07 mL, 12% in ether). Workup gave **36** (ca. 10%).

4′,5′-Dihydro-5′-methoxyspiro[bornane-2,2′(3′*H*)]furan (37). The epoxysilane **29** (0.5 g, 1.8 mmol) in methanol (3 mL) was treated with $BF_3 \cdot OEt_2$ (0.33 mL). Workup gave **37** (0.34 g, 84%). Anal. ($C_{14}H_{24}O_2$) C, 74.87; H, 10.83.

Treatment of 30 with $BF_3 \cdot OEt_2$/MeOH. The epoxysilane **30** (0.5 g, 1.9 mmol) in methanol (3.0 mL) was treated with $BF_3 \cdot OEt_2$ (1.25 g, 0.35 mL, 12% in ether) to give after workup 0.41 g of an oil which was purified by preparative layer chromatography (silica gel, eluting with 20:80 EtOAc/high petroleum ether). The main product was **38**, 4-(1-methyl-1-methoxyethyl)-1-(3,3-dimethoxypropyl)-1-cyclohexene (0.11 g, 22%); exact mass calcd for $C_{14}H_{25}O_3$ (M^+ – Me), *m/e* 241.180; found, 241.181.

4′,5′-Dihydro-5′-methoxyspiro[adamantane-2,3′(3′*H*)]furan (39). The epoxysilane **31** (0.75 g, 2.7 mmol) in methanol (5 mL) at 0 °C was treated with $BF_3 \cdot OEt_2$ (0.96 g, 12% solution in ether). Workup as described gave **39** (0.58 g, 97%). Anal. ($C_{14}H_{22}O_2$) C, 75.48; H, 10.14.

Spiro[4.4]-1-oxanonan-2-one (40).[18] Oxidation of **32** (0.40 g) as described for **45** gave the spirolactone **40** (0.27 g, 75%); exact mass calcd for $C_8H_{12}O_2$, *m/e* 140.084; found, 140.084.

Spiro[4.5]-1-oxadecan-2-one (41).[19] Oxidation of **33** (0.65 g) as described for **45** gave the spirolactone **41** (0.44 g, 76%); exact mass calcd for $C_9H_{14}O_2$, *m/e* 154.099; found, 154.100.

4-Cyclohexylbutyrolactone (42). The *O*-methyl lactol **34** (1.5 g, 6.7 mmol) in acetone (5 mL) at 0 °C was treated with Jones reagent (33 mmol, 4.2 mL of a solution 8 M in chromic acid). Workup in the usual way gave **42** (80%), ν_{max} 1775 cm^{-1}, identical with a sample prepared by the literature method.[20]

4-*p*-Tolylbutyrolactone (43).[21] Oxidation of **35** (0.44 g) as described for **45** gave the lactone **43** (77%).

1-Hydroxybornanepropionic Acid γ-Lactone (44).[22] Oxidation of **37** (0.12 g) as described for **45** gave the lactone **44** (75%): ν_{max} 1775 cm^{-1}; mp 83.5–87 °C. Anal. ($C_{13}H_{20}O_2$) C, 74.77; H, 9.76.

2-Hydroxyadamantanepropionic Acid γ-Lactone (45). The *O*-methyl lactol **39** (0.50 g, 2.2 mmol) in acetone (2 mL) at 0 °C was treated with Jones reagent (11 mmol, 1.4 mL of a solution 8 M in chromic acid). After 10 min, the mixture was quenched with 2-propanol (0.5 mL) and poured into saturated aqueous sodium bicarbonate solution (25 mL) layered with dichloromethane (10 mL). The aqueous phase was extracted with dichloromethane (4 × 10 mL), and the combined extracts were washed with water (25 mL). Evaporation in vacuo of the dried ($MgSO_4$) extract gave **45** (0.36 g, 80%), mp 124–128 °C. Anal. ($C_{13}H_{18}O_2$) C, 75.77; H, 8.77.

Direct Oxidation of the Adducts 11 and 19 to the Lactones 40 and 45. The adduct **11** (1.5 g, 7.6 mmol) in acetic acid (5 mL) at 0 °C was treated with peracetic acid (4.9 mL of a 40% solution in acetic acid). The stirred mixture was warmed to 25 °C and after 7 h poured into saturated aqueous sodium bicarbonate solution (5 mL) layered with dichloromethane (5 mL). The organic phase was dried ($MgSO_4$) and evaporated to give the lactone **40** (0.55 g, 52%), identical with an authentic sample. A similar procedure conducted on **23** gave **40** (60%).

