Table I

δ	Δδ	r_{measd}, Å	θ	r_{calcd}, Å	% r
4.35	3.376				
5.93	2.236	4.4	36	4.20	4.5
5.00	1.429	5.8	23	5.71	1.6
4.42	0.663	6.7	35	6.51	2.8
2.52	0.497	7.8	28	7.74	0.8
4.86	0.415	8.7	18	8.92	2.5
2.68	0.442	8.4	21	8.70	3.4
1.02	0.363	8.0	34	7.96	0.5
1.30	0.227	9.6	31	9.70	1.0

cess reagent in vacuo to yield 6 mg of the diacetate **12**: $[\alpha]^{23}_D$ −37.0° (*c* 0.33, $CHCl_3$); high-resolution mass measurement of $M^+ - HCl$ (obsd, *m/e* 330.044; calcd, *m/e* 330.047) and $M^+ - HOAC$ (obsd, *m/e* 307.014; calcd, *m/e* 307.010); ^1H NMR ($CDCl_3$) δ 1.07 (3 H, s), 1.18 (3 H, s), 2.07 (6 H, s), 2.35 (2 H, m), 3.64 (2 H, m), 4.27 (1 H, dd, *J* = 5.8 and 11.0 Hz), 5.31 (1 H, dd, *J* = 5.8 and 7.2 Hz), 5.39 (1 H, dd, *J* = 2.7 and 3.6 Hz), 5.91 (1 H, s).

Acknowledgment. We wish to acknowledge financial support for this work from the National Science Foundation, Oceanography Section, under Grant OCE 75-03824. The UCSD NMR Facility was supported by a grant from the National Institute of Health (RR-708). O.J.M. wishes to thank the Institute of Marine Resources, University of California, San Diego, Calif., for a Graduate Fellowship, 1977–1978.

Registry No.—**1**, 67237-02-9; **3**, 67237-01-8; **4**, 67237-03-0; **5**, 67237-04-1; **6**, 67237-05-2; **7**, 67237-06-3; **8**, 67237-07-4; **9**, 67237-08-5; **10**, 67237-09-6; **11**, 67237-10-9; **12**, 67237-11-0.

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(5) We wish to thank Dr. James Norris, Smithsonian Institution, for aid in the collection and identification of *O. secundiramea*. A voucher specimen has been deposited in the U.S. National Herbarium, Washington, D.C.
(6) We gratefully acknowledge F. X. Woolard and R. E. Moore for providing new structural information and a sample of authentic chondrocole A.[3a] The depiction of **2** with the halogens transposed relative to the published structure is due to a recent revision of structure based upon X-ray studies.
(7) The trisubstituted olefin in ochtodene could not be oxidatively cleaved under a variety of conditions: (a) O_3/CH_2Cl_2 or EtOAc, −78 °C to room temperature; (b) $KMnO_4$, 18-crown-6, benzene, room temperature, 20 h; (c) $RuO_2/NaIO_4$, CH_2Cl_2/H_2O, room temperature, 12 h; (d) $KMnO_4$, $MgSO_4$, H_2O/acetone, −78 °C to room temperature, 1 h.
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α,α-Dichlorocyclopropanols. Attenuation of Cyclopropyl Rearrangement Processes in the 3-Bicyclo[4.1.0]heptene System. A Novel Regiospecific 2-Chlorotropone Synthesis

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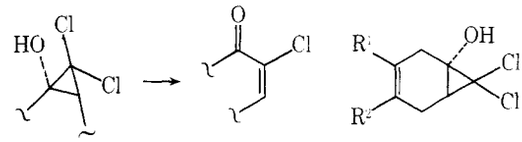
Received January 23, 1978

α,α-Dichlorocyclopropanols **1** rearrange with facility to α-chloroenones **2**, illustrating a transformation that has been synthetically employed in one-carbon ring expanding[1-3] or chain homologating[3,4] sequences. Indeed, these compounds are believed to thermally rearrange rapidly upon their in situ generation. However, we have recently uncovered a class of bicyclic, tertiary α,α-dichlorocyclopropanols which possess unusual thermal stability.[1,6b] The stable α,α-dichlorocyclopropanols were incorporated in the norcar-3-en-1-ol structure **3** and suggested an investigation of dichlorocyclopropanol stability with respect to olefin regioposition in the norcarene bicyclic system. We now report the results of these studies. In addition, we describe some chemistry of the compounds encountered in these studies, including a regiospecific cyclohexenone to α-chlorotropone conversion.



