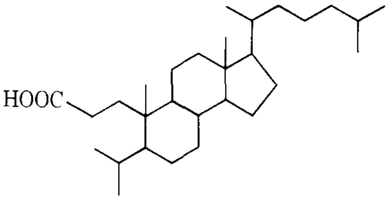
small amount of **9.** These same substances, which were identified by an alternate synthesis,[12] were also obtained by identical photolysis of **1.** Irradiation in the same manner for 12 hr of a solution of **4** in $BrCCl_3$ afforded 63% of **10.** This substance, again identified by synthesis,[13] was obtained in 32% yield by irradiation of **1** in $BrCCl_3$. These results suggest that facile oxidative cleavage[9] of the doxyl moiety was occurring and precluding the desired reaction.



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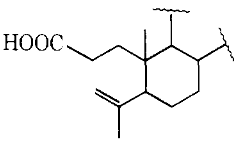

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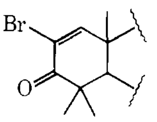

10

When **4** was simply photolyzed in the same manner in benzene solution under nitrogen, the following, more interesting, mixture of products was obtained:[14] 4% **4,** 34% hydroxylamine **11** (ir (film) 3500 cm^{-1}, readily oxidized to **4** by air or Ag_2O), 21% of oxazolidine **2,**[15] 10% of as yet unidentified material,[16] and **6** and **7,** in 17 and 8% yield, respectively.

The substance assigned structure **6** had mp 149-50°: M^+ (*m/e*) 513.4182 (calcd 513.4181); ir (KBr) 1765 cm^{-1};[17] nmr (PhH-d_6) δ 1.35 ppm (s, 3, $>C(CH_3)C{=}O$). Upon treatment with $HCl-H_2O-CH_3OH$ at reflux for 10 hr it afforded 4α-methylcholestan-3-one, thus proving beyond reasonable doubt that functionalization at a C-4 methyl group had occurred and in a manner conducive to oxidative demethylation in the laboratory. Proof that it was the 4β-methyl group which had been oxidized was obtained from the conversions shown in Scheme I, which led to previously prepared compounds of known stereochemistry.[1]

The substance assigned structure **7** had mp 201-202°: M^+ (*m/e*) 515.4335 (calcd 515.4338); ir (KBr) 3180 cm^{-1}; nmr ($CDCl_3$) δ 5.20 ppm (s, 1, $-CH(OH)OR$). Its structure was also confirmed by the chemistry displayed in Scheme I. The configuration of the hemiacetal hydroxyl group was assigned on the basis of examination of molecular models, which show severe nonbonded interaction between the angular methyl and that hydroxyl group when it has the opposite configuration.

No products involving C-4α methyl functionalization were found, despite the fact that the nitroxide oxygen can "reach" the hydrogens of both the 4α and 4β methyl groups in **4** if ring A has a chair conformation. Very likely the absence of such products is related to a conformational distortion of ring A which decreases the 1,3-diaxial methyl interaction in **4** but also moves the nitroxide moiety away from the 4α methyl.

Ideally, photolysis of the isomeric doxyl **5** would have yielded the stereoisomer of **6** with the 4α methyl group functionalized, thus permitting selective functionalization of either methyl group and providing a simulation of the enzymic demethylation sequence, in which the 4α methyl group is initially oxidized.[1-3] However, irradiation of **5** has to date yielded only a substance (39%), mp 78-82°, M^+ (*m/e*) 499.4384 (calcd 499.4389), tentatively assigned structure **12,** resulting from abstraction of the tertiary hydrogen from the 5α position.

Efforts are being made to improve the efficiency of the novel remote functionalization reaction leading to **6** and **7** by attempting to provide an alternate to **4** as the (apparent) source of incorporated oxygen and by studying the photochemical process involved.

Acknowledgment. This research was generously supported by National Institutes of Health Research Grant AM 12855. S. C. was a National Science Foundation Undergraduate Research Participant, summer, 1972. The authors thank Professor D. M. Lemal for permitting us extensive use of photochemical apparatus.

