of **10** was placed in a 400 °C oven for 2 min. After being cooled, the tube was opened and the contents were submitted to preparative-layer alumina chromatography. The major product (214 mg) was shown to be vinylogous imide **1** by comparison of ^1H and ^{13}C NMR spectra.

Intensity Data, Structure Determination, and Refinement. Integrated intensities were measured with an Oak Ridge computer-controlled diffractometer by the θ–2θ scan technique, to a limit of (sin θ)/$\lambda \leq 0.60$ Å^{-1}, using Nb-filtered Mo Kα radiation. Of the 1540 unique reflections measured, 1423 had intensities greater than 3 times their esd's and were used in the subsequent analysis. Each intensity was assigned an estimated variance, $\sigma^2(I)$, based on counting statistics plus an empirical correction of $(0.02I)^2$, determined during the final cycles of refinement from plots of $|\Delta F|^2$ vs. $|F_o|^2$.

The structure was solved using the MULTAN program[11] after calculating E's assuming an anisotropic thermal model with the ORESTES program.[12] The structure was refined by least-squares in two blocks (nonhydrogen atoms anisotropic, hydrogens isotropic), the refinement converging on a final conventional $R(F)$ value of 3.3% (4.4% weighted) and a goodness-of-fit of 1.49. No significant features were found in a final difference map. The programs used subsequent to structure solution were from the XRAY system.[13]

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Registry No.—**1**, 69089-06-1; **6**, 32917-19-4; **7**, 69089-07-2; **8**, 69089-08-3; **9**, 69120-34-9; **10**, 69089-09-4; **11**, 69089-10-7; 1-cyanocyclohexene, 1855-63-6; dimedone, 126-81-8.

Supplementary Material Available: Tables Ia and Ib, final parameters of the anisotropically and isotropically refined atoms, respectively, and Figures 2 and 3, bond angles and bond lengths, respectively, for compound **9** (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Department of Chemistry, University of Tennessee; (b) Department of Biochemistry, University of Tennessee; (c) Oak Ridge National Laboratory.
(2) Schell, F. M.; Cook, P. M. *J. Org. Chem.*, **1978**, *43*, 4420.
(3) Böhme, E. H.; Valenta, Z.; Wiesner, K. *Tetrahedron Lett.* **1965**, 2441.
(4) Cantrell, T. S. *Tetrahedron*, **1971**, *27*, 1227.
(5) Wiesner, D.; Musil, V.; Wiesner, K. J. *Tetrahedron Lett.* **1968**, 5643.
(6) Tamura, Y.; Ishibashi, H.; Hirai, M.; Kita, Y.; Ikeda, M. *J. Org. Chem.* **1975**, *40*, 2702.
(7) Tamura, Y.; Uraoka, J.; Fukumori, S.; Kita, Y. *Chem. Pharm. Bull.* **1973**, *21*, 1372
(8) Scheffer, J. R.; Wostradowski, A. *J. Org. Chem.* **1972**, *37*, 4317.
(9) Cotton, F. A.; Frenz, B. A. *Tetrahedron*, **1974**, *30*, 1587.
(10) House, H. O.; Paragamian, V.; Ro, R. S.; Wluka, D. J. *J. Am. Chem. Soc.*, **1960**, *82*, 1457.
(11) Germain, G.; Main, P.; Woolfson, M. W. *Acta Crystallogr., Sect. A* **1971**, *27*, 368.
(12) Thiessen, W. E.; Levy, H. A. Program Accession No. 247 in "World List of Crystallographic Computer Programs", 3rd ed., *J. Appl. Crystallogr.* **1973**, *6*, 309.
(13) Stewart, J. W.; Kruger, G. J.; Ammon, M.; Dickinson, C.; Hall, S. R. The XRAY system version of June 1972, Technical Report TR-192, Computer Science Center, University of Maryland, College Park, Md.

Steroid Photochemistry. Photocycloaddition of Cyclopropylenones to Dienes. An Example of a [$_\pi$2 + $_\pi$2 + $_\pi$2 + $_\sigma$2] Addition

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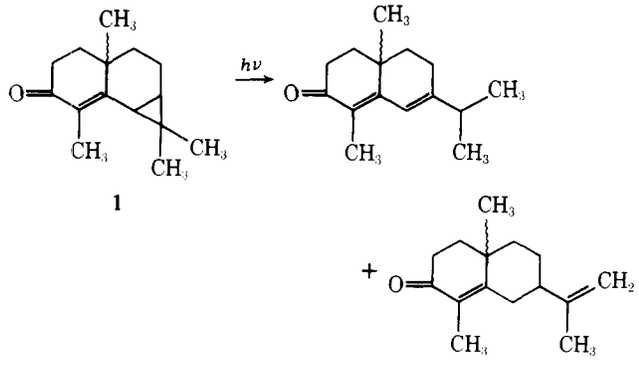
The photocycloaddition of a 3-keto-4,6-diene steroid **6** to 2,3-dimethylbutadiene formed the [4:4:4] ring adduct **7**, as well as the alternative [5:4:5] ring adduct **8**, which were differentiated mainly by their NMR spectra. The major product was the trans-4α,5β-[4 + 2] adduct **9**. Two other products were the 6α,7α- and 6β,7β-cis-[4 + 2] adducts. In agreement with past results, the direct irradiation of the 6α,7α- and 6β,7β-cyclopropylenones **4** and **5** demonstrated their remarkable photostability. They were also stereochemically stable when irradiated in the presence of dienes. However, the irradiation of both **4** and **5** in the presence of 2,3-dimethylbutadiene led to the same photoproduct **13** where both the double bond and the 6,7-cyclopropane bond of the steroids had added to both double bonds of the diene to form a [5:4:6] ring adduct. An equivalent head-to-head adduct is formed with 1-acetoxybutadiene. The photocycloaddition is not quenched with 3,3,4,4-tetramethyldiazetidine-1,2-dione indicating the singlet state, or a very short lived triplet, as the reactive state.

