concentrated at reduced pressure. The residual solid was extracted with acetone. The extract was concentrated to give 6.4 mg (94% yield) of the lactol. This (5.0 mg) in 0.5 mL of MeCN and 0.1 mL of water was treated with excess bromine (three drops). Calcium carbonate (10 mg) was then added immediately. After 1 h of stirring at room temperature, the mixture was filtered through Celite, washing with MeCN. The filtrate was concentrated at reduced pressure. The residual oil was flash chromatographed on silica gel, eluting first with 90:10 methylene chloride/acetone to remove yellow impurities and then with 65:35 methylene chloride/acetone to collect 2.6 mg (52% yield) of the lactone **5c**: R_F 0.49 (65:35 methylene chloride/acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, 3 H, J = 7.1 Hz, C2-Me), 1.39 (d, 3 H, J = 6.2 Hz, C5-Me), 2.00 (s, 3 H, Ac), 2.62 (m, 1 H, H2), 2.78 (t, 1 H, J = 10.6 Hz, H4), 3.73 (s, 3 H, CO_2Me), 4.25 (ddd, J = 10.97, 10.97, 9.04 Hz, H3), 4.57 (m, 1 H, H5), 5.54 (d, 1 H, J = 8.1 Hz, NH).

3-(Carbobenzyloxyamino)-4-*C*-carbomethoxy-2,3,4,6-tetradeoxy-2-*C*-methyl-D-glucono-1,5-lactone (5d). The compound **33b** (11.3 mg, 0.02 mmol) in 0.5 mL of THF was stirred with 0.2 mL of 12 M HCl for 13 h. The reaction was then diluted with two drops of water and neutralized with solid sodium bicarbonate. The mixture was filtered, washing with THF. The filtrate was concentrated at reduced pressure to give a solid, which was extracted with THF. The THF solution was concentrated at reduced pressure to give the crude lactol. This was taken up in 0.5 mL of MeCN and 0.1 mL of water. Three drops of bromine was added, followed by 10 mg of calcium carbonate. The mixture was stirred for 1.5 h at room temperature before filtering through Celite and washing with MeCN. The filtrate was concentrated at reduced pressure, and the residue was flash chromatographed on silica gel (75:25 petroleum ether/acetone). The product was rechromatographed with methylene chloride/EtOAc (90:10) to obtain 5.8 mg (60% yield from **33b**) of the lactone **5d**: R_f 0.33 (75:25 petroleum ether/acetone), 0.25 (CH_2Cl_2/EtOAc); $[\alpha]^{20}_D$ +20.17° (c 0.58, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (d, 3 H, J = 6.1 Hz, C2-Me, overlaps with C5-Me), 1.38 (d, 3 H, J = 6.9 Hz, C5-Me), 2.65 (m, 1 H, H2), 2.82 (t, 1 H, J = 10.9 Hz, H4), 3.63 (s, 3 H, CO_2Me), 3.92 (ddd, 1 H, J = 11.11, 11.11, 8.9 Hz, H3), 4.52 (m, 1 H, H5), 4.88 (d, 1 H, J = 8.5 Hz, NH), 5.08 (s, 2 H, Cbz-CH_2), 7.34 (m, 5 H, aromatic).

Acknowledgment. We are grateful to Dr. Isaac Oppong for his assistance in the early stages of this project.

Intramolecular Cycloadditions of Alkenes to Oxyallyl Zwitterions Generated from Photorearrangements of 2,5-Cyclohexadien-1-ones

Arthur G. Schultz* and Mark Plummer

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590

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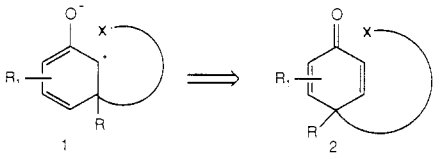
Photorearrangements of 2,5-cyclohexadien-1-ones containing a 3′-alkenyl substituent at C(4) provide intermediate alkenyl-substituted oxyallyl zwitterions **21** from which 5 + 2 cycloadditions give bridged cyclohexenones **22** and **23**. The occurrence of 3 + 2 cycloadditions to give dienol ethers **24** and bridged cyclopentanones **25** also is described.

We have reported that oxyallyl zwitterions **1** generated as transient intermediates from 2,5-cyclohexadien-1-ones **2** by two successive photorearrangements undergo intramolecular cycloaddition with tethered furans and alkyl azide substituents.[1] In these cycloadditions, the zwitterionophile X behaves as a four-electron component.

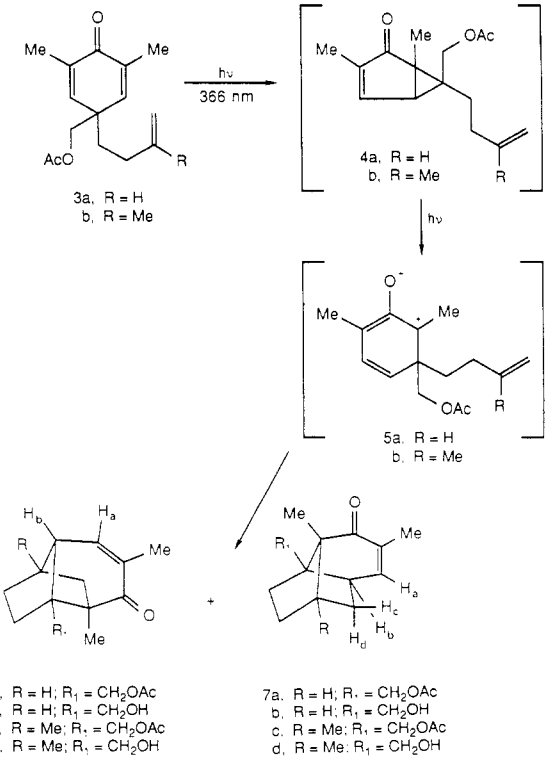


Herein, we report the complementary intramolecular cycloadditions of photogenerated zwitterions to alkene substituents (X = CR=CR_2).[2] These new tandem photorearrangement–cycloaddition processes are expected to have utility in carbocyclic and heterocyclic ring constructions.

Results and Discussion

As a result of previous work,[1,3] it was recognized that the group R in zwitterion **1** probably had to have a relatively low migration tendency to allow the cycloaddition process to be competitive with rearrangement to a phenol. Consequently, 4-(acetoxymethyl)-4-(3′-butenyl)-2,6-dimethyl-2,5-cyclohexadien-1-one (**3a**) was selected for initial study (Scheme I). Irradiation of a solution of **3a** in

Scheme I



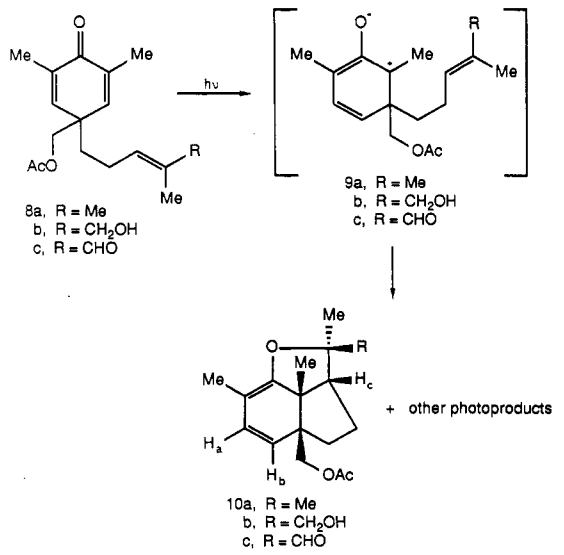
(1) (a) Schultz, A. G.; Myong, S. O.; Puig, S. *Tetrahedron Lett.* **1984**, *25*, 1011. (b) Schultz, A. G.; Puig, S.; Wang, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 785. (c) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391.