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(11) The conclusion that **5** but not **4** has a "W" is based on examination of Dreiding models using either planar or pyramidal nitrogen and with the steroid ring A in a normal or moderately distorted chair conformation.
(12) Baeyer-Villiger oxidation of **1** followed by treatment with H_2SO_4-HOAc according to J. S. E. Holker, W. R. Jones, and P. J. Ramm (*J. Chem. Soc. C*, 357 (1969)) produces **9,** which was reduced with H_2-Pd-C to **8.**
(13) Treatment of **1** sequentially with Br_2-HOAc, $CaCO_3$-DMA, and Br_2-CH_2Cl_2 afforded **10.**
(14) Exactly the same mixture of products is obtained whether the benzene is carefully degassed or not. Preliminary experiments using a Corning CS-3-73 filter (cutoff *ca.* 400 nm) suggest that the photochemistry is caused by excitation of the weak, long wavelength absorption of **4** ($\lambda_{max}^{Et_2O}$ 460 nm, ϵ = 6). The time required for completion of the photolysis of **4** can be reduced to 12 hr if the lamp is placed as close as possible to the reaction vessel and both are wrapped in Al foil. Under such conditions the reaction mixture refluxes, but this has no effect on the product distribution.
(15) Reference 5 provides a mechanistic scheme applicable to the formation of **2.**
(16) This material has the greatest tlc mobility of any of the products, has ir (film) 3500 cm^{-1}, and gives an unknown nitroxide on standing in air. Presumably therefore, it contains hydroxylamine other than **11.**
(17) H. A. Whaley, *J. Amer. Chem. Soc.*, **93,** 3767 (1971), reports an *O*-acylhydroxylamine with $\nu_{C=O}$ (Nujol) 1760 cm^{-1}.

James A. Nelson, Sunwen Chou, Thomas A. Spencer*
Department of Chemistry, Dartmouth College
Hanover, New Hampshire 03755

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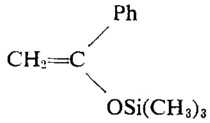
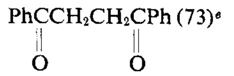
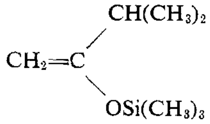
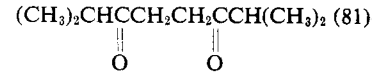
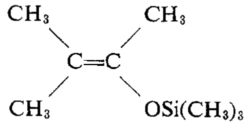
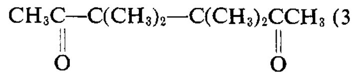
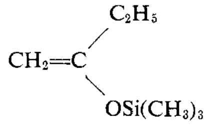
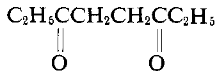
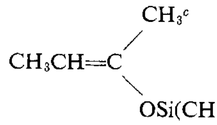
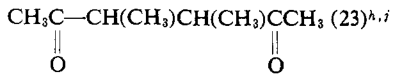
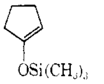
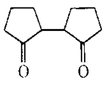
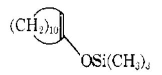
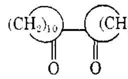
Synthesis of 1,4-Diketones by the Reaction of Silyl Enol Ether with Ag_2O. A Regiospecific Formation of Silver(I) Enolate Intermediates

Sir:

Synthetic utility of silyl enol ethers (**1**),[1] from which lithium enolates are regiospecifically produced using methyllithium, has been demonstrated in annelation reactions.[2] Herein, we wish to report the synthesis of 1,4-diketones by the reaction of silyl enol ethers with Ag_2O in dimethyl sulf-

Table I. Synthesis of 1,4-Diketones by the Reaction of Silyl Enol Ether with Ag_2O

Silyl enol ether		Reaction conditions[a,b]	1,4-Diketone[c] (Yield, %)[d]
	**1a**	65°, 2 hr	 $\mathrm{Ph}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH_2CH_2}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{Ph}$ (73)[e] **3a**
	**1b**	65°, 2 hr	 $\mathrm{(CH_3)_2CH}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH_2CH_2}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH(CH_3)_2}$ (81)[f] **3b**
	**1c**	100°, 5 hr	 $\mathrm{CH_3}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{{-}C(CH_3)_2{-}C(CH_3)_2}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH_3}$ (38)[f] **3c**
	**1d**	65°, 2 hr	 $\mathrm{C_2H_5}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH_2CH_2}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{C_2H_5}$ (76)[g] **3d**
	**1e**	80°, 3 hr	 $\mathrm{CH_3}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{{-}CH(CH_3)CH(CH_3)}\underset{\underset{\mathrm{O}}{\Vert}}{\mathrm{C}}\mathrm{CH_3}$ (23)[h,i] **3e**
	**1f**	100°, 2 hr	 3f (61)[i,j]
	**1g**	85°, 3 hr	 3g (45)[f,j]