1 2 3

The three isomeric 7,7-dichloronorcaren-1-ol compounds desired for our studies have structures **4a, 5a,** and **6a.** Facile entry into these materials was provided by sodium trichloroacetate mediated and regiospecific dichlorocyclopropanation of the corresponding dienol silyl ethers **4c, 5c,** and **6c.**[1,5] In this fashion, we have prepared the silyl ethers corresponding to the desired norcarenol olefin isomers **4b** and **5b** and to an alkylated derivative **7b.** In addition, the saturated parent trimethylsilyl 7,7-dichloronorcaran-1-yl ether **8b,** previously synthesized by Conia et al. as the dibromo derivative (Cl = Br),[3] was prepared. Methanolic acid-catalyzed hydrolysis of the trialkylsilyl ether is thought to release the desired dichlorocyclopropanol structures **4a, 5a, 7a,** and **8a.** Under these reaction conditions (vide infra), only dichloronorcarenol **4a** possesses stability. The products **9** and **10** (from **5b**) and **11** (from **7b**) of the isomeric silyl norcarenyl ether compounds **5b** and **7b** are exclusively ring-expanded α-chlorocycloheptenones, which arise by way of the intermediate α,α-dichlorocyclopropanols **5a** and **7a** via rearrangement. Such a sequence has been implied for the trimethylsilyl 7,7-norcaran-1-yl ether **8b** (Cl = Br) to 2-bromocycloheptenone **12** (Cl = Br) conversion.[3]

Our studies could not detect chemical intermediates in the silyl ether hydrolysis–hydroxy cyclopropyl ring expansion transformation of compounds **5b, 7b,** or **8b** (TLC) [room temperature, pH adjusted methanolic aqueous hydrochloric acid]. In these instances, formation of α-chloroenone products appeared coincident with norcarenyl silyl ether hydrolysis. In contrast, the isolated α,α-dichlorocyclopropanol **4a** was stable (85% recovery, no detectable UV absorption by TLC) to refluxing acidic aqueous 2-propanol for 20 h and could be purified via Kugelrohr distillation at 145 °C (0.1 mm). Two studies on alternate catalytic methodology to facilitate the rearrangement of **4a** deserve mention. Mildly basic treatment of cyclopropanol **4a** [methanolic $NaHCO_3$ or $Ba(OH)_2$] or base assisted hydrolysis of silyl ethers **5b, 7b,** or **8b** generated carboxylic acid compounds directly (no detectable intermediates), presumably via the corresponding α-chlorodienone, which is rapidly consumed in a Favorski ring contraction sequence. Attempted catalysis of chloride ionization with monovalent silver ion had little effect on **4a** with moderate substrate to Ag^+ ratios (3.0 equiv of $AgClO_4$ in refluxing methanol, 12 h) and converted **4a** directly to tropone with high ratios (1:15), albeit in low yield (~20%).[6]

The stability afforded the α,α-dichlorocyclopropanol function in **4a** by the appositely positioned carbon–carbon unsaturation is dramatic. However, stabilization of the cyclopropane moiety embraced in the Δ^3-norcarene system is not unique. In fact, such stabilization appears to be generally