(2) For recent explorations of processes patterned after the perezone to pipitzol transformation, another type of 3 + 2 intramolecular cycloaddition, see: Joseph-Nathan, P.; Garibay, M. E.; Santillan, R. L. *J. Org. Chem.* **1987**, *52*, 759. Heilmann, W.; Koschinsky, R.; Mayr, H. *J. Org. Chem.* **1987**, *52*, 1989 and references cited therein.

(3) Schultz, A. G.; Lavieri, F. P.; Macielag, M.; Plummer, M. *J. Am. Chem. Soc.* **1987**, *109*, 3991.

0022-3263/89/1954-2112$01.50/0

Scheme II



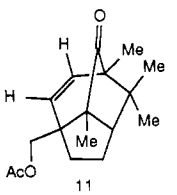
benzene (2.4×10^{-2} M) at 366 nm for 1.5 h gave a clean 3:1 mixture of tricycles **6a** and **7a** (^{1}H NMR analysis). The intramolecular cycloaddition products were inseparable, but alcohols **6b** and **7b**, obtained by acetate cleavage, were isolated by flash column chromatography on silica gel.

The structural assignments for tricyclodec-4-en-3-one **6b** (61% isolated yield) and tricyclodec-3-en-2-one **7b** (10%) were determined primarily by IR and ^{1}H and ^{13}C NMR spectral data. Analogues of **6b** and **7b** that incorporated methyl substituents at C(7) or C(9) were prepared to facilitate the ^{1}H NMR analysis. Thus, irradiation of **3b** gave tricycles **6c** and **7c**, which were isolated as alcohol derivatives **6d** and **7d**. The conversion of **3b** to **6d** and **7d** was not optimized, but examination of ^{1}H NMR spectra of the photoreaction mixture indicated that **6c** and **7c** were formed with good chemical efficiency.

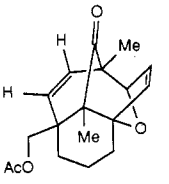
The ^{1}H NMR spectrum of **6d** showed a resonance for H_a at δ 6.58 as a doublet of doublets ($J_{a,b}$ = 6.8 Hz with allylic coupling to the vinyl methyl group of 1.4 Hz) and a resonance for H_b that appeared as a doublet ($J_{a,b}$ = 6.8 Hz). H_a in **7d** resonated further downfield (δ 7.15) than that in **6d** and, as would be expected, H_b appeared as a considerably more complex multiplet with coupling to not only H_a but also to H_c and H_d. These chemical shift and coupling patterns along with other spectral correlations made possible definitive assignments of structure to **6b** and **7b**.

Cyclohexadienes **8a–c** were prepared to examine steric and electronic effects on the course of zwitterion cycloaddition. Irradiation of **8a** gave a mixture of cycloadducts (Scheme II). The major product, isolated by flash chromatography on silica gel, was tricyclic dienol ether **10a** (~20% isolated yield). A fraction containing cycloadducts analogous to **6** and **7** also was obtained. Although this mixture of α,β-enones could not be separated, the constitution appeared certain on the basis of chemical shifts and coupling constants for protons corresponding to H_a (cf., scheme I).

The structural assignment for **10a** required a clear distinction to be made between **10a** and the isomeric bridged cyclopentanone **11**. Cyclopentanones have been obtained from cycloadditions of alkenes with oxyallyl-Fe(II) intermediates generated from α,α'-dibromo ketones and iron carbonyls,[4,5] and cycloadditions of enol ethers to an oxyallyl zwitterion presumably generated from photorearrangement of 2,7-cyclooctadienone.[6] To help distinguish between **10a** and **11** (and other possible isomers), we examined spectral data obtained from **12**, an intramolecular oxyallyl zwitterion–furan cycloadduct.[1c] The chemical shifts and coupling constants for H_a and H_b in **10a** and **12** are very similar; however, **10a** shows a sharp singlet for the vinyl methyl group at δ 1.60, and it is missing a carbonyl group absorption at 1715–1725 cm^{-1}, a frequency range compatible with the ketone carbonyl group of **12**. The IR spectrum of **10a** does show an acetate carbonyl stretch at 1740 cm^{-1} and a strong enol ether absorption at 1690 cm^{-1}. Furthermore, the ^{13}C NMR spectrum of **10a** displayed resonances at 128.33 and 121.52 for the disubstituted olefinic carbon atoms and at 97.74 and 158.40 for the enol ether carbon atoms.



11



12

In contrast to the complex product mixture obtained from **8a**, irradiation of the trans allylic alcohol derivative **8b** provided the tricyclic dienol ether **10b** in 71% isolated yield. The corresponding aldehyde **8c** gave a tricyclic dienol ether, **10c**, along with a substantial amount of uncharacterized material of high molecular weight. Some polymerization probably occurs on photoexcitation of **8c**, although it was determined that **8c** also undergoes decomposition in the absence of light. It is noteworthy that photorearrangements of **8b** and **8c** both appear to occur with complete retention of the configuration of the *E*-alkene unit. Relative configuration of **10c** was clearly established by the observation of a multiplet for H_c at δ 2.73, whereas H_c appeared at 2.19 in the ^{1}H NMR spectrum of **10a**. The large downfield shift results from deshielding of H_c by the adjacent aldehyde group in **10c**.