The adduct **19** (1.0 g, 3.8 mmol) in acetic acid (8 mL) was treated with peracetic acid (2.5 mL of a 40% solution in acetic acid) to give after workup, as above, the lactone **45** (31%), identical with an authentic sample.

1-[2,3-Epoxy-3-(trimethylsilyl)propenyl]-2-adamantane (46). The epoxysilane **31** (0.2 g, 0.71 mmol) in benzene (3 mL) at 10 °C was treated with a catalytic amount of *p*-toluenesulfonic acid (ca. 5 mg). After 48 h the mixture was poured into saturated aqueous sodium bicarbonate solution (5 mL) layered with dichloromethane (5 mL). Evaporation in vacuo of the dried ($MgSO_4$) extract gave **46**: yield 0.1 g; ν_{max} (Nujol mull) 2920, 1455, 1250, 1020, 1000, 845 cm^{-1}; NMR ($CDCl_3$) δ 5.04 (1 H, d, *J* = 5 Hz), 3.32 (1 H, m), 2.2–1.4 (15 H, br s), 0.05 (9 H, s); exact mass calcd for $C_{16}H_{26}OSi$, *m/e* 262.175; found, 262.176.

(Bromospiro[adamantane-2,2′-oxetan]-4′-ylmethyl)trimethylsilane (47). The adduct **19** (1.0 g, 3.8 mmol) in THF (20 mL) at 0 °C was treated with *N*-bromosuccinimide (1.0 g, 5.7 mmol). After the solution was stirred at 0 °C for 3 h, TLC (95:5 high petroleum ether/EtOAc) showed complete reaction. The mixture was quenched in saturated aqueous sodium bicarbonate solution (50 mL) layered with dichloromethane (20 mL). The aqueous phase was extracted with dichloromethane (4 × 15 mL), and the combined extracts were washed with water. Evaporation in vacuo of the dried ($MgSO_4$) extract gave **47**: yield 1.2 g, 92%; ν_{max} (thin film) 2900, 1450, 1250, 970, 850 cm^{-1}; ^1H NMR δ 4.59 (1 H, q, *J* = 7.8 Hz), 3.37 (1 H, d, *J* = 7.8 Hz), 2.37–1.81 (4 H, m), 1.66 (12 H, br s), 0.14 (9 H, s); ^{13}C NMR ($CDCl_3$, ppm decoupled) 85.446, 74.182, 47.723, 2.184. There were 14 signals in all, consistent with the proposed structure (other signals, adamantyl portion, not given). Further characterization by mass spectroscopy or microanalysis was not successful since **47** readily decomposed to give the diene **49**.

(*Z*)-[3-(2-Adamantylidene)-1-bromopropenyl]trimethylsilane (49). The adduct **19** (1.0 g, 3.8 mmol) in THF (20 mL) was heated at reflux, and *N*-bromosuccinimide (1.0 g, 5.7 mmol) was added. After 1 h, the solution was cooled to room temperature and worked up as for **48** to give the diene **49**: yield 1.24 g, 100%; mp 92–97 °C; ν_{max} (Nujol mull) 1632, 1246, 910, 840, 790, 760 cm^{-1}; ^1H NMR δ 6.55 (2 H, q, *J* = 11 Hz), 2.96 (1 H, s), 2.46 (1 H, s), 1.85 (2 H, br s), 0.17 (9 H, s); ^{13}C NMR ($CDCl_3$, ppm) 157.832, 133.588, 130.305, 115.643, 1.747, 41.218–28.546 (adamantyl carbons); exact mass calcd for $C_{16}H_{25}SiBr$, *m/e* 324.091; found, 324.092. Anal. Calcd for ($C_{16}H_{25}SiBr$) C, 59.25; H, 7.96.

Compound **47** (0.10 g, 0.29 mmol) in THF (2 mL) heated at reflux was treated with 1 M HCl (0.1 mL). After 7 h, workup as above gave **49** (90%), identical with the above authentic sample.

(*Z*)-2-(3-Bromoallyl)-2-adamantanol (50). The oxetane **47** (0.59 g, 1.7 mmol) in dry dimethyl sulfoxide (5 mL) was heated at 40–45 °C, and potassium fluoride dihydrate (0.48 g, 5.1 mmol) was added. After 6 h, TLC (95:5 high petroleum ether/EtOAc) indicated complete reaction. The mixture was poured into water (20 mL) layered with ether (10 mL). The aqueous phase was extracted with ether, and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo to give **50**: yield 0.35 g, 76%; mp 117–119 °C (from light petroleum ether/EtOAc); ν_{max} (Nujol mull) 3320, 2920, 1625, 1050, 745 cm^{-1}; ^1H NMR ($CDCl_3$) 6.23 (2 H, t, *J* = 5 Hz), 2.56 (2 H, d, *J* = 5 Hz), 2.2–1.3 (14 H); ^{13}C NMR $CDCl_3$, ppm) 130.669, 109.695, 75.347, 38.984–27.284 (other signals); exact mass calcd for $C_{13}H_{17}Br$ ($M^+ - H_2O$), *m/e* 252.051; found, 252.052.