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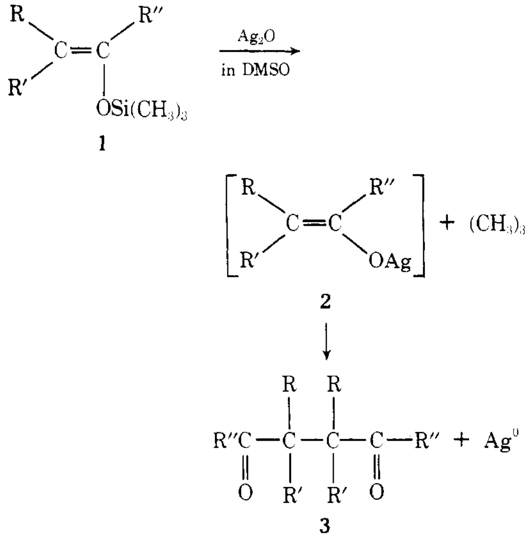
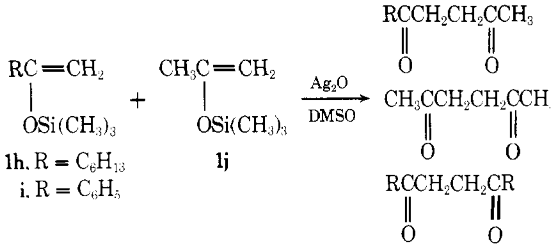
[a] No attempts have been made to optimalize the reaction conditions. [b] DMSO was used as solvent. [c] All products showed satisfactory analytical data and were identified by comparison of the ir and nmr spectra with those of the authentic samples. [d] Isolated yield based on the starting silyl enol ether. [e] Reference 4. [f] Reference 3. [g] Reference 5. [h] Reference 6. [i] Reference 7. [j] *dl*-meso mixture. [k] Cis-trans mixture.

oxide (DMSO), in which silver(I) enolates (**2**) generated regiospecifically are assumed to be a reactive intermediate. An important feature of the new reaction is regiospecific formation of 1,4-diketone according to the following equation.



A typical experimental procedure is illustrated by the reaction of a trimethylsilyl enol ether **1b** with Ag_2O in DMSO leading to the formation of 2,7-dimethyl-3,6-octanedione in high yield with regiospecificity. A heterogeneous mixture of 1.58 g (10 mmol) of a trimethylsilyl enol ether **1b**, 2.32 g (10 mmol) of Ag_2O, and 6 ml of DMSO was heated at 65° with stirring. As the reaction proceeded, metallic silver precipitated, and the formation of hexamethyldisiloxane was confirmed by glpc analysis of the reaction mixture. After 2 hr, ether was added to the reaction mixture, and the precipitated metallic silver was removed by filtration. The filtrate was washed with brine, dried, and evaporated to yield 2,7-dimethyl-3,6-octanedione (81% yield) uncontaminated with its isomers as judged by glpc. The structure was established by elemental analysis and spectral data.[3] This coupling reaction was very much influenced by the solvent. Similar results were obtained in aprotic polar solvents such as hexamethylphosphoric triamide, dimethylformamide, and acetonitrile. However, no reaction occurred in toluene and diglyme. Some representative results are summarized in Table I. As evident in Table I, the less substituted enol silyl ethers (**1a**, **1b**, and **1d**) are reactive toward Ag_2O and furnish regiospecific 1,4-diketones (**3a**, **3b**, and **3d**) in good yields. On the other hand, the more substituted enol silyl ethers (**1c** and **1e**) are less reactive toward Ag_2O and afford 1,4-diketones (**3c** and **3e**) in low yields,[8] but without loss of regiospecificity. These findings render the present reaction very useful in the preparation of symmetrical 1,4-diketones. So far, the selective couplings of unsymmetrical ketones, especially, at the less substituted α-position have been done with much difficulty; *e.g.*, the radical-induced dimerization[3,9] of unsymmetrical ketones produces mainly the most crowded 1,4-diketone, and the reductive coupling[3] of unsymmetrical α,α′-dibromo ketones with zinc–copper couple produces a mixture of all possible isomers of 1,4-diketones.

The present method is successfully applicable to some cross couplings leading to unsymmetrical 1,4-diketones, as exemplified by the synthesis of undecan-2,5-dione, a precursor of dihydrojasmone. Treatment of a mixture of trimethylsilyl enol ether **1h** and a threefold exess of trimethylsilyl enol ether **1j** with Ag_2O in dimethyl sulfoxide afforded undecan-2,5-dione (80% isolated yield based upon the starting **1h**) with hexan-2,5-dione and hexadecan-7,10-dione (yield <5%). Similarly, cross coupling of **1i** and **1j** gave 1-phenylpentan-1,4-dione in 60% isolated yield.



A detailed understanding of the reaction mechanism must await further mechanistic study. Now, we would like to propose an intermediate of silver(I) enolate (**2**) generated regiospecifically from silyl enol ether and Ag_2O, whose oxidative coupling may lead to the formation of 1,4-diketone. Oxidative couplings of organosilver[10] and organocopper compounds[11] are well known. We are currently exploring the full scope of the utility of silver(I) enolate in synthesis.