The formation of enol ethers from cycloaddition of oxyallyl zwitterions to alkenes is precedented in the chemistry of oxyallyl-Fe(II) and related intermediates. Dibromo ketone **13**, on reaction with $Fe_2(CO)_9$ in the presence of α-methylstyrene, has been reported to give alkylidenetetrahydrofuran **14** in 16% yield along with a cyclopentanone (5%) and acyclic ketonic products.[4] It was postulated that when the alkene and the carbon terminus of the oxyallyl species are sterically crowded, cycloaddition involving the oxygen terminus can compete with cyclopentanone formation. Furthermore, treatment of α,α'-dibromo ketone **15** with sodium iodide and copper powder in the presence of 1,1-dimethoxyethylene affords cycloadduct **16** in 90% yield instead of the corresponding cyclopentanone.[5]

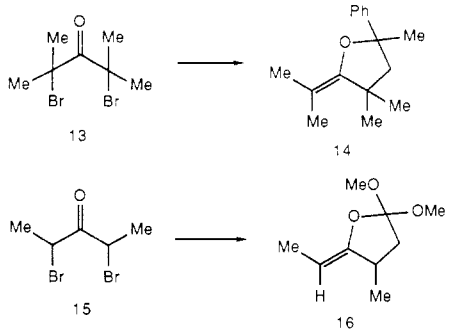
It is possible that oxyallyl zwitterion cycloadditions to give enol ethers **10a–c** are concerted (class c cycloadditions);[7] however, the formation of bridged cyclopentanones of type **11** must occur by stepwise bond formation rather than the thermally forbidden [$\pi^2 + \pi^2$] concerted process. Stepwise cyclization of **9a** to give **11** would result in severe steric crowding at adjacent quaternary centers. Instead, enol ether formation occurs,

(4) Hayakawa, Y.; Kokoyama, K.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1791.

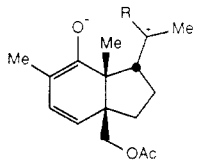
(5) Cowling, A. P.; Mann, J. *J. Chem. Soc., Chem. Commun.* **1978**, 1006.

(6) Matlin, A. R.; Jin, K. *Tetrahedron Lett.* **1989**, *30*, 637.

(7) Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*; Academic Press: New York, 1970.



possibly by way of the highly stabilized zwitterionic intermediate **17a**. Stepwise cyclization from oxyallyl zwitterions such as **5a** and **5b** would result in less stabilized zwitterionic intermediates and, for possibly this reason, the 4 + 2 cycloaddition (concerted?) operates to give bridged carbocycles **6** and **7**. Finally, it should be noted that electrostatic attractions between the enolate oxygen atom and the cationic center in **17b** and **17c** might be responsible for the stereoselectivity obtained from the cyclizations of **8b** and **8c** to **10b** and **10c**,[8] although this issue would have to be addressed by examination of the stereoselectivity of photorearrangement of the *Z* isomers of **8b** and **8c**.



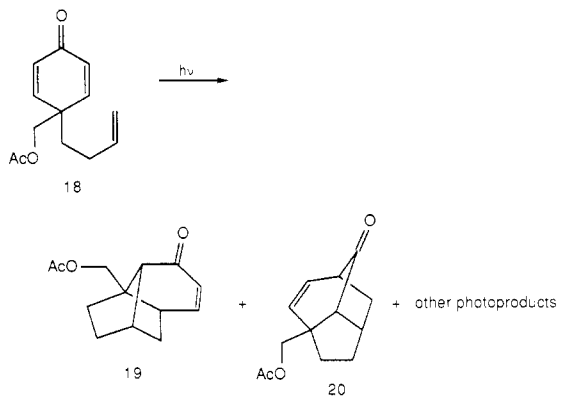
17a, R = Me
b, R = CH_2OH
c, R = CHO

The C(2) and C(6) unsubstituted 4-(3′-butenyl)-2,5-cyclohexadien-1-one **18** was prepared to test the hypothesis that steric crowding between the carbon terminus of the enolate residue in **17a–c** and C(4′) of the alkenyl substituent is responsible for the diversion of 3 + 2 cycloaddition from the type **11** products to dienol ethers **10a–c**. Irradiation of **18** in the usual manner resulted in the formation of four photoproducts (Scheme III). Flash column chromatography of the reaction mixture on silica gel gave 6-(acetoxymethyl)tricyclo[4.3.1^{5,9}.0^{1,6}]dec-3-en-2-one (**19**, 11%) and 4-(acetoxymethyl)tricyclo[5.2.1.0^{4,10}]dec-2-en-9-one (**20**, 16%). Bridged cyclopentanone **20** was immediately recognized by the presence of IR absorption for the ketone carbonyl group at 1725 cm^{-1}, which appeared as a shoulder on the band for the acetate carbonyl group at 1740 cm^{-1}. Another fraction containing a mixture of the remaining two photoproducts (51%) could not be separated even after conversion to the alcohol derivatives.[9]

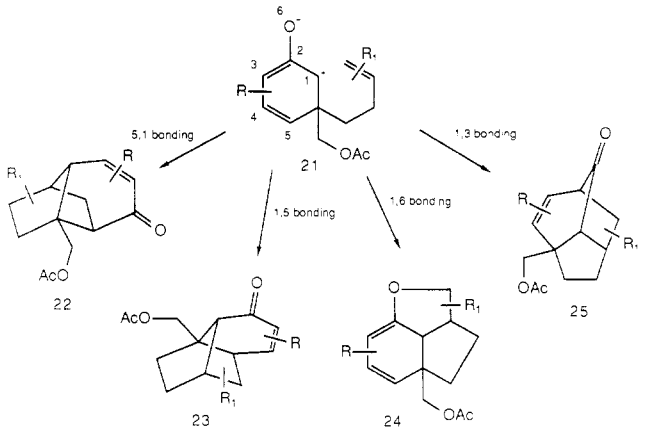
Conclusion

It has been possible to realize each of the oxyallyl zwitterion–alkene cycloadditions shown in Scheme IV. The alkenyl-substituted oxyallyl intermediate **21** behaves as a four-electron component in the two 5 + 2 cycloadditions resulting in product types **22** and **23**, while 3 + 2 cycloadditions give rise to either dienol ether **24** or bridged cyclopentanone **25**. Substituent effects (steric and electronic) appear to play dominant roles in the partitioning of reaction pathways. The observations outlined in this paper provide a foundation for further study of the synthetic potential of intramolecular cycloaddition reactions of oxyallyl zwitterions generated from successive photorearrangements of 2,5-cyclohexadien-1-ones.

Scheme III



Scheme IV



Experimental Section

The procedures for preparation of 2,5-cyclohexadien-1-ones have been described in detail.[1c,9] An improved procedure for bis(allylic) oxidations of 1,4-cyclohexadienes with *tert*-butyl hydroperoxide and pyridinium dichromate is available.[10]

General Procedure for the Irradiation of 2,5-Cyclohexadien-1-ones. The 2,5-cyclohexadienones were dissolved in spectrophotometric grade benzene unless otherwise indicated. The solutions were purged with dry nitrogen for 15 min prior to photolysis. The light source was a medium-pressure water-cooled 450-W Hanovia mercury arc lamp. The light was filtered through an uranyl glass sleeve to give predominantly the 366-nm ultraviolet emission of the mercury arc lamp, and irradiation times are as indicated. The crude photoproducts were isolated by removing the solvent under reduced pressure.[11]

3-(3′-Butenyl)-1,5-dimethyl-3-(methoxycarbonyl)-1,4-cyclohexadiene was prepared by Birch reduction–alkylation of methyl 3,5-dimethylbenzoate with 4-bromobutene.[1c,9] The crude product was used without further purification (1.09 g, 81% yield): ^{1}H NMR ($CDCl_3$) δ 5.70 (m, 1 H), 5.40 (s, 2 H), 4.91 (m, 2 H), 3.64 (s, 3 H), 2.41 (s, 2 H), 1.72 (s, 6 H) superimposed on 1.90–1.50 (m, 4 H); IR (film) 1730, 1640, 1430, 1220 cm^{-1}; CIMS *m/z* (relative intensity) 221 (M^+ + 1, 100), 189 (9.6).