The investigation of the photochemistry of conjugated cyclopropylenones has been primarily concerned with either bond reorganizations of the cyclopropyl group or the influence of the cyclopropyl group upon the di-π-methane rearrangement. Direct irradiation of the epimeric *gem*-dimethylcyclopropylenones **1** caused opening of the external cyclopropyl bond and formation of two dienones.[1,2] Incidental to these results was the observation that these cyclopropylenones do not interconvert under the irradiation conditions, i.e., they maintain their stereochemical integrity.[1]



1

In direct contrast to this facile ring opening was the total lack of reactivity found by Schaffner when the 6,7-cyclopropyl-3-keto-4-ene steroids were irradiated.[3] Again these isomeric cyclopropyl steroids **2** and **3** were not interconverted upon prolonged irradiation.[4] When the cyclopropylenone chromophore was part of a seven-membered ring, a bicyclic system was formed by a formal [$_\pi$2 + $_\sigma$2] cycloaddition between the internal cyclopropane bond and the double bond.[5] Our interest in this area stems from our investigations of the

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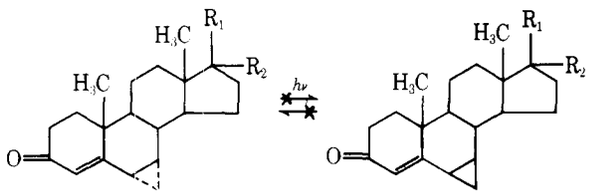
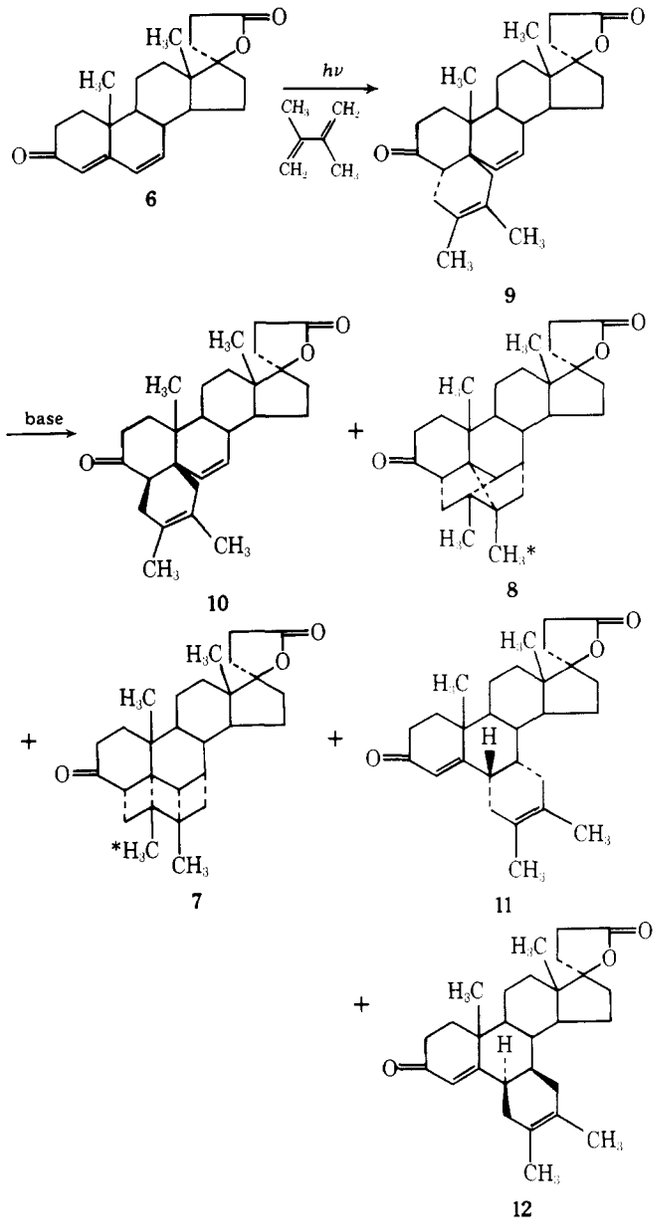


2, R_1 = H; R_2 = OAc
4, R_1 = R_2 = $-(CH_2)_2CO_2-$

3
5

photocycloaddition reactions of a linear steroidal dienone to various dienes whereby numerous novel cycloadducts are formed.[6] Adducts corresponding to [$_\pi$2 + $_\pi$2 + $_\pi$2 + $_\pi$2], cis-[$_\pi$4 + $_\pi$2] (across the γ,δ-steroid double bond), and trans-[$_\pi$4 + $_\pi$2] (for the α,β bond) additions of the dienone to the diene have been isolated and characterized. It was of interest to us to determine what the effect on the various cycloaddition modes would be if the γ,δ double bond of the dienone was replaced by a cyclopropane ring. This report then details the reaction of the cyclopropylenones **4** and **5** with dienes. Additionally, because of the importance of some of the diene adducts of the linear dienone to the structural elucidation of the adduct of **4** and **5** with dienes, this photocycloaddition is also described.

When the 3-keto-4,6-diene steroid **6** was irradiated in the presence of 2,3-dimethylbutadiene, a number of adducts were formed which could be separated by careful low-pressure chromatography on silica gel.[7] The first compound isolated in 6% yield was identified as the ladder compound **7** wherein both double bonds of the dienone had added across both diene double bonds in a [$_\pi$2 + $_\pi$2 + $_\pi$2 + $_\pi$2] cycloaddition to form a [4:4:4]-ring system. However, in contrast to the addition of dienone **6** to butadiene,[6] a second adduct **8**, closely following **7**, was isolated in 4% yield. This was identified as the alternative [$_\pi$2 + $_\pi$2 + $_\pi$2 + $_\pi$2] adduct where the dienone had added the diene to form a [5:4:5]-ring system. The same type of ring system was found by Srinivasan in the intramolecular photocycloaddition of 1,5-cyclooctadiene.[8] Although adducts **7** and **8** have many spectral similarities, they can be readily differentiated. The ^{13}C NMR spectra of **7** and **8** are both consistent with either structure, both compounds having the same number of carbon multiplicities. Their mass spectra are simple with the ladder compound **7** showing only a parent and a base peak corresponding to the retrocycloaddition, which is the loss of the diene with the transfer of a hydrogen to the dienone. Compound **8** is similar with the only notable difference being in the loss of a methyl group from the parent peak. The low positive molecular amplitude in the ORD spectrum and the positive CD spectrum of isomer **7** is consistent with α substitution and an almost planar AB-ring system and is very similar to the $4\alpha,5\alpha$-cyclobutane derivative of testosterone.[9] In contrast, in the alternative isomer **8**, the [5:4:5]-ring system allows the A ring of the steroid to more nearly approach the cyclohexanone chair form, although it is still significantly flattened. This is reflected in a greater molecular amplitude and molecular ellipticity for compound **8** than its isomer **7**. The most pertinent differences between these two compounds occur, however, in their NMR spectra and solvent-induced shifts.[10] Inspection of a model of **7** indicated that the methyl group at C-5′, which was derived from the diene (starred in formula), is in the deshielding cone of the C3-carbonyl group and would be expected to be further deshielded in benzene while the other diene derived methyl group would be unaffected. In a series of compounds related to **7**, this was borne out with the methyl group at C-5′ being deshielded and roughly equivalent to the chemical shift of the C-10 methyl group and further deshielded by δ 0.15 to 0.25 when the spectra were recorded in deuteriobenzene, while the methyl group attached to C-6′ was unaffected.[11] In the unsubstituted