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(8) About 40–50% of (**1c** + its original ketone) and (**1e** + its original ketone) were recovered in the coupling reaction of **1c** and **1e**, respectively, under the conditions indicated in Table I.

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Yoshihiko Ito, Toshiro Konoike, Takeo Saegusa*
Department of Synthetic Chemistry, Faculty of Engineering
Kyoto University, Kyoto 606, Japan
Received October 7, 1974

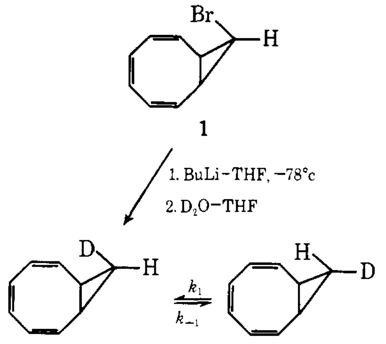
Epimerization of Bicyclo[6.1.0]nonatriene

Sir:

Since the initial observation of the thermal rearrangement of bicyclo[6.1.0]nonatriene by Vogel[1] in 1961, much effort has been directed toward unraveling the complex mechanistic details of the thermal isomerizations of bicyclo[6.1.0]nonatriene systems.[2] Epimerizations at C_9 have recently been observed for *syn*-9-carbomethoxy,[3] -cyano,[4] -fluoro,[5] and -methoxy[5] substituted systems, for which two different mechanisms have been proposed.[3,5] Since anti-9-substituted systems in general undergo skeletal rearrangements more rapidly than the corresponding syn-9-substituted systems, isomerizations of 9-syn systems may proceed *via* epimerization through 9-anti systems. Such an isomerization *via* the 9-anti epimer has been clearly demonstrated for *syn*-9-cyanobicyclo[6.1.0]nonatriene[4] and most likely occurs in other syn-9-substituted systems[3,5] but is an unsettled question for *syn*-9-methylbicyclo[6.1.0]nonatriene.[3,6]

We wish to report the stereospecific synthesis of bicyclo[6.1.0]nonatriene-*syn-9-d* and an investigation of its facile epimerization. This study clearly reveals the mechanism of epimerization of the unsubstituted bicyclo[6.1.0]nonatriene and suggests an alternative mechanism to those previously proposed for epimerization of syn-9 substitued systems.[3,5]

syn-9-Bromobicyclo[6.1.0]nonatriene (**1**) was prepared in a method similar to procedures used by Katz.[7a] A tetrahydrofuran (THF) solution of potassium cyclooctateaenide was added slowly to a stirred solution of bromoform in THF at −20°. Fractional distillation of the resulting mixture of products afforded a *ca.* 15% yield of **1** (32° (10^{-4} Torr)).[7] The syn bromide **1** was metalated with butyl lithium in THF at −78° and quenched with a D_2O–THF solution. Distillation at 0° gave in *ca.* 90% yield bicyclo[6.1.0]nonatriene-*syn-9-d* (*syn-d-***2**).[8] On warming to 30°, *syn-d-***2** epimerizes to *anti-d-***2** and after several hours an equilibrium mixture of 50% *syn-d-***2** and 50% *anti-d-***2** is obtained with neglible skeletal rearrangement to 8,9-dihydroindenes.[1,2]



*syn-d-***2** *anti-d-***2**

$k_1 = k_{-1} = 4.5 \times 10^{-5}\ sec^{-1}$

31°, CD_3CN

The rate of epimerization was determined by quenching at 15-min intervals and monitoring the pmr signal integrals at −25°. Treating the epimerization as a simple reversible first-order case ($k_1 = k_{-1}$), k_1 was determined as $(4.5 \pm 0.2) \times 10^{-5}\ sec^{-1}$ at 31.3° in CD_3CN ($\Delta G^* = 23.9$ kcal/mol) and $(4.7 \pm 0.2) \times 10^{-5}\ sec^{-1}$ at 35° in $CDCl_3$ ($\Delta G^* = 24.1$ kcal/mol).

When these data are combined with data recently reported by Boche, Weber, and Benz,[9] the mechanism of epimerization becomes obvious. Boche has presented strong evidence that the reaction of TCNE with **2** to yield adduct **3** occurs through formation and trapping of (*ZEZZ*)-cyclononatetraene **4** as an intermediate. At high concentrations of TCNE in CH_3CN, the rate of formation of **4** becomes rate limiting, the first-order rate constant for its formation being *ca.* $9 \times 10^{-5}\ sec^{-1}$ at 31.3°. Presuming **4** to be the intermediate responsible for epimerization of **2**, the rate of formation of **4** should be twice the rate of epimerization of