1,5-Dimethyl-3-(methoxycarbonyl)-3-(3′-methyl-3′-butenyl)-1,4-cyclohexadiene was prepared from methyl 3,5-di-

(8) For stepwise, stereospecific reactions, see ref 4 including examples noted in footnote 28.

(9) It has been shown that 4-(3′-alkenyl)-3-methoxy-2,5-cyclohexadien-1-ones undergo nearly quantitative intramolecular 2 + 2 photocycloaddition; see: Schultz, A. G.; Plummer, M.; Taveras, A. G.; Kullnig, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 5547.

(10) Schultz, A. G.; Taveras, A. G.; Harrington, R. E. *Tetrahedron Lett.* **1988**, *29*, 3907.

(11) For additional examples of oxyallyl zwitterion cycloaddition, see: Plummer, M. S. Ph.D. Thesis, Rensselaer Polytechnic Institute, 1986.

methylbenzoate and 1-bromo-3-methylbutene.[1c,9] The reaction mixture was chromatographed on silica gel (hexane–ethyl acetate, 5:1) to give the title compound (0.96 g, 67%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.40 (s, 2 H), 4.64 (s, 1 H), 4.62 (s, 1 H), 3.62 (s, 3 H), 2.40 (s, 2 H), 1.70 (s, 6 H), 1.65 (s, 3 H), 1.80–1.60 (m, 4 H); IR (film) 1720, 1650, 1605, 1430, 1210 cm^{-1}.

1,5-Dimethyl-3-(4′-methyl-3′-pentenyl)-3-(methoxycarbonyl)-1,4-cyclohexadiene was prepared from methyl 3,5-dimethylbenzoate and 1-bromo-4-methyl-3-pentene.[1c,9] The crude product, a light yellow oil, was used without further purification (3.57 g, 90%): ^{1}H NMR ($CDCl_3$) δ 5.42 (s, 2 H), 5.04 (m, 1 H), 3.63 (s, 3 H), 2.41 (s, 2 H), 1.73 (s, 6 H), 1.68 (s, 3 H), 1.62 (s, 3 H), 1.80–1.50 (m, 4 H); IR (film) 1730, 1430, 1220, 1190 cm^{-1}; CIMS m/z (relative intensity) 249 (M^+ + 1, 53.2), 217 (16.0), 189 (100), 167 (31.7).

3-(3′-Butenyl)-3-cyano-1,4-cyclohexadiene was prepared from benzonitrile and 4-bromobutene[1c,9,12] and was isolated as a colorless oil that was used without further purification (3.09 g, 100%): ^{1}H NMR δ 6.04 (d of t, 2 H, J = 10 Hz, J = 3 Hz), 5.84 (m, 1 H), 5.69 (m, 2 H), 4.94 (m, 2 H), 2.72 (m, 2 H), 2.14 (m, 2 H), 1.86 (m, 2 H); IR (film) 2220, 1635, 1410, 910 cm^{-1}; CIMS m/z (relative intensity) 160 (M^+ + 1, 6.1), 133 (100).

3-(3′-Butenyl)-3-(methoxycarbonyl)-1,4-cyclohexadiene was prepared from methyl benzoate and 4-bromobutene[1c,9] and was isolated as a colorless oil (1.15 g, 81%): ^{1}H NMR ($CDCl_3$) δ 5.88 (d of t, 2 H, J = 9.5 Hz, J = 1.4 Hz), 5.80 (m, 1 H), 5.70 (m, 2 H), 4.93 (m, 2 H), 3.66 (s, 3 H), 2.62 (m, 2 H), 2.00–1.62 (m, 4 H); IR (film) 1725, 1635, 1430, 1225 cm^{-1}; CIMS m/z (relative intensity) 193 (M^+ + 1, 100), 161 (22.6), 137 (46.0), 133 (94.0).

3-(3′-Butenyl)-1,5-dimethyl-3-(hydroxymethyl)-1,4-cyclohexadiene. Reduction of 3-(3′-butenyl)-1,5-dimethyl-3-(methoxycarbonyl)-1,4-cyclohexadiene with lithium aluminum hydride[1c,9] gave the title compound (0.86 g, 90%) as a colorless oil that was used without further purification: ^{1}H NMR ($CDCl_3$) δ 5.74 (m, 1 H), 5.04 (s, 2 H), 4.89 (m, 2 H), 3.29 (s, 2 H), 2.44 (s, 2 H), 1.74 (s, 6 H), 1.80 (m, 2 H), 1.33 (m, 2 H); IR (film) 3360 (broad), 1635, 1430, 1030 cm^{-1}; CIMS m/z (relative intensity) 193 (M^+ + 1, 16.9), 175 (100).

1,5-Dimethyl-3-(hydroxymethyl)-3-(3′-methyl-3′-butenyl)-1,4-cyclohexadiene was isolated by chromatography on silica gel (hexane–ethyl acetate, 2:1) as a colorless oil (0.77 g, 91%): ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 2 H), 4.64 (d, 2 H, J = 6 Hz), 4.32 (d, 2 H, J = 6 Hz), 2.46 (s, 2 H), 1.74 (s, 6 H), 1.67 (s, 3 H), 1.40–1.10 (m, 4 H); IR (film) 3470 (broad), 1640, 1435, 1030 cm^{-1}; CIMS m/z (relative intensity), 207 (M^+ + 1, 34.1), 189 (94.7), 177 (6.6), 133 (55.2), 119 (100).

1,5-Dimethyl-3-(hydroxymethyl)-3-(4′-methyl-3′-pentenyl)-1,4-cyclohexadiene was isolated by chromatography on silica gel (hexane–ethyl acetate, 3:1) as a colorless oil (1.75 g, 50%): ^{1}H NMR ($CDCl_3$) δ 5.05 (s, 3 H), 3.24 (d, 2 H, J = 6.2 Hz), 2.45 (s, 2 H), 1.74 (s, 6 H), superimposed on 1.75 (m, 2 H), 1.63 (s, 3 H), 1.53 (s, 3 H), 1.24 (m, 2 H); IR (film) 3370 (broad), 1430, 1075, 1030, 925 cm^{-1}; CIMS m/z (relative intensity) 221 (M^+ + 1, 25.1), 203 (100), 189 (27.9).

