a heavy-handed six-parameter combined reaction coordinate which can be termed the "percent completion" (Figure 2). It is seen that changing the dihedral angles and the C-C̈-C angle by 5% of their total changes in going from **1** to **2** (followed by reoptimizing the bond lengths and remaining angles) results in an immediate slight decrease in energy. Further changes (followed by reoptimization of the remaining variables) give a smooth decrease in energy until the allene **2** is reached. The same curve is generated if the optimized geometry of **2** is the starting point and the six parameters are changed until **1** is reached. While Figure 2 does not represent the MERP for **1** → **2** conversion, the actual MERP must be at least this favorable. Thus, according to MNDO, there is no barrier separating these structures, making **1** inaccessible to chemical interception. In this view, **1** could be very close to the transition state for the racemization of **2** and its enantiomer.[16]

It should be now recognized that the "aromatic" $\pi$ electron delocalization does not provide overriding stability for singlet **1**. This is, of course, because $\pi$ delocalization results in charge separation. In fact, MNDO calculations for triplet **1** (using the half-electron method) indicate the planar **1** is probably a ground-state triplet ($\Delta H_f$ = 97.4 kcal/mol).[17] The singlet allene **2** can successfully account for all of the chemistry previously ascribed to singlet **1**. The rearrangement chemistry can be attributed to singlet **2**.[11] If singlet **2** is considered as a conjugated tetraene whose termini share the same carbon ($C_2$), [${}_\pi 2_s + {}_\pi 8_s$] cycloadditions giving cyclopropane products can be envisaged. Finally, nucleophilicity is also a property of strained allenes.[18]

While any semiempirical calculation can not be considered the final answer to any chemical system, this work shows the importance of considering nonplanar structures when considering the geometries and properties of carbocyclic, completely conjugated carbenes. The results of MNDO calculations for cyclopropenylidene, cyclopentadienylidene, and cyclononatetraenylidene in their planar and nonplanar forms will be reported at a later time.

**Note Added in Proof:** The calculation of the MNDO-based vibrational force constant matrix and normal modes for **1** ("optimized" in a planar configuration but released from $C_{2v}$ symmetry; $\Delta H_f$ still is 114.4 kcal/mol) has now been accomplished. The vibrational force constant matrix shows a *single negative eigenvalue* corresponding to a "frequency" of 428 $cm^{-1}$. Inspection of the normal mode vectors for this "vibration" shows the precise atomic movement necessary to convert **1** into **2**. Thus, according to MNDO, **1** is a transition state. We thank Professor M. J. S. Dewar for making this program available and Mr. J. Ritchey for discussions on its use.

**Acknowledgment** is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. The assistance of Professor R. J. Field and the University of Montana Computer Center in installing the MNDO program is greatly appreciated. Stimulating discussions with Professors W. M. Jones and J. D. Scott and Dr. J. O. Jarvie have been especially helpful and enjoyable.

(15) Assuming the presence of a $C_2$ axis of symmetry in **1** and **2** and using the numbering convention of **2**, specifying the $C_1$-$C_2$-$C_3$-$C_4$, $C_2$-$C_3$-$C_4$-$C_5$, $H_3$-$C_3$-$C_2$-$C_1$, $H_4$-$C_4$-$C_3$-$C_2$, and the $H_5$-$C_5$-$C_4$-$C_3$ dihedral angles will uniquely describe the planarity or nonplanarity of **1** and **2**.

(16) (a) The location of transition states on a multidimensional energy surface can be a difficult and time consuming process.[14] McIver has shown that symmetrical transition states are unlikely (McIver, J. W., Jr. *Acc. Chem. Res.* **1974**, *7*, 72-77). A slight distortion of **1** could accommodate this point. (b) The structure **1** can only be energetically optimized if constrained to planarity.

(17) (a) The $C_7$-$\bar{C}_1$-$C_2$ angle for triplet **1** is 145.6°. The $C_1$-$C_2$, $C_2$-$C_3$, $C_3$-$C_4$, and $C_4$-$C_5$ bond lengths are 1.356, 1.435, 1.374, and 1.450 Å, respectively. The $C_1$-$C_2$-$C_3$, $C_2$-$C_3$-$C_4$, $C_3$-$C_4$-$C_5$, $H_2$-$C_2$-$C_1$, $H_3$-$C_3$-$C_2$, and $H_4$-$C_4$-$C_3$ bond angles are 120.3, 126.2, 130.6, 120.3, 115.9, and 116.3°, respectively. (b) Geometric optimization of nonplanar triplet **2** (starting with the singlet **2** geometry) resulted in an essentially planar structure, whose dihedral angles differed from planarity by no more than 0.17°. This structure ($\Delta H_f$ = 97.4 kcal/mol) was essentially the same as the triplet **1**. Although the energy surface was not completely searched, triplet **2** may not be an energy minimum.