6
9
10
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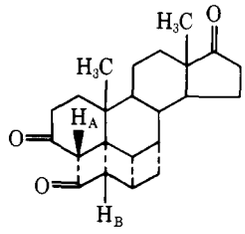
11
12

compounds related to **7**, the proton at C-5′ is much more deshielded and is shifted well out of the methylene envelope. Additionally, the structure represented by structure **7** is on firm ground since it can be related to the adduct, mp 291–294 °C, derived from the addition of the dienone to 1-acetoxybutadiene, which has been saponified and oxidized to a ladder compound containing a cyclobutanone carbonyl group.[11] The occurrence of the cyclobutanone carbonyl group at 1775 cm^{-1} confirms the ladder structure since the alternative addition mode would have generated a [5:4:5] ring system which would have yielded an additional cyclopentanone carbonyl group after hydrolysis and oxidation. The magnitude of the deshielding effect of the C-3-cyclohexanone carbonyl group on the C-5′-hydrogen (H_B) is demonstrated by its ^1H NMR resonance at δ 3.27 as a doublet (J = 2.5 Hz) while the C4-β-hydrogen (H_A), which is vicinal to the two carbonyl groups,



resonates as a singlet at δ 2.79. In addition, with the two isoprene ladder adducts, one shows a strongly deshielded proton and a tertiary methyl group at normal frequency while the other isomer does not have any single proton resonances below the normal values; the new tertiary methyl group is substantially deshielded. These observations hold for the entire series of ladder compounds synthesized by the photocycloaddition of linear dienones to acyclic dienes.

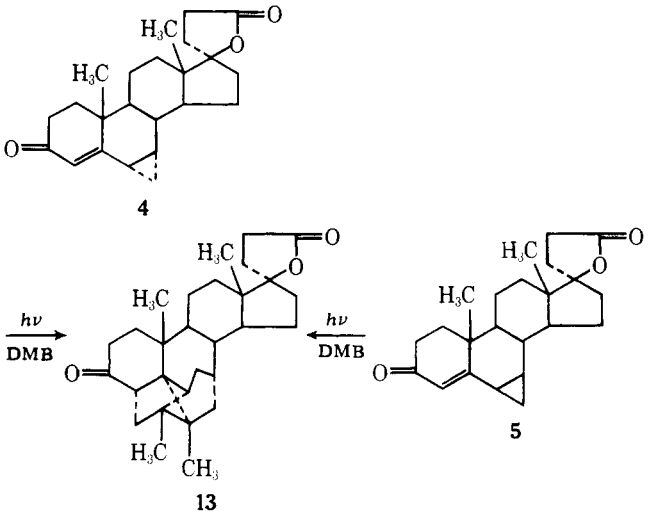
In contrast, inspection of a Dreiding model of the alternative isomer **8** indicated that one of the diene derived tertiary methyl groups, being remote from the functional groups, would appear at a normal chemical shift and would be relatively unaffected by aromatic solvents. However, the starred methyl group in **8** sits underneath the C-3 carbonyl group and the hydrogens of this methyl group are approximately 2 Å removed from the carbon–oxygen bond axis. As a result, this methyl group would be expected to be shielded, and even further shielded upon recording the spectrum in deuteriobenzene. In compound **8**, the methyl group remote from the carbonyl resonates at δ 1.07, while the other methyl group appears at δ 0.52, which further shifts to δ 0.35 in deuteriobenzene.[12]

The next chromatography fractions yielded a mixture of cis- and trans-[4 + 2] adducts **9** and **10** in 32% yield, from which a small amount of the trans-4α,5β-adduct **9** could be isolated by fractional crystallization. This compound was readily identified by the presence of two angular methyl groups and two vinylic methyl groups in its ^{1}H NMR spectrum, while the 4α substitution was indicated by a positive Cotton effect in its ORD spectrum and a positive CD curve. Epimerization with sodium methoxide in methanol yielded the cis-4β,5β-[4 + 2]-adduct **10**, as indicated by strongly negative ORD and CD curves. The reason for the ease of epimerization is the rigid 4α,5β-trans fusion forces the A ring of the steroid to adopt a conformation which is equivalent to that of an AB-trans steroid, i.e., planar. Epimerization at C-4 relieves the 1,2-diaxial interaction between the C-10 angular methyl group and the C-5 allylic methylene group. This also allows the AB-cis-ring fusion to attain its most thermodynamically stable configuration and also places the C4 substituent in the more stable equatorial configuration.

Closely following compound **9** was the cis-6α,7α-[4 + 2]-adduct **11** which was isolated in 27% yield. This compound was characterized by an enone absoption in UV and IR. The NMR spectrum again indicated the presence of two angular methyl groups and two vinylic methyl groups. The configuration was determined to be 6α,7α when allylic coupling was observed between the C-4 proton and the pseudoaxial 6β-hydrogen,[13] and when **11** was recovered unchanged from methanolic sodium methoxide solution. The 6β,7β-[4 + 2]-isomer **12** was isolated in 6% yield and possessed the expected spectral properties. In particular, the C-4 enone hydrogen appears as a sharp singlet due to the absence of allylic coupling between this proton and the pseudoequatorial 6α-hydrogen.[13] The 6β,7β isomer is the only one of the four possible cis and trans isomers where the C-6 proton is pseudoequatorial and would not be coupled to the allylic C-4-hydrogen. Compound **12** is also stable to sodium methoxide in methanol. Had either of these compounds **11** or **12** been trans fused, either 6α,7β or 6β,7α, the C-6-proton must necessarily be pseudoaxial and coupled to the C-4-hydrogen. The distortion caused by this ring fusion forces both the steroid A and B rings into the boat conformation. Then epimerization at C-6 with sodium methoxide would allow the steroid A and B rings to attain their stable conformations and also lead to a strain free ring junction between the newly formed ring and ring B. Therefore on the basis of their chemical and spectral properties, the 6,7-[4 + 2] adducts **10** and **11** were assigned the stable cis-6α,7α and cis-6β,7β stereochemistry, respectively.

The 6,7-cyclopropylenones **4** and **5** were prepared by 1,6 addition of dimethyloxosulfonium methylide to the dienone **6**[3,14,15] and were separated according to the published procedure.[16] Both compounds have a $\pi \rightarrow \pi^*$ transition at approximately 260 nm and a $n \rightarrow \pi^*$ band at approximately 325 nm. We have confirmed the surprising photostability of these steroidal cyclopropylenones, **4** and **5**. Under conditions of direct irradiation with a medium pressure mercury arc (Pyrex filter), the only observable reaction is a slow degradation of the steroids to undefined material. Under these conditions there is *no* detectable epimerization of the cyclopropane ring in either isomer from either direction, as was previously reported by Schaffner.[3] Gas chromatographic separation[16] of enones **4** and **5** would have allowed detection of a fraction of a percent of isomerization.