3-(3′-Butenyl)-3-(hydroxymethyl)-1,4-cyclohexadiene was isolated by chromatography on silica gel as a colorless oil (0.97 g, 98,%): ^{1}H NMR ($CDCl_3$) δ 5.98 (d of t, 2 H, J = 10 Hz, J = 4 Hz), 5.78 (m, 1 H), 5.35 (d of t, 2 H, J = 10 Hz, J = 2 Hz), 4.90 (m, 2 H), 3.30 (s, 2 H), 2.60 (m, 2 H), 2.00–1.82 (m, 2 H), 1.28 (m, 2 H); IR (film) 3360 (broad), 1630, 1410, 1020, 905 cm^{-1}; CIMS m/z (relative intensity) 165 (M^+ + 1, 3.7), 147 (72.7), 133 (11.9), 91 (100).

3-(Acetoxymethyl)-3-(3′-butenyl)-1,5-dimethyl-1,4-cyclohexadiene. The acetylation[1c,9] of 3-(3′-butenyl)-1,5-dimethyl-3-(hydroxymethyl)-1,4-cyclohexadiene provided the title compound (1.03 g, 95%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.76 (m, 1 H), 5.08 (s, 2 H), 4.89 (m, 2 H), 3.80 (s, 2 H), 2.39 (s, 2 H), 2.00 (s, 3 H), 1.80 (q, 2 H, J = 7 Hz), 1.70 (s, 6 H), 1.40 (m, 2 H); IR (film) 1740, 1640, 1430, 1370, 1225, 1030 cm^{-1}; CIMS m/z (relative intensity) 235 (M^+ + 1, 1.0), 175 (100).

3-(Acetoxymethyl)-1,5-dimethyl-3-(3′-methyl-3′-butenyl)-1,4-cyclohexadiene was obtained as a colorless oil (640 mg, 86%): ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 2 H), 4.60 (d, 2 H, J = 2.5 Hz), 3.81 (s, 2 H), 2.40 (s, 2 H), 2.01 (s, 3 H), 1.70 (s, 6 H), 1.67 (s, 3 H), 1.84–1.38 (m, 4 H); IR (film) 1735, 1645, 1435, 1370, 1225, 1030 cm^{-1}; CIMS m/z (relative intensity) 249 (M^+ + 1, 3) 189 (100), 133 (32).

3-(Acetoxymethyl)-1,5-dimethyl-3-(4′-methyl-3′-pentenyl)-1,4-cyclohexadiene was obtained as a colorless oil (1.88 g, 90%): ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 1 H), 3.78 (s, 2 H), 2.40 (s, 2 H), 1.99 (s, 3 H), 1.70 (s, 6 H) superimposed on (m, 2 H), 1.62 (s, 3 H), 1.52 (s, 3 H), 1.30 (m, 2 H); CIMS m/z (relative intensity) 263 (M^+ + 1, 1.9), 203 (50.2), 119 (100).

3-(Acetoxymethyl)-3-(3′-butenyl)-1,4-cyclohexadiene was obtained as a colorless oil (0.98 g, 80%): ^{1}H NMR ($CDCl_3$) δ 5.85 (d of t, 2 H, J = 10.4 Hz, J = 3.4 Hz), 5.80 (m, 1 H), 5.40 (d of t, 2 H, J = 10.4 Hz, J = 2.0 Hz), 4.96 (m, 2 H), 3.87 (s, 2 H), 2.60 (m, 2 H), 2.01 (s, 3 H), 1.94 (m, 2 H), 1.40 (m, 2 H); IR (film) 1735, 1635, 1370, 1225, 1030 cm^{-1}; CIMS m/z (relative intensity) 207 (M^+ + 1, 2.1), 147 (100).

General Procedure for Preparation of 2,5-Cyclohexadien-1-ones. The 1,4-cyclohexadiene was dissolved in ethanol-free chloroform to provide a 0.1 M solution. To this solution was added 3 equiv of pyridinium dichromate. The mixture was refluxed until the reaction was determined to be complete using thin-layer chromatographic (TLC) analysis (3–10 h). During this time, water was removed via a Dean–Stark apparatus. After the reaction was complete, the reaction mixture was filtered through a pad of Florisil to remove the chromium salts. The pad was washed with chloroform, and the filtrate was concentrated under reduced pressure to provide the 2,5-cyclohexadien-1-one. In certain cases the alternative bis(allylic) oxidation procedure might be preferred.[10]

4-(Acetoxymethyl)-4-(3′-butenyl)-2,6-dimethyl-2,5-cyclohexadienone (3a). The oxidation provided a dark oil that was chromatographed on silica gel (hexane–ethyl acetate, 3:1) to give **3a** (0.70 g, 66%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.49 (s, 2 H), 5.70 (m, 1 H), 4.98 (m, 2 H), 4.03 (s, 2 H), 2.00 (s, 3 H), 1.90 (s, 6 H), 1.84–1.54 (m, 4 H); IR (film) 1740, 1670, 1640, 1365, 1220, 1035 cm^{-1}; CIMS m/z (relative intensity) 249 (M^+ + 1, 7.1), 189 (100).

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.56; H, 8.11. Found: C, 72.71; H, 8.14.

4-(Acetoxymethyl)-2,6-dimethyl-4-(3′-methyl-3′-butenyl)-2,5-cyclohexadienone (3b). The oxidation and chromatography on silica gel (hexane–ethyl acetate, 2:1) provided **3b** (1.74 g, 94%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.49 (s, 2 H), 4.67 (s, 1 H), 4.59 (s, 1 H), 4.09 (s, 2 H), 1.99 (s, 3 H), 1.90 (s, 6 H), 1.73 (s, 3 H), 1.64 (s, 4 H); IR (film) 1745, 1670, 1635, 1370, 1220, 1035, 905 cm^{-1}; CIMS m/z (relative intensity) 263 (M^+ + 1, 8.2), 231 (7.3), 203 (100), 175 (9.6).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.29; H, 8.48.

4-(Acetoxymethyl)-2,6-dimethyl-4-(4′-methyl-3′-pentenyl)-2,5-cyclohexadienone (8a). The oxidation and chromatography on silica gel (hexane–ethyl acetate, 4:1) gave **8a** (0.32 g, 61%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.50 (s, 2 H), 4.96 (t, 1 H, J = 8 Hz), 4.01 (s, 2 H), 1.98 (s, 3 H), 1.90 (s, 6 H), 1.84–1.50 (m, 4 H), 1.62 (s, 3 H), 1.47 (s, 3 H); IR (film) 1745, 1670, 1640, 1360, 1220, 1040 cm^{-1}; CIMS m/z (relative intensity) 277 (M^+ + 1, 8.8), 217 (100), 189 (21.0), 161 (64.2).

Anal. Calcd for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.64; H, 8.60.

4-(Acetoxymethyl)-4-(3′-butenyl)-2,5-cyclohexadienone (18). The oxidation provided 18 (0.92 g, 88%) that was sufficiently pure for further use and elemental analysis: ^{1}H NMR ($CDCl_3$) δ 6.78 (d, 2 H, J = 10.2 Hz), 6.42 (d, 2 H, J = 10.2 Hz), 5.78 (m, 1 H), 5.04 (m, 2 H), 4.16 (s, 2 H), 2.02 (s, 3 H), 2.0–1.70 (m, 4 H); IR (film) 1745, 1665, 1630, 1370, 1220, 1040 cm^{-1}; CIMS m/z (relative intensity) 221 (M^+ + 1, 17.8), 191 (27.1), 161 (100), 133 (66.1).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.74; H, 7.38.