(18) Waali, E. E.; Wenslaff, J. B.; Rehrauer, L. F. American Chemical Society-Chemical Society of Japan Chemical Congress, Honolulu, April 1979.

## Minor and Trace Sterols in Marine Invertebrates. 23.[1] Xestospongesterol and Isoxestospongesterol—First Examples of Quadruple Biomethylation of the Sterol Side Chain

Lian Niang Li[2] and Carl Djerassi*

*Department of Chemistry, Stanford University*
*Stanford, California 94305*

*Received February 27, 1981*

The most characteristic difference between terrestrial and marine sterols resides in the side chain. The former contain side chains ranging from $C_8$ (e.g., cholesterol) to $C_{10}$ (e.g., sitosterol), while numerous marine sterols with $C_{11}$ side chains have recently been isolated[3]—i.e., products of *triple* biomethylation of an unsaturated precursor.[4] Indeed, recent work suggests that sterols resulting from a hitherto unprecedented *quadruple* biomethylation sequence may also exist in nature: GC–MS analysis of the trimethylsilylated sterol fraction of a tunicate[5] and a sponge[6] suggested the presence of trace quantities of unknown sterols with $C_{12}$ side chains. We report now the isolation, structure elucidation, and synthesis of the first two members of this new class of biosynthetically intriguing marine sterols from two sponges, which are rich in sterols with $C_{11}$ side chains.

Our first choice was a Caribbean *Xestospongia* species, which has been shown[7] to contain predominantly (71%) the $C_{30}$ sterol xestosterol (**1**) with a novel $C_{11}$ side chain. Capillary GC analysis[8] indicated the presence of a trace sterol (0.01% of total sterols) with relative retention time 2.38 (cholesterol 1.00) which was separated (absolute MeOH) by reverse-phase HPLC (Whatman Partisil M9 10/50 ODS-2) to afford another new sterol, xestospongesterol, of $M^+$ = 440.4013 ($C_{31}H_{52}O$). Assignment of structure **2** was based initially on mass spectrometric and proton NMR spectral analysis. Thus, its mass spectrum displayed the typical peaks[9] ($m/z$ 213, 231, 253, 271) of a $\Delta^5$-3$\beta$-hydroxy sterol nucleus (N), while its two most intense ions were of mass 328 and 111. The former has been shown[10] to be typical (McLafferty rearrangement) of $\Delta^{25}$-unsaturated sterol side chains, but such sterols also display[10] an intense $m/z$ 314 peak (associated with electron-impact-induced rearrangement to a $\Delta^{24}$ isomer, which then undergoes its own diagnostic McLafferty rearrangement). The virtual absence of such an $m/z$ 314 peak in the xestospongesterol (**2**) spectrum suggested the presence of a quaternary center at C-24, blocking rearrangement of the $\Delta^{25}$ double bond. The base peak at $m/z$ 111 is then clearly due to fission at the highly labilized allylic C-24 quaternary center (see wavy line in **2**). Given this mass spectral interpretation and the presence of vinylic methyl and ethyl functions as deduced from the 360-MHz proton NMR spectrum (Table I), one could readily assign the biosynthetically unusual structure **2** (except for double-bond stereochemistry) to xestospongesterol.

Our second choice was the Indopacific sponge *Strongylophora*

(1) For preceding paper, see E. Kho, D. K. Imagawa, M. Rohmer, Y. Kashman, and C. Djerassi, *J. Org. Chem.*, in press.

(2) Visiting investigator from the Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing, China.

(3) C. Djerassi, N. Theobald, W. C. M. C. Kokke, C. S. Pak, and R. M. K. Carlson, *Pure Appl. Chem.*, **51**, 1815-1828 (1979); C. Djerassi, *ibid.*, in press.

(4) For reviews of biosynthesis of sterol side chain, see L. J. Goad, *Mar. Nat. Prod.: Chem. Biol. Perspect.*, **28**, 75-172 (1978); E. Lederer, *Quart. Rev., Chem. Soc.*, **23**, 453-481 (1969).