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Anal. Calcd for ($C_{13}H_{17}OBr$) C, 57.35; H, 7.10.

(*Z*)-[3-(2-Adamantylidene)-1-bromopropene] (51). To **49** (0.34 g, 1.0 mmol) in dry dimethyl sulfoxide (5 mL) at 40–45 °C was added potassium fluoride dihydrate (0.28 g, 3.0 mmol), and the mixture was held at this temperature for 6 h (TLC, high petroleum ether). Workup as above gave **51**: yield 0.25 g, 100%; ν_{max} (thin film) 2900, 1650, 1450, 1295, 720 cm^{-1}; ^1H NMR ($CDCl_3$) 6.82 (1 H, m), 6.01 (2 H, m), 2.88 (1 H, s), 2.45 (1 H, s), 1.85 (12 H, s); ^{13}C NMR ($CDCl_3$) 157.007, 127.780, 113.313, 106.030, 41.120–28.546 (adamantyl carbons); exact mass calcd for $C_{13}H_{17}Br$, *m/e* 252.051; found 252.052.

The diene **51** was also prepared from **50** as follows. The alcohol **50** (0.10 g, 0.37 mmol) in dry pyridine (2 mL) at 0 °C was treated with thionyl chloride (0.8 mL). After 1 h, the mixture was poured into water (10 mL) and extracted with ether. Evaporation of the dried extract ($MgSO_4$) gave **51** (80%), identical with an authentic sample.

17α-Hydroxy-17β-(3-trimethylsilylprop-2-enyl)androst-4-en-3-one (57). To a stirred solution of *sec*-butyllithium (0.068 mol, 56.7 mL, 1.2 M solution in cyclohexane) in dry tetrahydrofuran (45 mL) at −78 °C under argon was added allyltrimethylsilane (0.076 mol, 8.7 g, 12.1 mL). To this mixture at −78 °C was added anhydrous zinc chloride (0.068 mol, 9.2 g), and the mixture was warmed to −35 °C, when the mixture became homogeneous. After 30 min, 3-methoxyandrosta-3,5-dien-17-one (**54**) (0.017 mol, 5.0 g) was added dropwise as a solution in tetrahydrofuran (40 mL). When the reaction was complete (0.5 h) (TLC, silica gel, 80:20 petroleum ether/EtOAc), saturated aqueous ammonium chloride (40 mL) was added, and the mixture was warmed to room temperature. The dense precipitate formed was filtered, and the cake was washed with water and THF. The aqueous phase was extracted with THF, and the combined organic phases were washed with saturated aqueous ammonium chloride and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure left a solid residue which was dissolved in dichloromethane (20 mL) and treated with concentrated sulfuric acid (7.5 mL) and water (20 mL) at 35 °C for 30 min. The above mixture was poured into saturated aqueous sodium bicarbonate solution (50 mL) layered with dichloromethane (25 mL). The aqueous phase was extracted with dichloromethane, washed with water, dried ($MgSO_4$), and evaporated under reduced pressure to give 17α-hydroxy-17β-(3-trimethylsilylprop-2-enyl)androst-4-en-3-one (**57**): yield 5.64 g, 82%; mp 116–118 °C (from EtOAc); ν_{max} ($CHCl_3$) 3440, 2940, 1670, 1615, 1250, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.83 (2 H, m, *J* = 19 Hz), 5.67 (1 H, s), 2.4–1.3 (22 H, envelope), 1.15 (3 H, s), 0.87 (3 H, s), 0.02 (9 H, s); $[\alpha]^{25}_D$ +48.4°; exact mass calcd for $C_{25}H_{40}O_2Si$, *m/e* 400.280; found, 400.280. Anal. Calcd for $C_{25}H_{40}O_2Si$: C, 75.07; H, 10.01. Found: C, 74.47; H, 9.97. On a 15-g scale, yields of 95% for **57** were obtained.