4-(Acetoxymethyl)-2,6-dimethyl-4-((*E*)-5′-hydroxy-4′-methyl-3′-pentenyl)-2,5-cyclohexadienone (8b) and 4-(Acetoxymethyl)-2,6-dimethyl-4-((*E*)-5′-oxo-4′-methyl-3′-pentenyl)-2,5-cyclohexadienone (8c). To dichloromethane (1 mL) was added selenium dioxide (20 mg, 0.5 equiv) and *tert*-butyl hydroperoxide 70% (123 μL, ~2.5 equiv).[13] This mixture was

(12) Schultz, A. G.; Macielag, M. *J. Org. Chem.* **1986**, *51*, 4983.

stirred at room temperature until the selenium dioxide had dissolved. To this solution was added a solution of dichloromethane (2 mL) containing **8a** (100 mg, 0.36 mmol). After the mixture was stirred 10 h at room temperature, the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (hexane–ethyl acetate, 1:1) to give **8b** (41 mg, 39%)[14] as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.49 (s, 2 H), 5.25 (t, 1 H, J = 7 Hz), 4.00 (s, 2 H), 3.92 (s, 2 H), 1.97 (s, 3 H), 1.89 (s, 6 H), 1.84–1.53 (m, 4 H), 1.51 (s, 3 H); IR (film) 3450 (broad), 1740, 1670, 1635, 1435, 1370, 1220, 1040 cm^{-1}; CIMS m/z (relative intensity) 293 (M^+ + 1, 23.9), 275 (24.1), 233 (89.9), 215 (100).

Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.55; H, 8.34.

Utilization of the same reaction conditions, but with stirring at room temperature for 24 h, also provided **8c**: ^{1}H NMR ($CDCl_3$) δ 9.35 (s, 1 H), 6.51 (s, 2 H), 6.33 (d of t, 1 H, J = 7.2 Hz, J = 1.3 Hz), 4.05 (s, 2 H), 2.10 (m, 2 H), 2.05 (s, 3 H), 1.92 (s, 6 H), 1.80 (m, 2 H), 1.63 (s, 3 H); IR (film) 1740, 1685, 1635, 1425, 1360, 1220, 1035 cm^{-1}; CIMS m/z (relative intensity) 291 (M^+ + 1, 12.0), 231 (57.4), 203 (64.4), 173 (100).

Anal. Calcd for $C_{17}H_{22}O_4$: C, 70.33; H, 7.63. Found: C, 70.05; H, 7.81.

Note: **8c** undergoes polymerization on standing.

2,4-Dimethyl-1-(hydroxymethyl)tricyclo[4.3.1^{2,7}.0^{1,6}]dec-4-en-3-one (6b). Irradiation of **3a** for 1.5 h gave a mixture of **6a** and **7a** that was inseparable (TLC analysis). Treatment with sodium methoxide in methanol gave a mixture of alcohols. Chromatography on silica gel (hexane–ethyl acetate, 1:1) gave a colorless oil (high R_f fraction) containing **6b** (167 mg, 61%): ^{1}H NMR ($CDCl_3$) δ 6.60 (dd, 1 H, J = 6.8 Hz, J = 1.4 Hz), 3.46 (s, 2 H), 2.50 (d, 1 H, J = 6.8 Hz), 2.23 (b s, 1 H), 1.76 (d, 3 H, J = 1.4 Hz), 1.82–1.54 (m, 4 H), 1.20 (m, 2 H), 1.08 (s, 3 H); IR (film) 3440, 1660, 1440, 1360, 1025 cm^{-1}; CIMS m/z (relative intensity) 207 (M^+ + 1, 100), 189 (27.6), 161 (29.7); ^{13}C NMR ($CDCl_3$) δ 203.87, 141.79, 134.45, 63.22, 60.80, 54.47, 49.24, 41.42, 40.21, 30.72, 25.48, 15.28, 13.61.

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.70; H, 8.79. Found: C, 75.81; H, 8.86.

1,3-Dimethyl-6-(hydroxymethyl)tricyclo[4.3.1^{5,9}.0^{1,6}]dec-3-en-2-one (7b) was obtained as a colorless oil (low R_f fraction, 25 mg, 10%): ^{1}H NMR ($CDCl_3$) δ 7.15 (dd, 1 H, J = 7.4 Hz, J = 1.4 Hz), 3.77 (d, 1 H, J = 10.8 Hz), 3.50 (d, 1 H, J = 10.8 Hz), 2.52 (d of t, 1 H, J = 7.4 Hz, J = 1.3 Hz), 1.85–1.48 (m, 7 H) superimposed on 1.73 (d, 3 H, J = 1.4 Hz), 1.07 (s, 3 H); IR (film) 3430, 1650, 1440, 1375, 1355, 1050, 1015, 975 cm^{-1}; CIMS m/z (relative intensity) 207 (M^+ + 1, 100), 189 (24.3), 177 (21.1), 165 (25.5), 161 (22.7), 135 (55.6); ^{13}C NMR ($CDCl_3$) δ 201.92, 152.20, 135.74, 63.48, 61.89, 42.28, 41.66, 41.23, 30.84, 30.21, 15.17, 12.75 (1 carbon missing).

Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.70; H, 8.79. Found: C, 75.71; H, 8.67.

1-(Hydroxymethyl)-2,4,7-trimethyltricyclo[4.3.1^{2,7}.0^{1,6}]-dec-4-en-3-one (6d). Irradiation of **3b** for 1.5 h gave a mixture of **6c** and **7c** that was inseparable (TLC analysis). Treatment with sodium methoxide in methanol gave a mixture of alcohols (process not optimized). Chromatography on silica gel (hexane–ethyl acetate, 1:1) gave **6d** (30 mg, 20%): ^{1}H NMR ($CDCl_3$) δ 6.58 (dd, 1 H, J = 6.8 Hz, J = 1.4 Hz), 3.42 (s, 2 H), 2.28 (d, 1 H, J = 6.8 Hz), 1.79 (d, 3 H, J = 1.4 Hz), 1.60 (t, 2 H, J = 7.2 Hz), 1.65–1.10 (m, 4 H), 1.06 (s, 3 H), 1.04 (s, 3 H); IR (film) 3440 (broad), 1660, 1440, 1365, 1035, 1020 cm^{-1}; CIMS m/z (relative intensity) 224 (M^+ + 1, 100) 203 (27); ^{13}C NMR ($CDCl_3$) δ 141.09, 135.43, 68.57, 63.92, 55.57, 53.63, 47.84, 47.34, 38.08, 25.43, 20.09, 15.38, 13.89 (carbonyl carbon missing).