(5) J. A. Ballantine, A. Lavis, J. C. Roberts, and R. J. Morris, *J. Exp. Mar. Biol. Ecol.*, **30**, 29-44 (1977).

(6) P. R. Bergquist, W. Hofheinz, and G. Oesterhelt, *Biochem. Syst. Ecol.*, in press.

(7) W. C. M. C. Kokke, C. Tarchini, D. B. Stierle, and C. Djerassi, *J. Org. Chem.*, **44**, 3385-3388 (1979).

(8) Carlo Erba Fractovap model 4160, carrier gas hydrogen, oven temperature 270 °C, capillary column 15 m (0.3-mm i.d.) packed with Se-52.

(9) S. G. Wyllie, B. A. Amos, and L. Tökes, *J. Org. Chem.*, **42**, 725-731 (1977).

(10) C. Djerassi, *Pure Appl. Chem.*, **50**, 171-184 (1978); I. J. Massey and C. Djerassi, *J. Org. Chem.*, **44**, 2448-2456 (1979).

0002-7863/81/1503-3606$01.25/0 

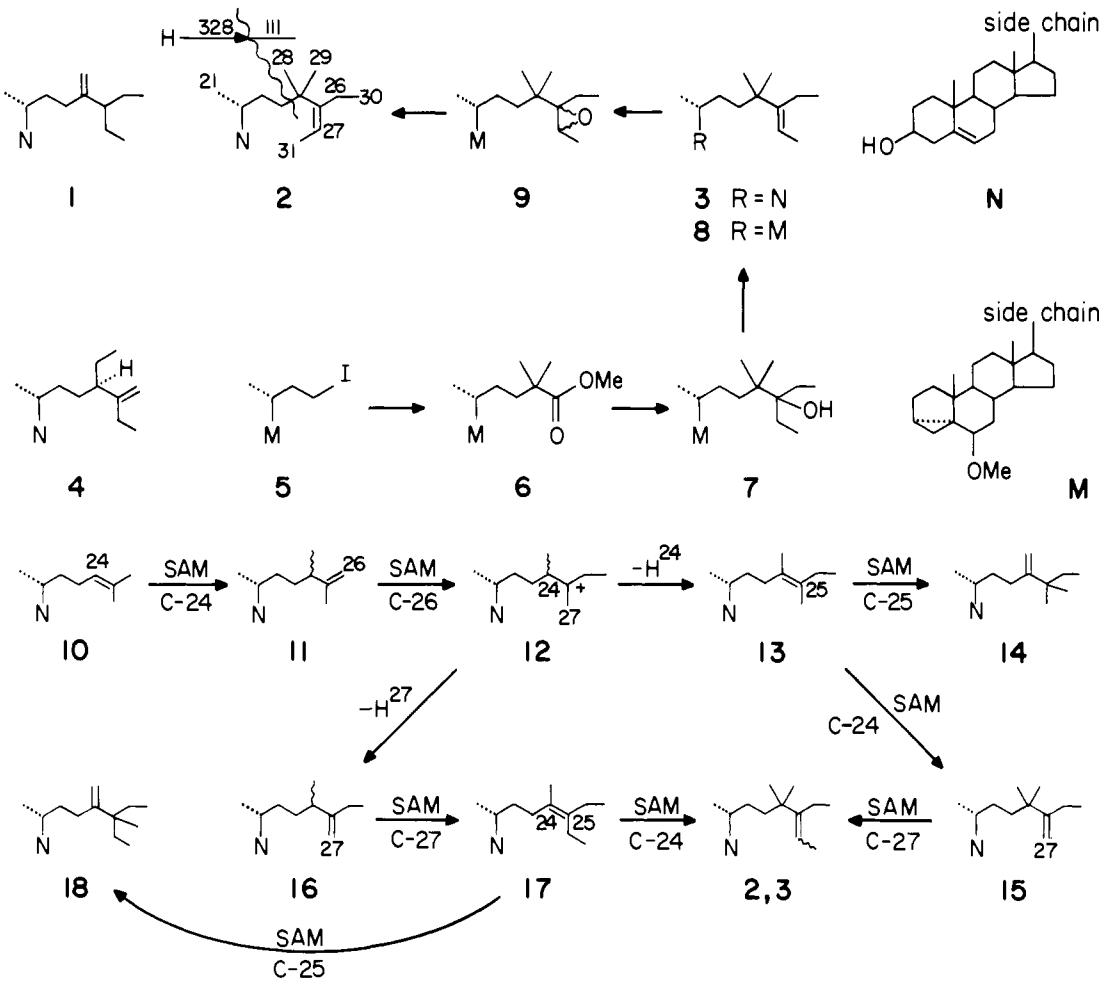



Table I. Selected $^1$H NMR Chemical Shifts ($C_6D_6$) of Xestospongesterol (2) and Isoxestospongesterol (3)