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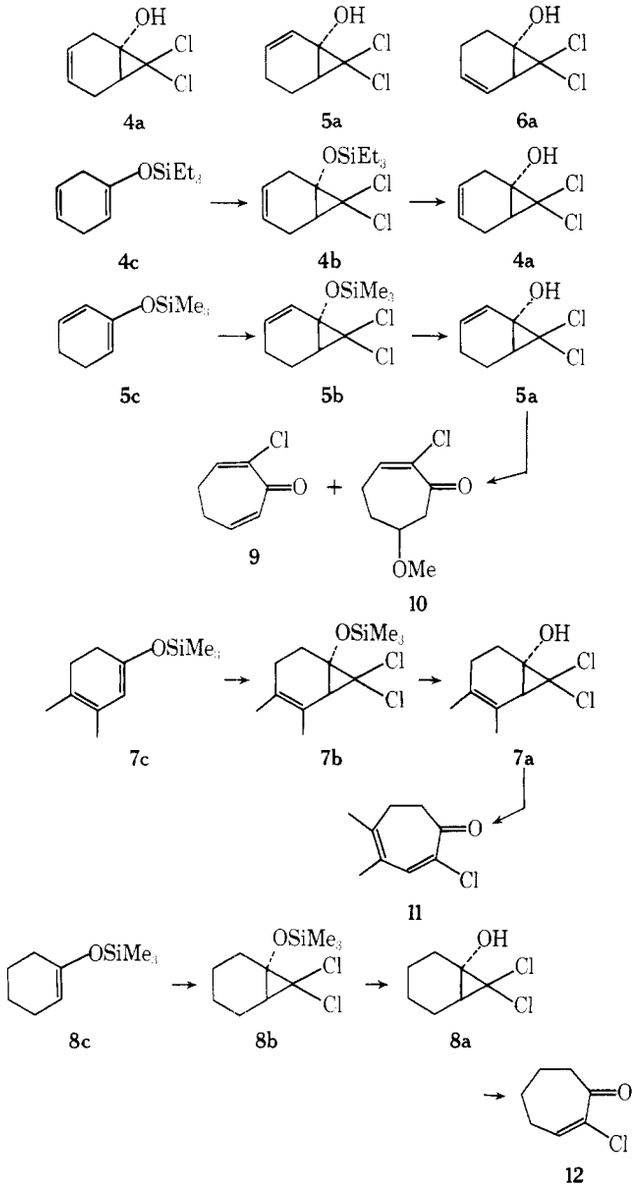
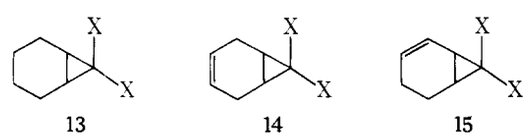
Scheme I

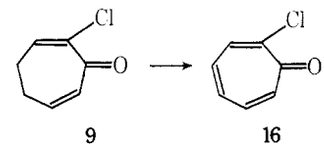


observed in cyclopropane rearrangement processes of bicyclo[4.1.0]hept-3-ene systems relative to their isomeric Δ^2-unsaturated or saturated counterparts. For example, "unusual thermal stability"[7a] of the parent Δ^3-unsaturated hydrocarbon and of 3-carene[7b] has been noted and the facility of ring expansion for the Δ^2-[9a] and saturated[9b,c] 7,7-dihalonorcarane systems relative to the Δ^3 skeleton has been described. Furthermore, the corresponding Δ^2- and Δ^3-carane oxides exhibit a pronounced difference in ease of cyclopropane (and epoxide) rearrangement.[8] Taken together,[9] studies on the rearrangement of 7,7-dihalonorcarane (-2- or -3-ene) systems would suggest the "cyclopropane rearrangement ease" relationship to be **15** > **13** ≫ **14**.

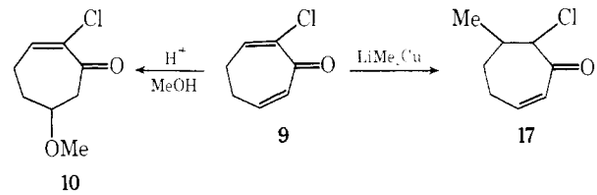


The underlying rationale for this "site specific olefin" stabilizing effect inherent in the bicyclo[4.1.0]heptane system is not clear. Allylic stabilization of the transition state incipient carbocation generated during thermal ring expansion of **15** has been suggested to facilitate its rearrangement (relative to **13** and **14**).[9a] Postulated allylic cationic stabilization may well play a role in isomeric norcarene rearrangements, although such effects are probably minimal in the molecules examined here due to distortion of the incipient charge distribution resulting from strong nucleophilic oxygen participation in the activated complex for ring expansion (cf. no discernible difference under our conditions in the rate of rearrangement of **5a, 7a,** and **8a**). It is relevant to note the findings of Ledlie et al.[9c] on the rate parameters for cyclopropane rearrangement of the bicyclic dibromides **13** and **14** (X = Br). The Ledlie group found *entropic factors* to be the primary source of k_{13}–k_{14} rate difference in silver ion assisted solvolysis. Apparently, subtle geometric factors occur in the isomeric norcarene–norcarane structures which have substantial impact on activation entropies for cyclopropane rearrangement. However, despite lack of understanding of the source of such 3-norcarene "stabilization factor(s)", the 3-norcarene system represents a structural device which may have general mechanistic utility in attenuating rearrangement processes of reactive cyclopropanes.

