^{13}C NMR has been utilized to assign stereochemistry in an acyclic system. We anticipate the continued use of ^{13}C NMR for the assignment of stereochemistry to acyclic systems.

Experimental Section

FT ^{13}C NMR spectra were recorded at 25.144 MHz by using a Nicolet Technology Corp. TT-23 spectrometer. The sweep width was 5 or 6 kHz, with a heteronuclear lock on deuterated solvent (deuteriochloroform). Chemical shift values were determined by computer analysis of the spectra and are accurate to ±0.1 ppm. Repetition rates of 2 s with pulse angles of 70° were typical. All spectra were recorded by using ^{1}H-noise decoupling. Chemical shift values are given relative to internal deuteriochloroform signals (77.0 ppm relative to external Me_4Si).

Acknowledgment. This work was supported in part by grants from the United States Public Health Services (NIH Grant No. AI-11607 and AI-15027) and the National Science Foundation (Grant No. CHE 75-23368). M.C.P. gratefully acknowledges the Fannie & John Hertz Foundation for financial support in the form of a fellowship. We are also grateful to the National Science Foundation for providing funds for the purchase of the ^{13}C NMR spectrometer (NSF Departmental Equipment Grant No. CHE 76-05512).

Registry No. *erythro*-I-1, 14366-89-3; *threo*-I-1, 17226-79-8; *erythro*-I-2, 71699-15-5; *threo*-I-2, 71699-16-6; *erythro*-I-3, 61878-66-8; *threo*-I-3, 61878-67-9; *erythro*-I-4, 71699-17-7; *threo*-I-4, 71699-18-8; *erythro*-I-5, 36677-29-9; *threo*-I-5, 36677-30-2; *erythro*-I-6, 71699-19-9; *threo*-I-6, 71699-20-2; Cram's-I-7, 71748-71-5; anti-Cram's-I-7, 71748-75-9; *threo*-I-8, 71699-21-3; Cram's-I-9, 71699-22-4; anti-Cram's-I-9, 71748-76-0; *erythro*-I-10, 71699-23-5; *threo*-I-11, 71699-24-6; I-12, 71699-25-7; I-13, 71748-72-6; *erythro*-I-14, 71699-26-8; *erythro*-I-15, 17226-86-7; *threo*-I-15, 17226-85-6; I-16, 71699-27-9; *erythro*-I-17, 71699-28-0; *threo*-I-17, 71699-29-1; Cram's-I-18, 71699-30-4; anti-Cram's-I-18, 71748-77-1; *erythro*-I-19, 71699-31-5; *threo*-I-19, 71699-32-6; *erythro*-I-20, 67498-18-4; *threo*-I-20, 67498-07-1; *erythro*-I-21, 67498-21-9; *threo*-I-21, 67498-06-0; *erythro*-I-22, 71699-33-7; *threo*-I-22, 71699-34-8; *erythro*-I-23, 71699-35-9; *threo*-I-23, 71699-36-0; *erythro*-I-24, 71699-37-1; *threo*-I-24, 71699-38-2; *erythro*-I-25, 71699-39-3; *threo*-I-25, 71699-40-6; *erythro*-I-26, 71699-41-7; *erythro*-I-27, 71699-42-8; *threo*-I-27, 71699-43-9; *erythro*-III-1, 71699-44-0; *threo*-III-1, 71699-45-1; *erythro*-III-2, 71699-46-2; *threo*-III-2, 71699-47-3; *erythro*-III-3, 71699-48-4; *threo*-III-3, 71699-49-5; *erythro*-III-4, 71699-50-8; *threo*-III-4, 71699-51-9; *erythro*-III-5, 71699-52-0; *threo*-III-5, 71699-53-1; *erythro*-III-6, 71733-84-1; *threo*-III-6, 71699-54-2; *erythro*-III-7, 71699-55-3; *threo*-III-7, 71699-56-4; *erythro*-III-8, 71699-57-5; *threo*-III-8, 71699-58-6; *erythro*-III-9, 71699-59-7; *threo*-III-9, 71699-60-0; *erythro*-III-10, 71699-61-1; *threo*-III-10, 71699-62-2; *erythro*-III-11, 71699-63-3; *erythro*-III-12, 71699-64-4; *threo*-III-12, 71699-65-5; III-13, 71699-66-6; *erythro*-III-14, 71699-67-7; *threo*-III-14, 71699-68-8; *erythro*-III-15, 71699-69-9; *threo*-III-15, 71699-70-2; *erythro*-III-16, 71699-71-3; *threo*-III-16, 71699-72-4; *erythro*-III-17, 71699-73-5; *threo*-III-17, 71699-74-6; III-18, 71699-75-7; **14**, 50693-03-3; **15**, 71699-76-8; **16**, 71748-73-7; **17**, 71748-74-8; **18**, 71686-69-6; **19**, 71686-70-9; **20**, 71686-71-0; **21**, 54008-25-2; **22**, 71686-79-8; **23**, 71686-78-7; **24**, 71699-77-9; **25**, 71686-76-5; **26**, 54008-24-1; benzaldehyde, 100-52-7.