17α-Hydroxy-17β-(2,3-epoxy-3-trimethylsilylpropyl)androst-4-en-3-one (58). The above adduct **57** (7.5 mmol, 3.0 g) in benzene (20 mL) was treated with $VO(acac)_2$ (0.075 mmol, 0.02 g), and the mixture was heated at reflux. *tert*-Butyl hydroperoxide (8.2 mmol, 0.74 g) was added dropwise, and the mixture was held at reflux for several hours. When the reaction was judged complete by TLC (80:20 high petroleum ether/EtOAc), the solution was cooled and poured into saturated aqueous sodium bisulfite. The aqueous phase was extracted with dichloromethane (5 × 15 mL) and washed with water. Evaporation of the dried ($MgSO_4$) extract under reduced pressure gave the required epoxide: yield 3.03 g, 97%; mp 147–150 °C (from EtOAc/light petroleum ether); ν_{max} ($CHCl_3$) 3480, 2955, 1665, 1615, 1250, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.64 (1 H, s), 3.00 (1 H, m), 2.5–1.3 (23 H, envelope), 1.15 (3 H, s), 0.86 (3 H, s), −0.02 (9 H, s); exact mass calcd for $C_{25}H_{40}O_3Si$, *m/e* 461.275; found, 416.275.

(17β)-4′,5′-Dihydro-5′-methoxyspiro[androst-4-ene-17,2′(3′*H*)-furan]-3-one (59). The epoxide **58** (0.50 g, 1.2 mmol) in methanol (2 mL) at 0 °C was treated with boron trifluoride etherate (2.4 mmol, 0.34 g, 0.30 mL), and the solution was allowed to warm to room temperature. When the reaction was judged complete (TLC, 80:20 high petroleum ether/EtOAc) after 24 h, the solution was poured into saturated aqueous sodium bicarbonate layered with dichloromethane. The aqueous phase was extracted with dichloromethane, and the combined extracts were washed with water. Evaporation of the dried ($MgSO_4$) extract under reduced pressure gave the *O*-methyl lactol **59**: yield 0.40 g, 93%; ν_{max} (CCl_4) 2950, 1680, 1620, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.69 (1 H, s), 4.80 (1 H, m), 3.30 (3 H, s), 2.6–1.4 (23 H, envelope), 1.17 (3 H, s), 0.92 (3 H, d, epimers at C-22); exact mass calcd for $C_{23}H_{34}O_3$, *m/e* 358.251; found, 358.251.

(17β)-4′,5′-Dihydrospiro[androst-4-ene-17,2′(3′*H*)-furan]-3-one (60).[16] The *O*-methyl lactol **59** (2.0 g, 5.6 mmol) in acetone (10 mL) at 0 °C was treated with excess Jones reagent (3.5 mL of a solution 8 M in CrO_3). After complete reaction (0.5 h), 2-propanol was added, and the solution was poured into saturated aqueous sodium bicarbonate solution layered with dichloromethane. The aqueous phase was extracted with dichloromethane (4 × 15 mL), and the combined extracts were washed with water. Evaporation of the dried ($MgSO_4$) extract under reduced pressure gave the lactone **60** (1.31 g, 68%). Chromatography of the crude lactone over silica gel, eluting with low petroleum ether/EtOAc, gave **60** (0.92 g, 48%), mp 148–151 °C (from EtOAc).

3-Methoxy-17α-(3-trimethylsilylprop-2-enyl)-1,3,5(10)-estratrien-17β-ol. To a stirred solution of *sec*-butyllithium (70.7 mL of a 1.4 M solution in cyclohexane) in dry THF (60 mL) at −78 °C was added trimethylallylsilane (12.5 g, 0.11 mol). To this mixture was added anhydrous zinc chloride (13.5 g). The heterogeneous reaction mixture was warmed to −20 °C whereupon the mixture became homogeneous. After 45 min, estrone methyl ether (5.0 g, 18 mmol) was added as a slurry in THF (10 mL). When the reaction was complete (ca. 1 h; TLC, 70:30 high petroleum ether/EtOAc), saturated aqueous ammonium chloride (60 mL) was added, and the precipitate was filtered. The precipitate was washed with THF and water. The aqueous phase was extracted with THF, and the combined extracts were washed with saturated aqueous ammonium chloride and dried ($MgSO_4$). Evaporation of the extract in vacuo gave a residue which was chromatographed over silica gel to give 3-methoxy-17α-(3-trimethylsilylprop-2-enyl)-1,3,5(10)-estratrien-17β-ol: yield 4.71 g, 66%; mp 110–112 °C (from diisopropyl ether); ν_{max} ($CHCl_3$) 3540, 2950, 1610, 1500, 1250, 870, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3–6.5 (3 H, m), 5.90 (2 H, m, J_{AB} = 19 Hz), 3.72 (3 H, s), 2.70 (3 H, m), 2.33 (2 H, d, J_{AX} = 5 Hz), 1.9–1.1 (14 H, m), 0.90 (3 H, s), 0.05 (9 H, s); exact mass, calcd for $C_{25}H_{38}O_2Si$, *m/e* 398.264; found, 398.265.