Apart from their mechanistic interest, the 2-chlorocycloheptadienone systems prepared in the course of these studies have considerable synthetic value. The present work describes new, regiospecific syntheses of 2,6-cycloheptadienones[10] and 2,4-cycloheptadienones[11] for which few preparations are currently available. The synthetic utility of the regiospecifically generated 2-chloro-2,6-cycloheptadienone system can be illustrated by its facile dehydrogenation into the 2-chlorotropone system. Thus, chlorodienone **9** can be converted into chlorotropone **16** with dichlorodicyanoquinone.[10c] This regiospecific conversion of cyclohexenones into α-chlorotropones complements our reported phenol to α-chlorotropone transform.[1] In contrast to the facile dehydrogenation of chlorodienone **9** with DDQ, 2-chloro-2,4-cycloheptadienone **11** yields a one to one adduct, presumably a cycloaddition product. We are currently elucidating the structure of this adduct.



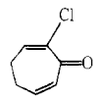
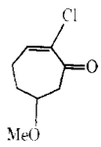
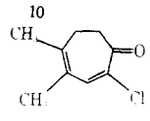
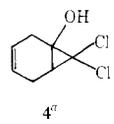
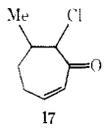
In addition, 2-chlorocycloheptadienone **9** serves as a useful probe into chloro-substituent perturbation on cyclic α-enone reactivity. Thus, **9** under acidic methanolysis adds methanol exclusively to the more electron rich olefin forming 2-chloro-6-methoxycycloheptadienone **11**. In contrast, nucleophilic lithium dimethylcuprate addition occurs exclusively across the chlorodienone system in **9** to give chlorodienone **17** (configuration based on NMR analysis).



Experimental Section

General. Melting points were taken with a Thomas-Hoover apparatus using open capillaries and are uncorrected. Proton magnetic resonance spectra were recorded at 100 MHz with a Joel JNM-MH-100 spectrometer employing tetramethylsilane as an internal standard. Low resolution mass spectra were obtained by direct insertion with an LKB 9000 spectrometer at 70 eV. The parent ion and the most intense peaks (2–4) are reported. Infrared spectra were obtained on a Perkin-Elmer 727 infrared spectrometer. Elemental analyses on all used compounds were performed by Galbraith Laboratories, Inc., Knoxville, Tenn; results were within acceptable limits.

Table I. Physical Data for Products from Silyloxy Diene Dichlorocyclopropanation–Aqueous Hydrolysis

compd	registry no.	bp (mm) or mp, °C	IR (neat), cm^{-1}	NMR ($CDCl_3$, Me_4Si), δ	MS m/e rel abundance
 9[a]	67382-58-5	thermally labile mp ≃ 8–11	1655 (stg) 1635 (med) 790 (stg)	2.5 (t, J = 4.0 Hz, 4 H) 6.20 (d, J = 12.5 Hz, 1 H) 6.72 (m of d, J = 12.5 Hz, 1 H) 7.12 (m, 1 H)	142 (51) 125 (35) 107 (79) 79 (100)
 10	67382-59-6	thermally labile	1695 (stg) 1625 (med) 725 (st)	2.00 (qt, J = 7.5 Hz, 2 H) 2.60 (m, 2 H) 2.95 (d, J = 10.5 Hz, 2 H) 3.60 (s, 3 H) 3.87 (aquint, J = 10.5 Hz, 1 H) 7.20 (t, J = 11.0 Hz)	 174 (12) 142 (24) 79 (100)
 11[a]	67382-60-9	160 (0.1 mm)	1660 (stg) 1620 (m) 1595 (w)	2.12 (s, 6 H) 2.52 (s, 4 H) 6.08 (s, 1 H)	170 (72) 155 (68) 107 (100) 90 (75)
 4[a]	67382-61-0	145 (0.1 mm)	3375 (stg) 820 (stg)	1.82 (d,d, J = 8.0 Hz, 1 H) 2.20–2.80 (m centered at 2.60, 4 H) 5.60 (s, 2 H) 2.2 (s, 1 H(OH))	178 (8) 143 (100) 115 (45)
 17	67382-62-1			1.08 (d, J = 6.0 Hz, 3 H) 1.89 (m, 2 H) 2.2 (brm, 3 H) 7.58 (d, J = 3.5 Hz, 1 H) 6.05 (d, J = 12.5 Hz, 1 H) 6.60 (d,d,d, J = 12.5, 4.0, 6.5 Hz, 1 H)	158 (37) 123 (72) 95 (100)