6-(Hydroxymethyl)-1,3,9-trimethyltricyclo[4.3.1^{5,9}.0^{1,6}]-dec-3-en-2-one (7d) also was isolated (15 mg, 10%): ^{1}H NMR ($CDCl_3$) δ 7.15 (dd, 1 H, J = 7.5 Hz, J = 1.5 Hz), 3.78 (d, 1 H, J = 10.7 Hz), 3.50 (d, 1 H, J = 10.7 Hz), 2.48 (t, 1 H, J = 8 Hz), 2.0–1.0 (m, 6 H), 1.71 (d, 3 H, J = 1.5 Hz), 0.97 (s, 3 H), 0.86 (s, 3 H); IR (film) 3440 (broad), 1650, 1440, 1375, 1355, 1030, 1015 cm^{-1}; CIMS m/z (relative intensity) 221 (M^+ + 1, 100), 203 (70), 191 (25), 175 (13).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.14. Found: C, 76.18; H, 9.20.

1-(Acetoxymethyl)-4,7,7′,11-tetramethyl-6-oxotricyclo-[5.3.1.0^{8,11}]undeca-2,4-diene (10a). Irradiation of **8a** for 1.5 h and chromatography on silica gel (hexane–ethyl acetate, 4:1) gave **10a** as a colorless oil (25 mg, 17%): ^{1}H NMR ($CDCl_3$) δ 5.69 (d, 1 H, J = 9.4 Hz), 5.26 (d, 1 H, J = 9.4 Hz), 3.98 (AB quartet, 2 H, J = 20 Hz, J = 11 Hz), 2.19 (m, 1 H), 2.07 (s, 3 H), 1.69 (m, 4 H), 1.60 (s, 3 H), 1.48 (s, 3 H), 1.27 (s, 3 H), 1.09 (s, 3 H); IR (film) 1740, 1690, 1580, 1445, 1380, 1360, 1235, 1030 cm^{-1}; CIMS m/z (relative intensity) 277 (M^+ + 1, 100), 276 (92.7), 217 (86.1); ^{13}C NMR ($CDCl_3$) δ 170.85, 158.40, 128.33, 121.52, 97.74, 89.28, 66.22, 56.68, 51.09, 33.47, 31.27, 25.95, 25.42, 20.71, 17.65, 12.83.

Also isolated (48 mg, 32%) was a mixture of two cycloadducts containing an α,β-unsaturated carbonyl group. Selected ^{1}H NMR ($CDCl_3$) δ 6.80 (dd, 1 H, J = 8 Hz, J = 1 Hz) and 6.60 (dd, 1 H, J = 8 Hz, J = 1 Hz).

1-(Acetoxymethyl)-7-(hydroxymethyl)-4,7,11-trimethyl-6-oxatricyclo[5.3.1^{1,5}.0^{8,11}]undeca-1,3-diene (10b). Irradiation of **8b** for 1.5 h provided a single cycloadduct. Chromatography on silica gel (hexane–ethyl acetate, 1:1) gave **10b** (106 mg, 71%) as a colorless oil that slowly decomposes on standing: ^{1}H NMR ($CDCl_3$) δ 5.69 (d, 1 H, J = 9.3 Hz), 5.30 (d, 1 H, J = 9.3 Hz), 3.99 (AB quartet, 2 H, J = 18.4 Hz, J = 11.0 Hz), 3.55 (m, 2 H), 2.07 (s, 3 H), 2.05–1.60 (m, 5 H), 1.60 (s, 3 H), 1.26 (s, 3 H), 1.05 (s, 3 H); IR (film) 3460, 1740, 1690, 1585, 1440, 1370, 1235, 1030 cm^{-1}; EIMS m/z (relative intensity) 292 (M^+, 100), 201 (30.4); ^{13}C NMR ($CDCl_3$) δ 171.03, 129.04, 128.01, 111.31, 85.13, 75.20, 68.03, 57.72, 57.07, 51.36, 36.38, 30.01, 25.46, 20.87, 16.17, 14.59, 14.06.

1-(Acetoxymethyl)-7-formyl-4,7,11-trimethyl-6-oxatricyclo[5.3.1^{1,5}.0^{8,11}]undeca-1,3-diene (10c). Irradiation of **8c** for 1.5 h provided a single cycloadduct as well as polymeric material. Chromatography on silica gel (hexane–ethyl acetate, 3:1) gave **10c** (5 mg, 10%) as an oil: ^{1}H NMR ($CDCl_3$) δ 9.86 (s, 1 H), 5.72 (d, 1 H, J = 9.3 Hz), 5.23 (d, 1 H, J = 9.3 Hz), 3.99 (s, 2 H), 2.73 (m, 1 H), 2.07 (s, 3 H), 2.00–1.70 (m, 4 H), 1.66 (s, 3 H), 1.32 (s, 3 H), 0.83 (s, 3 H); IR (film) 1735, 1690, 1580, 1440, 1360, 1230, 1030 cm^{-1}; EIMS m/z (relative intensity) 290 (M^+, 100), 261 (69.9), 217 (8.4), 201 (8.9), 189 (15.6), 173 (33.1), 159 (37.8), 135 (40.6).

4-(Acetoxymethyl)tricyclo[5.2.1.0^{4,10}]dec-2-en-9-one (20). Irradiation of **18** for 1.5 h gave four cycloadducts and a trace of starting material (^{1}H NMR analysis). Chromatography on silica gel (hexane–ethyl acetate, 3:1) resulted in the isolation of two products: **20** (colorless oil, 41 mg, 16%); ^{1}H NMR ($CDCl_3$) δ 6.20 (m, 2 H), 4.11 (AB quartet, 2 H, J = 24.5 Hz, J = 11.2 Hz), 3.12 (m, 1 H), 2.79 (m, 1 H), 1.89 (s, 3 H), superimposed on 2.22–1.30 (m, 7 H); IR (film) 1740, shoulder 1725, 1325, 1310, 1230, 1030 cm^{-1}; CIMS m/z (relative intensity) 221 (M^+ + 1, 48.1), 179 (16.9), 161 (7.8), 133 (100); ^{13}C NMR ($CDCl_3$) δ 212.95, 132.91, 128.17, 64.74, 54.26, 47.79, 46.69, 35.06, 32.56, 31.20, 29.70, 20.77.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.03; H, 7.40.

6-(Acetoxymethyl)tricyclo[4.3.1^{5,9}.0^{1,6}]dec-3-en-2-one (19) also was isolated (colorless oil, 27 mg, 11%): ^{1}H NMR ($CDCl_3$) δ 6.63 (dd, 1 H, J = 10.1 Hz, J = 4.8 Hz), 5.94 (dd, 1 H, J = 10.1 Hz, J = 0.9 Hz), 4.31 (d, 1 H, J = 10.9 Hz), 3.76 (d, 1 H, J = 10.9 Hz), 3.15 (m, 1 H), 2.97 (m, 2 H), 2.57 (q, 1 H, J = 12.0 Hz), 2.20–1.40 (m, 5 H), superimposed on 1.98 (s, 3 H); IR (film) 1740, 1670, 1450, 1375, 1230, 1040 cm^{-1}; CIMS m/z (relative intensity) 221 (M^+ + 1, 67.6), 179 (48.5), 161 (100), 133 (21.7); ^{13}C NMR ($CDCl_3$) δ 200.42, 171.01, 147.98, 125.95, 65.40, 54.10, 42.51, 36.51, 36.10, 30.14, 28.28, 20.77.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.05; H, 7.38.