| | chemical shift, ppm | | | |
|---|---|---|---|---|
| | xestospongesterol (2) | | isoxestospongesterol (3) | |
| group | natural | synthetic | natural | synthetic |
| C-18 Me | 0.670 | 0.670 | 0.667 | 0.668 |
| C-19 Me | 0.945 | 0.945 | 0.944 | 0.945 |
| C-21 Me | 1.021 (d, $J$ = 6.4[a]) | 1.021 (d, $J$ = 6.5) | 1.009 (d, $J$ = 6.49) | 1.009 (d, $J$ = 6.44) |
| C-28 Me | 1.204 | 1.204 | 1.084 | 1.083 |
| C-29 Me | 1.204 | 1.204 | 1.084 | 1.083 |
| C-30 Me | 1.056 (t, $J$ = 7.4)[b] | 1.056 (t, $J$ = 7.4) | 1.049 (t, $J$ = 7.4) | 1.049 (t, $J$ = 7.7) |
| C-31 Me | 1.776 (d, $J$ = 7.4)[c] | 1.776 (d, $J$ = 7.305) | 1.633 (d, $J$ = 6.8) | 1.633 (d, $J$ = 6.8) |
| C-27 H | 5.319 (q, $J$ = 7.2) | 5.32 (q, $J$ = 7.4) | 5.339 (q, $J$ = 6.7) | 5.34 (q, $J$ = 6.7) |

[a] $J$ is in Hz. [b] Collapsed to singlet upon irradiation of 2.02-ppm quartet (allylic C-26 protons). [c] Coupled to C-27 proton.

*durissima*, which has been reported[11] to contain over 90% of a single $C_{30}$ sterol, strongylosterol (4), whose sterol mixture was subjected to the same type of capillary GC and reverse-phase HPLC analysis as described above to yield a new trace (0.6%) sterol ($M^+$ = 440), which we have named isoxestospongesterol. Its mass spectrum was indistinguishable from that of xestospongesterol (2), but its GC mobility[8] was slightly different (relative retention time 2.31 vs. 2.38 for 2). Its proton NMR spectrum (Table I) was very similar to that of xestospongesterol (2) except for the high field shifts of the signals associated with the C-31 vinyl methyl substituent and the two quaternary methyl groups (28 and 29) attached to C-24. We conclude, therefore, that isoxestospongesterol is the 25*E* isomer (3) of xestospongesterol (2) (25*Z*).[12]

In order to verify these structural assignments, both isomers were synthesized by the following unambiguous route. 3$\alpha$, 5-Cyclo-6$\beta$-methoxy-23-iodonorcholane (5)[13] was coupled in THF with the enolate produced from methyl isobutyrate and lithium diisopropylamine[14] to yield the ester 6 ($M^+$ = 444, NMR consistent with structure), which was subjected to Grignard reaction with ethylmagnesium bromide, dehydration (thionyl chloride–pyridine) of the resulting tertiary alcohol 7 and removal of the i-methyl ether protecting group (*p*-TsOH, dioxane) of 8 to provide isoxestospongesterol (3), mp 117–118 °C, $[\alpha]^{28}_D$ −34.2° (*c* 0.11,

(11) M. Bortolotto, J. C. Braekman, D. Daloze, and B. Tursch, *Bull. Soc. Chim. Belg.*, **87**, 539–543 (1978). For stereochemistry, see N. Theobald and C. Djerassi, *Tetrahedron Lett.*, 4369–4372 (1978). We are indebted to Dr. J. C. Braekman for providing the sponge.

(12) The assignment of the $\Delta^{25}$-double-bond stereochemistry is based on the $^{13}$C (Table II) NMR measurements. cf. E. Breitmaier and W. Voelter, "C NMR Spectroscopy", H. F. Ebel, Ed., Verlag Chemie, Weinheim Bergstr., Germany, 1978, p 137.