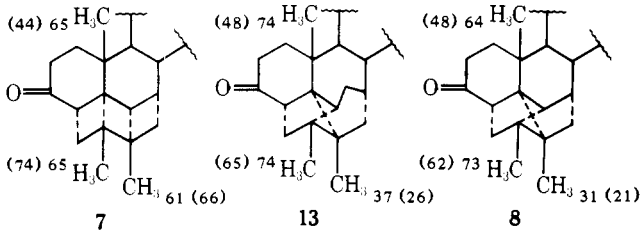
When the 6α,7α-cyclopropylenone **4** was irradiated in the presence of 2,3-dimethylbutadiene, a slow reaction occurred to form a single compound **13** in 69% yield. In addition, 16% of unisomerized starting material **4** was recovered. That the new product **13** was indeed an adduct of enone **4** and the diene was proven by its analysis and mass spectrum. In the NMR spectrum of adduct **13**, there were no olefinic resonances corresponding to the initial five olefinic protons, and the appearance of two new tertiary methyl group signals indicated that both the steroidal double bond and one of the cyclopropyl bonds had added to both diene double bonds. The ^{13}C NMR spectrum of **13** demonstrated the loss of all the olefinic carbons and the cyclopropane carbon atoms. The spectrum also



demonstrated that the only remaining functional group in the molecule, excepting the remote C-17 lactone, was the carbonyl group at C-3. An analysis of the off-resonance proton-decoupled spectrum indicated that compound **13** was a homologue of either **7** or **8**, which contained an extra methylene unit. The ORD/CD spectra indicated 4α substitution and **13** was recovered unchanged from refluxing methanolic sodium methoxide solution. When the 6β,7β-cyclopropyl isomer **5** was irradiated under equivalent conditions, a much slower reaction occurred to again generate a single photoproduct in 12% yield (20% based on recovered starting material **5**), together with substantial steroid degradation, although 29% of the unepimerized 6β,7β isomer was recovered. This photoproduct **13** was identical in all respects to that obtained from the 6α,7α-isomer **4**. When either **4** or **5** was irradiated in the presence of dimethylbutadiene and monitored as a function of time by gas chromatography, no epimerization into the other isomer was observed. This precluded an exiplex mediated isomerization analogous to the diene-catalyzed dimerization of 9-phenylanthracene.[17] On this basis, the photoepimerization of the cyclopropylenones and subsequent opening of an exocyclic cyclopropyl ring bond was excluded.[18] Indeed,

this mechanism was not very probable, for epimerization would involve opening of the steroidal 6,7-cyclopropane bond, followed presumably by a second photochemical reaction with specific opening of the exocyclic cyclopropane bond to generate the observed adduct. This is especially so since the quantum yield for adduct formation is obviously very low and epimerization would have been observed in view of the 50:1 ratio of resultant photoproduct **13** to contaminating 6α,7α-cyclopropyl-**4** in the starting 6β,7β-cyclopropyl-**5** had this mechanism been operative. The result then of these experiments is that the internal 6,7-steroidal cyclopropane bonds in the cyclopropylenones **4** and **5** are involved in the cycloaddition.

Since the 6,7-steroid cyclopropyl bond is involved in the cycloaddition, the structure of the photoproduct **13** is a ring B homologue of either the ladder compound **7** or the alternate isomer **8**. Consideration of Dreiding models of both homologues leads to the conclusion that while the seven-membered steroid B ring allows a small amount of flexibility in the A ring, the chemical shifts of the substituents observed in either adduct **7** or the alternative **8** should be very similar to those of the photoproduct **13**. The only functional group remaining in the photoproduct from the dienone and diene chromophores is the C-3 carbonyl group. In the ladder compound **7**, one of the diene derived methyl groups is moderately deshielded by this carbonyl group while in the alternate isomer **8** one of these methyl groups is strongly shielded. The difference in chemical shifts between **7** and **8** is δ 0.57 in deuteriochloroform, and the opposite direction in chemical shifts expands this to δ 0.88 in deuteriobenzene. Therefore comparison of the chemical shifts of the methyl groups in the photoproduct **13** with those of the model compounds **7** and **8** will allow a choice between the [4:4:5] ring and the [5:4:6] ring adducts. The numbers given next to the methyl substituents on the partial structures **7**, **8**,



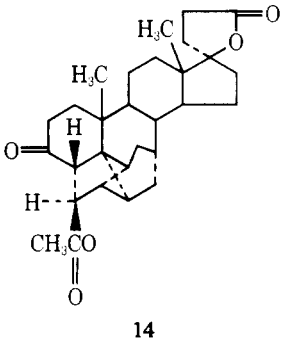
7 **13** **8**

and **13** are the chemical shifts in hertz at 60 MHz in deuteriochloroform, while the numbers in parentheses correspond to the chemical shift in deuteriobenzene. As can be readily seen, one of the diene derived methyl groups is strongly shielded in **13**, and is even more strongly shielded in deuterobenzene, analogous to the alternative diene dienone isomer **8**. In contrast, there are no downfield shifts as is observed in the [4:4:4]-ladder compounds, of which **7** is a member. On this basis, **13** was assigned the [5:4:6]-ring structure, homologous to **8**.

Addition of the 6α,7α-cyclopropylenone **4** to 1-acetoxybutadiene was also studied. Again the reaction was very slow, 8.5 mmol of **4** were irradiated for 71 h until the reaction stopped, due to polymerization of the diene, at approximately 50% consumption of **4**. However, chromatography and careful crystallization allowed the isolation of one of the photoproducts **14** in about 90% purity. The photoproduct was one of a pair of epimers and was determined to have the structure indicated by **14** by decoupling experiments in deuteriobenzene. The α-acetoxy proton resonated at δ 4.38 as a slightly broadened doublet which double irradiation indicated was coupled to the 4β proton at δ 3.12. Irradiation of the 4β proton collapsed the α-acetoxyproton into a slightly broadened singlet. This is clearly incompatible with this proton being part of a cyclobutane ring.[19] Inspection of a model of **14** indicates that the α-acetoxyproton forms approximately an 85° dihedral angle with the vicinal hydrogen and little, if any, coupling would be expected.[20] Hydrolysis of **14** and subsequent oxidation unfortunately did not lead to definable products probably due to fragmentation and oxidation of the intermediate aldol.[21] The presence of the head-to-tail isomers has not been rigidly excluded but the head-to-tail ladder adducts are not observed in the dienone–diene photocycloadditions.