Another fraction (127 mg, 51%) contained two additional photoproducts, but cleavage of the acetate groups with sodium methoxide in methanol resulted in an inseparable mixture of two alcohols that could not be further characterized.

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Registry No. **3a**, 119694-20-1; **3b**, 119694-21-2; **6a**, 119694-34-7; **6b**, 119694-26-7; **6c**, 119720-73-9; **6d**, 119694-28-9; **7a**, 119694-35-8;

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7b, 119694-27-8; **7c**, 119694-36-9; **7d**, 119694-29-0; **8a**, 119694-22-3; **8b**, 119694-24-5; **8c**, 119694-25-6; **10a**, 119694-30-3; **10b**, 119694-31-4; **10c**, 119694-32-5; **18**, 119694-23-4; **19**, 119694-33-6; **20**, 119720-72-8; 4-bromobutene, 5162-44-7; methyl 3,5-dimethylbenzoate, 25081-39-4; 1-bromo-3-methylbutene, 20038-12-4; 1-bromo-4-methyl-3-pentene, 2270-59-9; benzonitrile, 140-29-4; methyl benzoate, 93-58-3; 3-(3'-butenyl)-1,5-dimethyl-3-(methoxycarbonyl)-1,4-cyclohexadiene, 119694-07-4; 1,5-dimethyl-3-(methoxycarbonyl)-3-(3'-methyl-3'-butenyl)-1,4-cyclohexadiene, 119694-08-5; 1,5-dimethyl-3-(4'-methyl-3'-pentenyl)-3-(methoxy carbonyl)-1,4-cyclohexadiene, 119694-09-6; 3-(3'-butenyl)-3-cyano-1,4-cyclohexadiene, 119694-10-9; 3-(3'-butenyl)-3-(methoxycarbonyl)-1,4-cyclohexadiene, 119694-11-0; 3-(3'-butenyl)-1,5-dimethyl-3-(hydroxymethyl)-1,4-cyclohexadiene, 119694-12-1; 1,5-dimethyl-3-(hydroxymethyl)-3-(3'-methyl-3'-butenyl)-1,4-cyclohexadiene, 119694-13-2; 1,5-dimethyl-3-(hydroxymethyl)-3-(4'-methyl-3'-pentenyl)-1,4-cyclohexadiene, 119694-14-3; 3-(3'-butenyl)-3-(hydroxymethyl)-1,4-cyclohexadiene, 119694-15-4; 3-(acetoxymethyl)-3-(3'-butenyl)-1,5-dimethyl-1,4-cyclohexadiene, 119694-16-5; 3-(acetoxymethyl)-1,5-dimethyl-3-(3'-methyl-3'-butenyl)-1,4-cyclohexadiene, 119694-17-6; 3-(acetoxymethyl)-1,5-dimethyl-3-(4'-methyl-3'-pentenyl)-1,4-cyclohexadiene, 119694-18-7; 3-(acetoxymethyl)-3-(3'-butenyl)-1,4-cyclohexadiene, 119694-19-8.

Scope and Regiochemical Control of the Allylpotassium Reaction in the Synthesis of Sterols with Unsaturated Side Chains

José-Luis Giner, Christian Margot, and Carl Djerassi*

Department of Chemistry, Stanford University, Stanford, California 94305

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Allylpotassium derivatives were prepared from a variety of olefins by using Schlosser's base (BuLi/KOt-Bu). Reaction with (20*S*)-20-(iodomethyl)pregnane *i*-methyl ether (**1**) followed by deprotection gave in high yields a wide variety of Δ^{24} and $\Delta^{24(28)}$ sterols, including the naturally occurring desmosterol (**37**), fucosterol (**33**), 24(*E*)-propylidenecholesterol (**35**), 24-methylenecholesterol (**3**), dehydroaplysterol (**10**), 25-methyl-24-methylenecholesterol (**11**), mutasterol (**12**), and 25-methylxestosterol (**13**). Control of the regiochemistry of unsymmetrical allylmetals was achieved through the addition of Li_2CuCl_3. Rules concerning the high regioselectivities and stereoselectivities are discussed.

Sterols containing the Δ^{24} and $\Delta^{24(28)}$ double bond are common in nature and represent key intermediates in sterol biosynthesis.[1] In this paper we present our application of allylpotassium compounds[2] to the synthesis of a wide variety of such unsaturated sterol side chains from simple olefins and a common steroidal precursor.

It has become increasingly necessary in our biosynthetic studies of sterols of marine origin[3] to be able to synthesize a wide variety of sterol side chains as precursors in feeding experiments, for structure proofs, and as cold carriers for the chromatographic and degradative analyses of feeding experiments. With the allylmetal method we describe a means by which a great number of sterols containing unsaturated side chains may be conveniently prepared in high yields by a single reaction.

Results and Discussion

Our initial success in the coupling the steroidal iodide **1**[4] with the allylpotassium derived by deprotonation of 2,3-dimethyl-1-butene (**2**) with Schlosser's base[2] (BuLi/KOt-Bu) to give the *i*-methyl ether of 24-methylenecholesterol (**3**)[5] (Figure 1) prompted further investigation of this procedure with results summarized in Table I.

Substitution of the Δ^7 iodide (**4**) for **1** gave the protected Δ^7 24-methylene sterol (**5**). Reaction of the *i*-methyl iodide **1** with the allylpotassiums derived from 2,3-dimethyl-1-pentene (**6**) and especially the olefins **7–9** containing quaternary centers gave aplysterol (**10**),[6] 25-methyl-24-methylenecholesterol (**11**),[7] mutasterol (**12**),[8] and 25-methylxestosterol (**13**)[9] as their *i*-methyl ethers in good yields (72–95%). Regeneration of the Δ^5-3β-hydroxy moiety was then accomplished in high yield by the conventional procedure.[4] In this series, the yield of the reaction decreased with increasing steric hindrance (Table I). The steric hindrance of the tertiary amyl group in **12** and the yet bulkier group in **13** has been a problem leading to low yields in our previous syntheses of **12**[8] and **13**[9] by aldol condensations followed by Wittig reaction of the resulting ketones. Allylpotassiums derived from isobutylene (**14**) and propylene (**15**) gave the unnatural sterols **16** and **17** with shortened side chains.[10]

The regiochemical outcome of the reactions of unsymmetrical allylpotassiums generated from olefins **18–32** can be seen in Table II: attack at both termini of the allyl system gives rise to sterols **33–68** with a preference for attack at the less substituted terminus. Provided that the products are easily separable, this can be a satisfactory way of preparing certain sterols. For instance desmosterol

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