[a] Satisfactory elemental analysis was obtained (C, H = ±0.3%).

For all column chromatography, E. Merck (type 60) silica gel and short column techniques were utilized and for TLC analysis, E. Merck Silica Gel 60, F-254 precoated (0.25 mm) plates were employed. Magnesium sulfate was used as drying agent throughout and all experimental procedures were performed under an atmosphere of dry nitrogen.

Trialkylsilyl Cyclohexadienyl Ethers 4c, 5c, and 7c. (a) Triethylsilyloxy-1,4-cyclohexadiene (4c). This dihydroaromatic ether was prepared as described in ref 1. Treatment of triethylsilyl phenyl ether (2.420 g, 12.0 mmol) in anhydrous THF (55 mL), *tert*-butyl alcohol (10 mL), and ammonia (120 mL) at −33 °C with lithium wire (75.0 mmol) for 45 min, followed by ammonium chloride (4.0 g) quench and rapid pentane (300 mL) saturated aqueous ammonium chloride (200 mL) partitioning, gave crude (>90% pure by NMR) **4c** (2.112 g, 87%). The sole impurity was unreduced (and noninterfering) starting material and the product was consequently utilized without further purification: NMR δ 1.10–0.40 (m, 15 H), 2.68 (s, 4 H), 4.88 (s, 1 H), 5.65 (s, 2 H); IR 1605 and 1240 cm^{-1}.

(b) Cyclohexadienyl Trimethylsilyl Ethers 5c and 7c. These compounds were prepared according to Rubottom and Gruber.[5] Ether **5c** is described therein, although data for **7c** are not presented. Silyloxy diene **7c**: bp 65–72 °C (0.1 mm); NMR δ 0.30 (s, 9 H), 1.58 (s, 6 H), 2.08 (s, 4 H), 4.90 (s, 1 H); IR 1655 and 1250 cm^{-1}.

General Procedures for Sequential Dichlorocyclopropanation–Hydrolysis of 4c, 5c, 7c, and 8c. (a) Dichlorocyclopropanation. The requisite trialkylsilyl cyclohexadienyl ether (4.00 mmol) was dissolved in freshly distilled tetrachloroethylene (5 mL) and anhydrous dimethoxyethane (5 mL). Anhydrous sodium trichloroacetate (1.20 g, 6.00 mmol) was introduced and the suspension refluxed for 1.5 h. The solution was then cooled, poured into pentane (150 mL), and washed rapidly twice with water and then brine and the organic layer dried. Solvent removal in vacuo afforded the crude siloxy norcarene compounds: **4b, 5b, 7b,** and **8b.** These materials were somewhat unstable to distillation;[3] however, for comparative rate study, partial purification (>80%) could be effected via rapid (<5 min) silica gel chromatography (20 g) using pentane as eluent giving **4b** (~65%), **5b** (~80%), **7b** (~70%), and **8b** (~65%) in the noted approximate yields. These compounds did not give satisfactory elemental analysis.