The photocycloaddition of **4** to 2,3-dimethylbutadiene was not quenched by Ullman's quencher, 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide, implicating the singlet state of **4**, or a very short-lived triplet state, as the reactive species.[22]

Thus the cycloaddition of 6,7-cyclopropylenones to dienes is a unique example of a [$_{\pi}2 + _{\pi}2 + _{\pi}2 + _{\sigma}2$] cycloaddition which is "allowed" suprafacially between an even number of components.[23] However, an initial [$_{\pi}4 + _{\pi}2 + _{\sigma}2$] cycloaddition, followed by either a second photochemical, or a thermal, ring closure, cannot be excluded.[24] This type of cycloaddition is unlikely, however, since although inspection of a model of the [$_{\pi}4 + _{\pi}2 + _{\sigma}2$] adduct does indicate some unfavorable steric interactions, there is nothing which would obviously preclude its existence. Since the [4:4:4]-ring system found in dienone–diene ladder compounds of type **7** is undoubtedly less stable than the [5:4:5] system obtained as an additional product in the addition of the excited dienone to dimethylbutadiene, formation of compounds like **7** must occur via maximum orbital overlap between the π systems of the diene and the dienone.[25] The addition of the cyclopropylenones to dienes reflects the less common reaction mode in dienone cycloadditions. However, this does offer the advantage of minimizing



14

the steric interference between the α-cyclopropane ring and the diene in the approach of the excited enone to the diene, and additionally offers the potential for secondary orbital overlap between the diene and the exocyclic cyclopropyl bonds.[26] This lack of secondary orbital overlap may be the reason that the cycloaddition of the 6β,7β-cyclopropylenone to dimethylbutadiene is less facile than with its 6α,7α isomer. Also, since the cycloaddition of 6α,7α-cyclopropylenone to the diene involves inversion at both steroid 6,7 positions and since at some point along the reaction coordinate for the 6α,7α-cyclopropylenone cycloaddition this reaction coordinate becomes identical with that of the 6β,7β-cyclopropylenone and, if the reaction were not concerted, reversal would lead to photoepimerization of the cyclopropane rings. Since this is not observed with either isomer, the reaction has to be concerted.

Experimental Section

General. Melting points were taken on a Thomas-Hoover Uni-Melt capillary apparatus and are uncorrected. IR spectra were run in potassium bromide and UV spectra were run in methanol and are not reported if only n → π^* absorption was observed. A Varian Associates A-60 or HA-100 nuclear magnetic resonance spectrometer was used to record spectra, which were run in deuteriochloroform, unless otherwise stated, using tetramethylsilane as an internal standard. Spectra are reported as chemical shifts, followed by the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; the coupling constant, in hertz, where appropriate, which is followed by integrated signal intensity. ^{13}C NMR spectra were run in deuteriochloroform at 25.7

MHz. Optical Rotatory Dispersion–Circular Dichroism spectra were obtained on methanol solutions using a Durrum-Jasco J-20 spectrometer. Optical rotations were determined in chloroform on a Perkin-Elmer Model 141 polarimeter.

The sample of the dienone **6** (Searle Chemicals) used in this study showed only one peak on a GLC trace and has UV absorption at 282 nm (ε 27 000) in methanol and n → π* absorption which is resolved in benzene at 350 nm (ε 90). The 6,7-cyclopropylenones were prepared according to the published procedure.[3,14-16] The 6β,7β-cyclopropylenone **5**, 6α,7α-dihydro-17β-hydroxy-3-oxo-3′*H*-cyclopropa[6,7]-pregna-4,6-diene-21-carboxylic acid γ-lactone, possesses: mp 171.5–175.5 °C; UV 263.5 nm (ε 18 750), [C_6H_6] 328 nm (ε 80), [ethyl acetate] 325 nm (ε 75); $[\alpha]^{25}_{589}$ −173° (*c* 1.04%), $[\alpha]^{25}_{365}$ −6.2°. The sample of **5** used was analyzed by GLC, according to published procedure,[16] and contained 98.6% **4**, 0.4% of the α-isomer **5**, and 1.0% of the dienone **6**. The isomeric 6α,7α-cyclopropylenone **4**, 6β,7β-dihydro-17β-hydroxy-3-oxo-3′*H*-cyclopropa[6,7]-pregna-4,6-diene-21-carboxylic acid γ-lactone, possesses: mp 169–171 °C; UV 260 nm (ε 16,750), [C_6H_6] 326 nm (ε 75), [ethyl acetate] 326 nm (ε 75); $[\alpha]^{25}_{589}$ +99° (*c* 1.026%), $[\alpha]^{25}_{365}$ +2035°. The sample of **4** used contained 95.2% of **4**, 1.3% of isomeric 6β,7β-cyclopropylenone **5**, and 3.5% of the dienone **6**.

The Photocycloaddition of the 4,6-Diene-3-one 6 to 2,3-Dimethylbutadiene. A solution of 5.00 g (14.7 mmol) of the dienone **6** in 165 mL of ethyl acetate and 25 mL of redistilled 2,3-dimethylbutadiene (99%, Chemical Samples) was irradiated, under argon, with a 450-W medium-pressure mercury arc (Pyrex) for 2.5 h. The solvent was evaporated and the residue chromatographed on 250 g of Woelm silica utilizing low pressure. Elution with 9:91 ethyl acetate–toluene yielded 284 mg (0.67 mmol, 6%) of the ladder compound **7**, [3*S*-(3α,3aα,5aβ,5bα,9β,9a*R**,10α,11α,11aα,12β,12aα,12bβ)]-hexadecahydro-3a,5b,10,11-tetramethylspiro[9,10:11,12-dimethanocyclobuta[*k*]cyclopenta[*a*]phenanthrene-3,2′(5′*H*)-furan]-5′,8-dione:[27] mp 224–226 °C (ethyl acetate–petroleum ether); IR 1775 cm^{-1}, 1700; NMR δ 1.09 (s, 6 H), 1.03 (s, 3 H), 0.97 (s, 3 H), [C_6D_6] 1.24 (s, 3 H), 1.10 (s, 3 H), 0.85 (s, 3 H), 0.73 (s, 3 H); ^{13}C NMR δ 213.8 (s), 176.7 (s), 96.0 (s), 60.5 (s), 56.1 (s), 53.8 (d), 53.7 (t), 47.2 (d), 46.1 (s), 44.8 (d), 43.5 (s), 42.6 (d), 40.4 (d), 39.1 (s), 37.6 (t), 35.5 (t), 34.6 (t), 34.0 (d), 32.0 (t), 31.9 (t), 31.4 (t), 29.4 (t), 22.9 (t), 20.8 (t), 17.7 (q), 17.1 (q), 14.8 (q), 12.1 (q); ORD $[\phi]_{317}$ + 2872°; $[\phi]_{283}$ + 1270°, *a* = +16; CD $[\theta]_{297}$ + 2316°; $[\alpha]^{25}_{589}$ + 95.8° (*c* 0.992%), $[\alpha]^{25}_{365}$ +409°; MS *m/e* (rel %) 422 (parent peak, 12%), 407 (-methyl, 6%), 341 (-diene + H, 100%).

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.42; H, 9.05.