17α-(2,3-Epoxy-3-trimethylsilylpropyl)-3-methoxy-1,3,5(10)-estratrien-17β-ol. The above adduct (4.1 g, 10 mmol) in benzene (20 mL) heated at reflux was treated with $VO(acac)_2$ (0.026 g, 0.10 mmol). To this mixture was added *tert*-butyl hydroperoxide (0.99 g, 11 mmol). After 6 h, the mixture was cooled to room temperature and poured into saturated aqueous sodium bisulfite solution layered with dichloromethane. The aqueous phase was extracted with dichloromethane, and the combined extracts were washed with water. Evaporation of the dried ($MgSO_4$) extract gave 17α-(2,3-epoxy-3-trimethylsilylpropyl)-3-methoxy-1,3,5(10)-estratrien-17β-ol: yield 3.76 g, 91%; ν_{max} ($CHCl_3$) 2920, 1610, 1500, 1255, 845 cm^{-1}; ^1H NMR δ 7.3–6.5 (3 H, m), 3.76 (3 H, s), 3.17 (1 H, m), 2.82 (3 H, m), 3.0–1.1 (16 H, m), 0.92 (3 H, s), 0.09 (9 H, s). The above crude product (0.35 g, 0.84 mmol) in methanol (3 mL) at 0 °C was treated with $BF_3{\cdot}OEt_2$ (0.26 mL). After 72 h, workup gave 17β-4′,5′-dihydro-3,5′-dimethoxyspiro[1,3,5(10)estratrien-17,2′-(3′*H*)-furan]: yield 0.24 g, 80%; ν_{max} ($CHCl_3$) 2940, 1610, 1500, 1040 cm^{-1}; ^1H NMR δ 7.3–6.4 (3 H, m), 4.86 (1 H, m), 3.70 (3 H, s), 3.26 (3 H, s), 2.73 (3 H, m), 2.3–1.1 (16 H, m), 0.86 (3 H, d, epimers); exact mass calcd for $C_{23}H_{23}O_3$, *m/e* 256.235; found, 356.236.

The above methoxy lactol (1.8 g, 5.0 mmol) in acetone (10 mL) at 0 °C was treated with Jones reagent (3.1 mL of a 8 M solution in CrO_3). Workup gave 3′-[3-methoxy-17β-hydroxy-1,3,5(10)estratrien-17α-yl]-propanoic acid lactone (**62**): yield 1.12 g, 66%; mp 150–152 °C (from EtOAc); ν_{max} ($CHCl_3$) 2940, 1765, 1610, 1500, 1170 cm^{-1}; ^1H NMR δ 7.3–6.5 (3 H, m), 3.76 (3 H, s), 2.84 (3 H, m), 2.6–1.1 (16 H, m), 0.95 (3 H, s); $[\alpha]^{25}_D$ +11.8°; exact mass calcd for $C_{22}H_{28}O_3$, *m/e* 340.204; found, 340.204.

3-(2-Adamantylidene)propene (66). To the adduct **19** (0.25 g, 0.95 mmol) in dry THF (10 mL) was added potassium hydride (0.04 g, 1.0 mmol) followed by dicyclohexano-18-crown-6 (0.04 g, 0.095 mmol). The mixture was stirred at 20 °C for 4 days. Further dicyclohexano-18-crown-6 (0.02 g) was added, and the mixture was heated at reflux for 48 h. The mixture was poured into saturated aqueous ammonium chloride (10 mL) layered with dichloromethane (10 mL). The organic phase was washed with water, dried with $MgSO_4$, and evaporated to give **66**: yield 0.14 g, 88% (purified by TLC); ν_{max} (thin film) 2900, 1670, 1645, 1445, 985, 890 cm^{-1}; ^1H NMR (CCl_4) δ 6.8–4.7 (4 H, m), 2.97 (1 H, br s), 2.35 (1 H, br s), 1.85 (12 H, br s). Anal. Calcd for ($C_{13}H_{18}$) C, 89.50; H, 10.35.

Acknowledgments. Support from the National Institutes of Health and Upjohn Co. is gratefully acknowledged, and Dr. Jake Parikh is thanked for initially demonstrating the effect of zinc chloride on the (trimethylsilyl)allyl anion. Dr. Charles Cottrell is thanked for NMR experiments to assign the configuration of **51**. Sherry Anthony of Chemical Abstracts Service is thanked for assistance with naming certain compounds.

Supplementary Material Available: Further experimental details for compound preparations (20 pages). Ordering information is given on any current masthead page.