(13) N. Theobald, R. J. Wells, and C. Djerassi, *J. Am. Chem. Soc.*, **100**, 7677–7684 (1978).

(14) We are indebted to Dr. S. F. Lee (Zoecon Corp.) for experimental details.

Table II. $^{13}C$ NMR Chemical Shifts ($CDCl_3$) of Side Chain and Angular Methyl Carbons

| carbon | chemical shift, ppm: xestospongesterol (2) | chemical shift, ppm: isoxestospongesterol (3) |
|---|---|---|
| C-18 | 11.84 | 11.83 |
| C-19 | 19.40 | 19.40 |
| C-20 | 36.34 | 36.20 |
| C-21 | 18.89 | 18.89 |
| C-22[b] | 30.88 | 30.61 |
| C-23[b] | 38.78 | 37.29 |
| C-24 | 39.18 | 39.48 |
| C-25 | 146.96 | 148.15 |
| C-26[b] | 28.62 | 20.22 |
| C-27 | 118.37 | 116.96 |
| C-28[a] | 28.94 | 27.68 |
| C-29[a] | 28.68 | 27.20 |
| C-30 | 15.06 | 14.37 |
| C-31[a] | 15.63 | 13.60 |

[a] Assignment proved by selective decoupling. [b] These assignments were confirmed by comparing the observed chemical shifts with those calculated by the procedures described by Kelecom [A. Kelecom, *Bull. Soc. Chim. Belg.*, 89, 343-352 (1980)].

$CHCl_3$), which was shown to be identical with the natural material (cf. Table I).

Isomerization of the double bond was achieved by the procedure of Dervan and Shippey[15] through conversion (*m*-chloroperbenzoic acid, $CH_2Cl_2$, 0 °C, 24 h) of isoxestospongesterol i-methyl ether (**8**) to the epoxide **9** ($M^+$ = 470; NMR consistent with structure) and exposure (100 °C, 2 h) to excess hexamethyldisilane and potassium methoxide in hexamethylphosphoramide, followed by removal of the i-methyl ether protecting group. The resulting xestospongesterol (**2**), mp 133-134 °C, $[\alpha]^{28}_D$ -46.6° (*c* 0.07, $CHCl_3$) was identical in all respects (cf. Table I) with the natural sponge sterol.

The two most plausible biosynthetic paths involve well-documented[4] processes: one-step SAM [(*S*)-adenosylmethionine] biomethylation of a double bond (e.g., **10**, **11**, **13**, **15-17**) and proton elimination from a carbon adjacent to the resulting carbonium ion (e.g., **12** → **13** or **16**). The key precursor is either codisterol or 24-epicodisterol (**11**), both of them naturally occurring[16,17] and easily derivable[4] by SAM biomethylation of desmosterol (**10**). A second SAM biomethylation of C-26 would provide the carbonium ion **12**, which through proton loss from either C-24 (**12** → **13**) or C-27 (**12** → **16**) can initiate two further, alternative biomethylation processes. Indirect evidence for either scheme to (iso)xestospongesterol (**2**, **3**) is provided by our recent isolation of the postulated biosynthetic intermediates **15**[18] and **16**.[17] While the highly alkylated desmosterol (**10**) analogues **13** and **17** have not yet been encountered in nature, their intermediacy seems highly likely, since we have not only found in marine sponges the products of SAM biomethylation at C-24 (i.e., **17** → **2** or **3**; **13** → **15**) but also the products **14**[19] and **18**[20] arising from SAM attack at C-25. In summary, the continuing isolation of highly branched marine sterols has no terrestrial counterpart and most likely is associated with a special biological function[21] in these marine organisms. However, as the various "missing links" are isolated and identified, their biosynthesis fits beautifully into the currently accepted[4] scheme of sequential single-step biomethylations of olefinic precursors.

(15) P. B. Dervan and M. A. Shippey, *J. Am. Chem. Soc.*, **98**, 1265-1267 (1976).
(16) I. Rubinstein and L. J. Goad, *Phytochemistry*, **13**, 481-484 (1974).
(17) W. C. M. C. Kokke, C. S. Pak, W. Fenical, and C. Djerassi, *Helv. Chim. Acta*, **62**, 1310-1318 (1979).
(18) L. N. Li and C. Djerassi, to be published.
(19) L. N. Li, U. Sjöstrand, and C. Djerassi, *J. Am. Chem. Soc.*, **103**, 115-119 (1981).
(20) L. N. Li, U. Sjöstrand, and C. Djerassi, to be published.
(21) R. M. K. Carlson, C. Tarchini, and C. Djerassi in "*Frontiers of Bioorganic Chemistry and Molecular Biology*", S. N. Anachenko, Ed., Pergamon, Oxford, 1980, pp 211-224.