Continued elution with the same solvent combination yielded 251 mg (0.59 mmol, 4%) of the alternative isomer **8**, [3′*R*-(3′α,3′aα,5′aβ,5′bα,8′aα,10′α,10′aβ,10′bα,12′α,12′aα,12′bβ,13′*R**)]-octadecahydro-3′a,5′b,10′,10′a-tetramethylspiro[furan-2(5*H*),3′-[3*H*-10,10b,12]methenobenz[*cd*]indeno[5,4-f]azulene]-5,8′(3′a*H*)-dione:[27] mp 202–204.5 °C (ether–petroleum ether); IR 1775 cm^{-1}, 1700; NMR δ 1.22 (s, 3 H), 1.07 (s, 3 H), 0.90 (s, 3 H), 0.52 (s, 3 H), [C_6D_6] 1.03 (s, 3H), 0.93 (s, 3 H), 0.80 (s, 3 H), 0.35 (s, 3 H); ^{13}C NMR δ 216.1 (s), 176.7 (s), 96.0 (s), 52.3 (s), 48.6 (s), 48.2 (d), 45.6 (t), 45.2 (d), 43.1 (d), 42.9 (d), 40.3 (s), 35.6 (t), 35.1 (s), 34.5 (d), 33.8 (t), 32.0 (t), 31.4 (s), 30.9 (2 × t), 29.3 (t), 29.0 (d), 28.1 (t), 22.7 (t), 20.3 (t), 18.2 (q), 17.7 (q), 14.6 (q), 12.2 (q); ORD $[\phi]_{310}$ + 1890°, $[\phi]_{280}$ 0°, $[\phi]_{275}$ −175°, *a* = +21; CD $[\theta]_{290}$ +2180°; $[\alpha]^{25}_{589}$ +33.2° (*c* 0.112%); $[\alpha]^{25}_{365}$ +180.3°; MS *m/e* (rel %) 422 (parent, 17%), 407 (-methyl, 29%), 341 (-diene + H, 100%).

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.40; H, 8.99.

Further elution gave a mixture of the cis-4β,5β-[4 + 2]-epimer **10** and the trans-4α,5β-[4 + 2]-adduct **9**. The fairly unstable trans-isomer **9** could be isolated in low yield, 350 mg (0.83 mmol, 6%), by careful and slow crystallization of the mixture from ether. Compound **9**, 3′,6′-dihydro-17-hydroxy-4′,5′-dimethyl-3-oxo-1′*H*,4β,5β,17α-benzo[4.5]androst-6-ene-17α-propionic acid γ-lactone, possesses: mp 218–223 °C; IR 1775 cm^{-1}, 1720; NMR δ 5.58 (s, 2 H), 1.66 (d, 6 H), 0.97 (s, 6 H); ORD $[\phi]_{305}$ +4360°, $[\phi]_{285}$ 0°, $[\phi]_{274}$ −1635°, *a* = +60; $[\theta]_{289}$ +5535°; $[\alpha]^{25}_{589}$ +52° (*c* 0.108%), $[\alpha]^{25}_{365}$ +250°.

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.40; H, 9.09.

The remainder was dissolved in 100 mL of methanol and 2 g of sodium methoxide was added. After standing for 18 h, and subsequent neutralization with dilute hydrochloric acid, the methanol was evaporated and the crystalline residue filtered. Recrystallization from methanol–water yielded 1.58 g (3.74 mmol, 26%) of the 4β,5β-[4 + 2] epimer, **10**, 3′,6′-dihydro-17-hydroxy-4′,5′-dimethyl-3-oxo-1′*H*,4α,5β,17α-benzo[4,5]androst-6-ene-17α-propionic acid γ-lactone: mp 180–183 °C; IR 1770 cm^{-1}, 1720; NMR δ 5.53 (s, 2 H), 1.68 (broad s, 3 H), 1.58 (broad s, 3 H), 1.00 (s, 3 H), 0.86 (s, 3 H); ORD $[\phi]_{307}$ −7440°, $[\phi]_{294}$ 0°, $[\phi]_{250}$ + 12 680, *a* = −201; CD $[\theta]_{291}$ −15380°.

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.37; H, 9.36.

Closely following this mixture was 1.60 g (5.79 mmol, 27%) of the *cis*-6α,7α-[4 + 2]-adduct **11**, 3′,6β,6′,7β-tetrahydro-17-hydroxy-4′,5′-dimethyl-3-oxo-17α-benzo[6,7]androsta-4,6-diene-17α-propionic acid γ-lactone, possesses: mp 143 °C (methanol–water); IR 1780 cm^{-1}, 1675, 1620; UV 240 nm (ε 12 500); NMR δ 5.58 (d, *J* ≃ 1.5 Hz, 1 H), 1.65 (broad s, 3 H), 1.56 (broad s, 3 H), 1.38 (s, 3 H), 1.00 (s, 3 H); $[\alpha]^{25}_{589}$ −31° (*c* = 1%), $[\alpha]^{25}_{365}$ −228°.

Anal. Calcd for $C_{28}H_{38}O_3 \cdot 0.5H_2O$: C, 77.92; H, 9.11. Found: C, 77.73; H, 8.94.

Elution with ethyl acetate–toluene (14:86) furnished 345 mg (0.82 mmol, 6%) of the highly crystalline *cis*-6β,7β-[4 + 2]-adduct **12**, 3′,6α,6′,7α-tetrahydro-17-hydroxy-4′,5′-dimethyl-3-oxo-17α-benzo[6,7]androsta-4,6-diene-17α-propionic acid γ-lactone: mp 249–252 °C (ether); IR 1775 cm^{-1}, 1665, 1615; UV 244 nm (π 14 400); NMR δ 5.72 (s, 1 H), 1.61 (s, 6 H), 1.36 (s, 3 H), 0.98 (s, 3 H); $[\alpha]^{25}_{589}$ −18.7° (*c* 0.097%), $[\alpha]^{25}_{365}$ +877°.

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.88; H, 9.04.

Further elution with 1:4 ethyl acetate–toluene returned 785 mg (16%) of starting dienone **6**.