(b) Methanolic Aqueous Hydrochloric Acid Hydrolysis. The crude product silyloxy norcanene **4b, 5b, 7b,** and **8b** was dissolved in a solution of methanol (80 mL) and 10% (by volume) aqueous hydrochloric acid (25 mL) then stirred at room temperature for 2.0 h. The mixture was partitioned between ether (300 mL) and water (200 mL) and the ethereal layer was washed once with water and then brine and dried. Chromatography (ethyl acetate/petroleum ether) afforded the described compounds in the noted yields. The principle recovered by-product in all cases was the unreacted (or hydrolyzed) cyclohexenone derivative. See Table I for the physical constants of reported compounds.

From triethylsilyl cyclohexadienyl ether (**4b**) was obtained 7,7-dichloro-3-norcaren-1-ol (**4a**) (59% based on starting trimethylsilyl phenyl ether; 73% mass material balance based on starting phenylsilyl ether).

From trimethylsilyl cyclohexadienyl ether (**5b**) was obtained 2-chloro-2,5-cycloheptadienone (**9**) (73%) and 2-chloro-5-methoxy-2-cycloheptenone (**10**) (8%). A mass balance (total material derived from **5b**) of 89% was obtained.

From trimethylsilyl dimethylcyclohexadienyl ether (**7b**) was obtained 2-chloro-4,5-dimethyl-2,4-cycloheptadienone (**11**) (72%). A mass balance of 88% was obtained.

From trimethylsilyl cyclohexenyl ether (**8b**) was obtained 2-chloro-2-cycloheptenone **12** (62%) (reported for the α-bromo compound 90%;[3] mass balance 77%).

2-Chlorotropone (16). 2-Chlorocycloheptadienone **9** (0.210 g, 1.5 mmol), dichlorodicyanoquinone (0.450 g, 2.0 mmol), and *p*-toluenesulfonic acid (~15 mg) was refluxed in benzene (10 mL) for 6.5 h. The reaction mixture was cooled and the bulk of the solvent removed in vacuo. The residue was then chromatographed [ethyl acetate (30%)/pentane] affording 2-chlorotropone (**16**) (0.165 g, 78%) identical in spectral and physical characteristics with an authentic sample (prepared from α-tropolone and thionyl chloride[12]).

Methyl Chloroenone (17). Lithium dimethylcuprate (1.5 mmol) was generated by methyllithium (1.5 mL of a 2.0 M ethereal solution, 3.0 mmol) addition to a cold (−10 °C) suspension of cuprous iodide (0.288 g, 1.5 mmol) in anhydrous ether (10 mL). The solution was stirred for 10 min then cooled to −40 °C and 2-chlorocycloheptadienone **9** (0.178 g, 1.25 mmol) in ether (3 mL) was added dropwise. After 30 min, the reaction was poured into saturated aqueous ammonium chloride overlayered with pentane. The layers were separated and the organic phase dried. The solvent was removed in vacuo and the residue chromatographed [ethyl acetate (10%)/pentane] affording chloroenone **17** (0.181 g, 91%).

Acknowledgment. The author is grateful for the financial assistance of the Vanderbilt University Natural Sciences Committee and the donors of the Petroleum Research Fund, administered by the American Chemical Society.

Registry No.—**4b,** 67382-63-2; **4c,** 67382-64-3; **5b,** 67382-65-4; **5c,** 54781-19-0; **7b,** 67382-66-5; **7c,** 67382-67-6; **8b,** 67382-68-7; **8c,** 6651-36-1; **12,** 67382-69-8; **16,** 3839-48-3; triethylsilyl phenyl ether, 5888-66-4; tetrachloroethylene, 127-18-4.

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(13) After submission of this manuscript, Torii et al. reported the isolation of dichloronorcaranol **8a** via cold methanolysis of the precursor silyl ether **8b.** Although thermal unstability was not noted, their subsequent employment of this substance required low temperatures (−10 °C): S. Torii, T. Okamoto, and N. Ueno, *J. Chem. Soc., Chem. Commun.*, 293 (1978).