**Acknowledgment.** Financial support was provided by NIH Grants GM-06840 and GM-28352. We thank Annemarie Wegmann, Sakiko Hirano, and Pierre Tecon for mass spectral measurements, Dr. J. N. Shoolery (Varian Associates, Palo Alto, CA) for $^{13}C$ measurements and assignments, and Dr. Lois Durham for the 360-MHz NMR spectra, which were obtained at the Stanford NMR facility funded by NIH Grant RR-0711 and NSF Grant GP-23622. We thank Dr. Karl Heusler (Ciba-Geigy Ltd., Basel) for a generous gift of methyl 3β-acetoxychol-5-enate.

## Silver(I) Photocatalyzed Addition of Acetonitrile to Norbornene

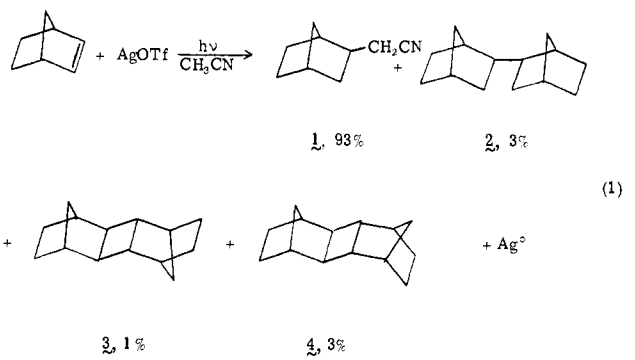
Joseph W. Bruno, Tobin J. Marks,* and Frederick D. Lewis*

*Department of Chemistry, Northwestern University Evanston, Illinois 60201*

*Received February 2, 1981*

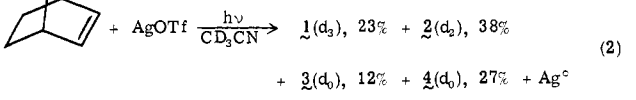
We have recently reported that the cationic polymerization of cyclic ethers can be photoinitiated with metal ions such as Ag(I) and Cu(I).[1] The metal ion serves as a one-electron oxidant upon ligand-to-metal charge-transfer excitation and ultimately forms a metallic precipitate, thus rendering electron transfer irreversible. The contrasting failure of strong organic electron acceptors to effect charge-transfer photoinitiated polymerization of cyclic ethers presumably is due to rapid back electron transfer from the acceptor anion radical to a cationic species.[2] We have now extended our investigations to the photochemical behavior of Ag(I)-alkene complexes and here report the efficient conversion of norbornene to *exo*-2-(cyanomethyl)bicyclo[2.2.1]heptane (**1**) upon irradiation of the Ag(I)-norbornene complex in acetonitrile solution. The novel mechanism of this reaction involves ligand-to-metal charge-transfer photoinitiation and, ultimately, free radical chain addition of the cyanomethyl radical to norbornene.

Irradiation of an acetonitrile solution of norbornene (0.25 M) and silver trifluoromethanesulfonate (AgOTf, 0.002-0.02 M) with a medium pressure mercury lamp in a Vycor lamp well results in the formation of **1**, minor amounts of the norbornene dimers **2-4**, and a silver mirror (eq 1).[3] Conversions of norbornene to




(1)

**1** in preparative scale reactions were typically 35-40%, even when the initial norbornene-Ag(I) ratio was 15:1. Irradiation in acetonitrile-$d_3$ yields the same norbornene-containing products, albeit in greatly different relative yields (eq 2). Mass spectral analysis




(2)

(1) (a) Woodhouse, M. E.; Lewis, F. D.; Marks, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 996. (b) Submitted for publication.
(2) Achiba, Y.; Kimura, K. *Chem. Phys. Lett.* **1976**, *39*, 515.
(3) Spectroscopic properties of **1-4** were identical with those of independently synthesized samples.

0002-7863/81/1503-3608$01.25/0 