The Photocycloaddition of the 6α,7α-Cyclopropylenone 4 to Dimethylbutadiene. A solution of 3.00 g (8.47 mmol) of **4** in 160 mL of ethyl acetate and 30 mL of redistilled 2,3-dimethylbutadiene (Chemical Samples) was irradiated, under argon, with a 450-W medium-pressure mercury arc (Pyrex filter) for 47.5 h. After 23 h, an additional 10 mL of diene was added to replace lost solvent. During the irradiation, a new compound slowly appeared on the TLC plates and grew at the expense of starting material. After the irradiation was terminated the TLC plates showed diene dimer formation and some degradation as evidenced by substantial streaking, although the irradiation solution was still clear. After removal of the solvent, the residue was chromatographed on 400 g of Mallinckrodt CC-7 silica. Elution with 5% ethyl acetate–benzene furnished 2.53 g (5.80 mmol, 69%) of the 1:1 adduct **13**, [3*R*-(3α,3aα,5aβ,5bα,9β,-10α,11α,11aβ,13α,13aα,13bβ)]octadecahydro-3a,5b,10,11-tetramethylspiro[9,11:10,13]dimethano-3*H*-benzo[3,4]cyclobuta[4,5]-cyclohept[1,2-*e*]indene[3,2′(5′H)-furan]-5′,8(9*H*)-dione:[27] mp 214–218 °C (ether–petroleum ether); IR 1780 cm^{-1} (lactone), 1705 (cyclohexanone); NMR δ 1.24 (s, 6 H), 1.08 (s, 3 H), 0.61 (s, 3 H), [C_6D_6] 1.08 (s, 3 H), 1.02 (s, 3 H), 0.78 (s, 3 H), 0.44 (s, 3 H); ^{13}C NMR δ 214.3 (s), 176.1 (s), 95.7 (s), 52.5 (s), 50.3 (d), 47.2 (s), 47.1 (s), 45.8 (2 × s), 45.4 (s), 40.6 (d), 39.0 (d), 37.5 (t), 37.3 (s), 35.5 (t), 34.7 (d), 32.9 (t), 31.6 (t), 31.5 (t), 31.3 (t), 29.2 (2 × t), 28.3 (t), 23.2 (t), 22.3 (q), 20.5 (t), 18.3 (q), 14.2 (q), 12.6 (q); $[\alpha]^{25}_{589}$ +118° [*c* 1 ($CHCl_3$)], $[\alpha]^{25}_{365}$ +1010°; ORD $[\phi]_{307}$ +2860°, $[\phi]_{291}$ 0°, $[\phi]_{266}$ −3929°, *a* = +68; CD $[\theta]_{288}$ +5414°; MS 436 (74%, parent), 421 (100%, −methyl).

Anal. Calcd for $C_{29}H_{40}O_3$: C, 79.77; H, 9.23. Found: C, 79.46; H, 9.21.

Elution with ethyl acetate–benzene (15:85) returned 0.466 g of starting cyclopropyl enone **4**. GLC on a 6 ft OV-17 column at 290 °C indicated the returned starting material was the pure α isomer and contained none of the β isomer.

Reaction of 268 mg of **13** with sodium methoxide in methanol at room temperature for 16 h returned 255 mg of unchanged **13**.

The Photocycloaddition of the 6β,7β-Cyclopropylenone 5 to 2,3-Dimethylbutadiene. A solution of 1.09 g (3.08 mmol) of **5** (98.6% β by GLC) in 160 mL of ethyl acetate and 30 mL of redistilled 2,3-dimethylbutadiene was irradiated as above. After 24 h, TLC indicated that the starting enone was mostly consumed and one new spot had appeared which had the same mobility as **13**. In addition the TLC plates were heavily streaked indicating extensive decomposition of the steroid. Chromatography yielded a fraction containing the photoproduct and crystallization over night from ether–petroleum ether yielded 144 mg (12%) of **13** which was identical in physical spectra, TLC, mp, mmp, and GLC behavior with material prepared from the 6α,7α-isomer **4**. In addition 305 mg of starting compound **5** was recovered. GLC indicated that no epimerization had occurred.

Attempted Photoepimerization of the Cyclopropylenones 4 and 5. A solution of 121 mg of **4** in 250 mL of ethyl acetate was dissolved in 250 mL of ethyl acetate and apportioned, under nitrogen, among eight Pyrex tubes. The tubes were irradiated on a merry-go-round in a Rayonet Photoreactor using eight 3000-Å lamps. Samples withdrawn at 0.5-h intervals over 4 h indicated a slow decrease in the total amount of steroid present but no conversion into the β-isomer **5**.

The same experimental procedure on 124 mg of the β-isomer **5** yielded identical results, with no isomerization into the α-isomer **4**.

Attempted Photoisomerization of 4 and 5 in the Presence of 2,3-Dimethylbutadiene. A solution of 111.7 mg of **5** in 40 mL of ethyl acetate and 10 mL of 2,3-dimethylbutadiene was apportioned among eight Pyrex tubes and irradiated on a merry-go-round in a Rayonet Photoreactor equipped with eight 3000-Å lamps. Samples were withdrawn over 2.5 h and analyzed by GLC. Although the dienone was partially consumed, there was no change in the amounts of the cyclopropyl enones.

Equivalent results were obtained using 111.6 mg of the α-isomer **4**. The dienone was partially consumed and there was no change in the relative amounts of the cyclopropylenones.

The Photocycloaddition of the 6α,7α-Cyclopropylenone 4 to 1-Acetoxybutadiene. A solution of 3.00 g (8.47 mmol) of **4** was dissolved in 160 mL of ethyl acetate and 29.5 mL of freshly distilled 1-acetoxybutadiene was added. The irradiation was conducted under argon with a 450-W medium-pressure mercury arc (Pyrex filter). After 71 h of irradiation, the reaction had stopped after about 50% disappearance of starting steroid due to consumption of the diene. TLC indicated that in addition to starting material, one new product had appeared and substantial degradation was indicated by heavy streaking on the TLC plates. After removal of solvent, the residue was subjected to low-pressure liquid chromatography. Initial elution gave 9.4 g of diene dimers. Elution with ethyl acetate–benzene (18:85) gave a substantial oil from which 350 mg of the photoproduct **14** was obtained in two crops by careful dilution of an ether solution of the oil with petroleum ether. Compound **14** shows: mp 152–160 °C; IR 1780 cm^{-1} (lactone), 1740 (acetate), 1710 (cyclohexanone); NMR δ 4.60 (d, J = 3 Hz, 1 H, α-acetoxy H), 2.98 (broad s, 1 H, C-4-β-H), 1.99 (s, 3 H, acetate methyl), 1.15 (s, 3 H), 0.92 (s, 3 H), [C_6D_6] 4.83 (d, J = 3 Hz), 3.12 (apparent triplet, 1 H, C-4-β-H), 1.72 (s, 3 H, acetate methyl), 0.87 (s, 3 H), 0.72 (s, 3 H). Irradiation of the signal at δ 4.83 collapsed the δ 3.12 signal to a doublet ($J \leq 1$ Hz), while irradiation of the δ 3.12 signal collapsed the signal at δ 4.83 to a slightly broadened singlet: ORD $[\phi]_{309}$ + 1350°, $[\phi]_{296}$ 0°, $[\phi]_{267}$ −3775°, a = +51; CD $[\theta]_{290}$ +2516°.

Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.65; H, 8.21. Found: C, 74.45; H, 8.55.

Starting material was eluted closely following the photoproduct but was not recovered due to accidental breakage of the recovery flask. However, a portion of the solution which was saved again showed no isomerization of the α isomer to the β isomer.