Solvolysis of Virescenol B 19-Tosylate

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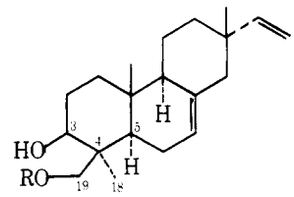
Received March 21, 1978

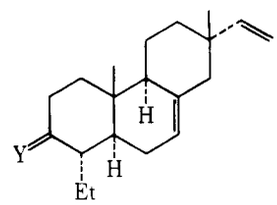
In continuation of a study of the chemistry of virescenol B (**1a**),[1] the aglycon of several of the fungal, virescenoside metabolites,[3] the solvolysis of the 19-tosylate (**1b**)[4] in dimethyl sulfoxide was investigated. It produced two carbonyl-containing substances whose structures are the subject of this note.

One of the products could be shown to be ketone **2a** on the basis of the following facts. Its infrared absorption at 1708 cm^{-1} revealed it to be a cyclohexanone. The disappearance of the oxymethine, oxymethylene, and 4-methyl ^1H NMR signals normally associated with the C(3) and C(4) substitution pattern of the virescenol B skeleton and the exhibition of a methyl triplet (J = 6 Hz) in the ^1H NMR spectrum of the product suggested the latter to be an α-ethyl ketone. Finally,

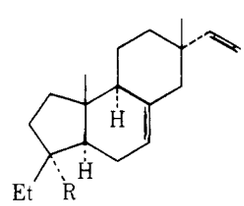


1a, R = H
b, R = Ts

its ^{13}C NMR spectra confirmed the structural changes at C(3) and C(4), showed rings B and C of virescenol B (**1a**)[5] to be affected only minimally, and ring A reminiscent of a 3-keto-steroid.[6] Sodium borohydride reduction of the ketone yielded a ca. 2:1 mixture of alcohols, whose ^1H NMR spectra indicated them to be equatorial and axial isomers, respectively. The low equatorial–axial isomer ratio, in contrast to the high ratio resulting from the hydride reduction of a 3-ketosteroid,[7] was in accord with the presence of a 4α-ethyl-3-keto system whose ethyl group offered resistance to the normal α attack by borohydride. The ^{13}C NMR spectra of the alcohols confirmed fully structures **2b** and **2c** for the reduction products.

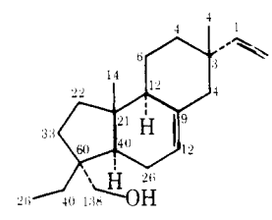


2a, Y = O
b, Y = α-H, β-OH
c, Y = α-OH, β-H

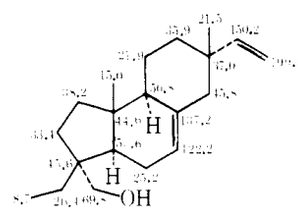


3a, R = CHO
b, R = CH_2OH

The minor product of the solvolysis of **1b** was shown by its infrared absorption bands of 2670 and 1722 cm^{-1} to be an aldehyde and by its ^1H NMR spectrum to have its carboxaldehyde unit in an equatorial orientation[8] next to a nonprotonated carbon center. Once again the structural change at C(3) and C(4) was revealed not only by the new carbonyl group, but also by a methyl triplet (J = 5 Hz) indicative of the presence of an ethyl group. Sodium borohydride reduction of the aldehyde yielded an alcohol whose ^1H NMR spectral characteristics revealed the presence of an equatorial hydroxymethyl group[8,9] next to a nonprotonated carbon and an ethyl group. The ^{13}C NMR spectra of the alcohol exhibited virescenol B-like ring B and C carbon signals and a homoneopentyl carbon signal customary for a methyl group on an ethyl function terminating on a nonprotonated carbon site. A Yb(DPM)$_3$ shift study (cf. $\Delta\delta$ values on formula **4**) permit-



4



5

ted a carbon signal assignment and structure analysis as depicted by formula **5** (**3b**), thus showing the aldehyde to possess structure **3a.**

The simplest explanation for the production of the two carbonyl compounds, **2a** and **3a,** on solvolysis of tosylate **1b** involves the migration of the 4α-methyl group to the site of the departing tosylate group with concommitant O–C(4) bond formation by the neighboring 3β-hydroxy group. Hydride migration from C(3) to C(4) of the resultant conjugate acid of a 3β,4β-epoxide (**6**) leads to an O-protonated 4β-ethyl 3-

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