Attempted Quenching of the Photocycloaddition of the α Isomer 4 to 2,3-Dimethylbutadiene. A 3.16×10^{-2} M solution of **4** in a 15:35 v/v mixture of 2,3-dimethylbutadiene and ethyl acetate was irradiated simultaneously in the presence and absence of 1.16×10^{-2} M 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide using a 450-W mercury arc (Pyrex filter). The reaction was conducted to 20% formation of the photoadduct, and allowing for the partial absorbtion of the quencher, there was no evidence for quenching of the reaction.

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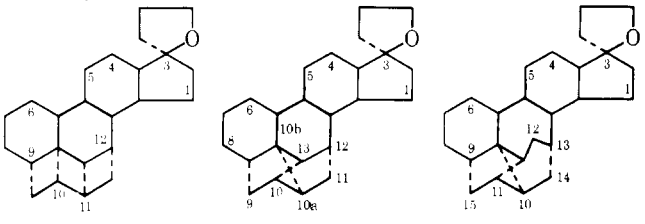
Registry No.—**4**, 49848-04-6; **5**, 40574-52-5; **6**, 976-71-6; **7**, 69330-99-0; **8**, 69331-00-6; **9**, 69331-01-7; **10**, 69331-02-8; **11**, 69331-03-9; **12**, 69331-04-0; **13**, 69352-38-1; **14**, 69352-37-0; 2,3-dimethylbutadiene, 513-81-5; 1-acetoxybutadiene, 1515-76-0.

References and Notes

(1) β-Methyl: A. E. Greene, J.-C. Muller, and G. Ourisson, *Tetrahedron Lett.*, 4147 (1971).
(2) α-Methyl: P. J. Kropp and H. J. Krauss, *J. Org. Chem.*, **32**, 4118 (1967).
(3) J. Pfister, H. Wehrli, and K. Schaffner, *Helv. Chim. Acta*, **50**, 166 (1967).
(4) A personal communication from Professor D. Arigoni to Professor K. Schaffner, quoted in ref 3, indicated that 9α,10α- and 9β,10β-3-oxo-1-ene-9,10-cyclopropyltriterpene derivatives were interconverted by a reversible opening of the internal (9,10) cyclopropane bond.
(5) (a) L. A. Paquette, G. V. Meehan, and R. F. Eizember, *Tetrahedron Lett.*, 995 (1969); (b) L. A. Paquette, G. V. Meehan, and R. F. Eizember, *ibid.*, 999 (1969); (c) L. A. Paquette, G. V. Meehan, R. P. Henzel, and R. F. Eizember, *J. Org. Chem.*, **38**, 3250 (1973); (d) L. A. Paquette, R. P. Henzel, and R. F. Eizember, *J. Org. Chem.*, **38**, 3257 (1973).
(6) (a) G. R. Lenz, *Tetrahedron Lett.*, 3027 (1972); (b) *ibid.*, 2483 (1977).
(7) This diene was chosen because of the facility of differentiating between the various adducts by differences in their NMR spectra due to the 2,3-methyl groups.
(8) (a) R. Srinivasan, *J. Am. Chem. Soc.*, **85**, 819 (1963); (b) R. Srinivasan, *ibid.*, **85**, 3048 (1963); (c) R. Srinivasan and K. A. Hill, *ibid.*, **87**, 4988 (1965).
(9) G. R. Lenz, *Tetrahedron*, **28**, 2195 (1972).
(10) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964, p 172.
(11) G. R. Lenz, unpublished observations. The full report detailing the photocycloaddition of dienones to Diels–Alder dienes is in preparation.
(12) The apparent reason for obtaining both isomers (**7** and **8**) with 2,3-dimethylbutadiene, as opposed to only the ladder compound **7** with butadiene (ref 6), appears to be steric in origin. The [5:4:5]-ring system is undoubtedly more stable than the [4:4:4]-ring system. When a substituent, other than hydrogen, is attached to C-5′ severe steric interactions occur between it and the axial protons at C-1 and C-9. The interactions appear to be strong enough to overcome the orbital overlap effects and allow formation of the [5:4:5]-ring system which minimizes the steric interactions.
(13) (a) D. J. Collins, J. J. Hobbs, and S. Sternhell, *Aust. J. Chem.*, **16**, 1030 (1963); (b) T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Am. Chem. Soc.*, **85**, 1699 (1963).
(14) G. E. Arth, G. F. Reynolds, G. H. Rasmusson, A. Chen, and A. A. Patchett, *Tetrahedron Lett.*, 291 (1974).
(15) H. Laurent and R. Wiechert in "Organic Reactions in Steroid Chemistry", Vol. II, J. H. Fried and J. A. Edwards, Eds., Van Nostrand-Reinhold, New York, 1972, Chapter 10.
(16) J. F. Zawadzki and L. J. Chinn, German Offen., 2410853 [*Chem. Abstr.*, **82**, P31462Z (1975)].
(17) R. O. Campbell and R. S. H. Liu, *Chem. Commun.*, 1191 (1970).
(18) An opening of the exocyclic cyclopropane bonds in **2** and **3** was reasonably postulated by Schaffner (ref 3) to account for their photostability and their lack of phosphoresence, or triplet energy transfer to naphthalene. An alternative possibility involves stretching of the disubstituted steroidal 6,7-cyclopropane bond, but not breaking of it, so that the cyclopropane ring does not achieve coplanarity with the steroid B ring. In this way, photoepimerization is avoided and the reversible opening of the tetrasubstituted internal cyclopropane bond observed by Arigoni (ref 4) can be accommodated.
(19) (a) J. Fleming and D. H. Williams, *Tetrahedron*, **23**, 2747 (1967); (b) H. Weitkamp and F. Korte, *Tetrahedron, Suppl.*, **7**, 75 (1966).
(20) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
(21) (a) P. DeMayo, *Acc. Chem. Res.*, **4**, 41 (1971); (b) P. G. Sammes, *Q. Rev., Chem. Soc.*, **24**, 37 (1970); (c) P. G. Sammes, *Synthesis*, 636 (1970).
(22) E. Ullman and P. Singh, *J. Am. Chem. Soc.*, **94**, 5077 (1972).
(23) R. B. Woodward and R. Hoffman, "The Conservation of Orbital Symmetry", Verlag Chemie, Weinheim/Bergstrasse, 1970, p 112.
(24) Similar cycloadducts have been observed by Yang in the photocycloaddition of anthracenes to dienes: (a) N. C. Yang, D. M. Shold, and J. K. McVey, *J. Am. Chem. Soc.*, **97**, 5004 (1975); (b) N. C. Yang, K. Srinivasachar, B. Kim, and J. Libman, *ibid.*, **97**, 5005 (1975).
(25) R. A. Caldwell and L. Smith, *J. Am. Chem. Soc.*, **96**, 2994 (1974).
(26) H. Prinzbach, G. Sedelmeier, and H.-D. Martin, *Angew. Chem., Int. Ed. Engl.*, **16**, 103 (1977).
(27) Compounds **7**, **8**, and **13** are named as furan derivatives and are numbered thusly:



7 **8** **13**