Supplementary Material Available: The complete ^{13}C NMR spectra of the compounds reported herein (4 pages). Ordering information is given on any current masthead page.

Steroid Photochemistry. Photocycloaddition of a Linear Dienone to Diels–Alder 1,3-Dienes[1]

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The photocycloaddition of 3-keto-4,6-dienic steroids to seven *s*-trans, one *s*-cis, and one cis Diels–Alder dienes has been studied. The products obtained do not correlate with either the predominant configuration of the diene nor its triplet energy, but do correlate with the diene ionization potential. The dienes, butadiene, 2-methylbutadiene, 1-acetoxybutadiene, and 2,4-dimethyl-1,3-pentadiene, all undergo two competing cycloadditions. The first is a [2 + 2 + 2 + 2] cycloaddition on the α face of the steroid where both dienone double bonds add across the diene double bonds to form three annulated cyclobutane rings. The structure was confirmed by the isolation of the cyclobutanone derived from 1-acetoxybutadiene. The alternative [2 + 2 + 2 + 2] adduct, yielding a 5:4:5 ring system, was also obtained in a low yield with 2,3-dimethylbutadiene. The adducts with terminally substituted dienes are formed in a tail-to-tail manner. The second type of cycloaddition observed is a photo-Diels–Alder reaction to yield [4 + 2] adducts. The addition across the α,β dienone double bond yields exclusively the symmetry-allowed trans-4α,5β [4 + 2] adduct in a head-to-tail manner. This reaction is ascribed to an excited-state reaction rather than a ground-state trans double bond. Accompanying this product were tail-to-tail cis [4 + 2] cycloadditions across the γ,δ double bond. A transition occurs at approximately 8.4 eV, where the products are best described as being formed through a diradical with initial bonding at C4 of the dienone, followed by ring closure to generate cis and trans [2 + 2] as well as cis-4α,5α [4 + 2] adducts. This transition is characterized by 1-vinylcyclohexene, which gave a mixture of all the observed adducts with the exception of the [2 + 2 + 2 + 2] adduct. Below approximately 8.4 eV, the [2 + 2 + 2 + 2] and γ,δ [4 + 2] adducts were not formed. Thus, *trans,trans*-2,4-hexadiene, 1,1′-bicyclohexenyl, and 1,3-cyclohexadiene, normally a very reactive Diels–Alder diene, gave mainly [2 + 2] adducts across the α,β-dienone double bond, together with lesser amounts of the cis [4 + 2] adduct. The dienone does not phosphoresce but does fluoresce and the fluorescence is quenched by *trans, trans*-2,4-hexadiene. The photocycloadditions are efficiently, and differentially, quenched by 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide. The reactions are postulated to occur through the $\pi\pi^*$ triplet excited state of the dienone. The cycloadditions are discussed in terms of Epiotis and Shaik's theoretical $\pi\pi^*$ triplet photocycloaddition model.

The study of the photocycloaddition of steroidal enones to olefins succeeded the original discovery of the photocycloaddition of simple cyclohexenones to olefins.[2] Although there are many similarities between these enones,

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Table I. The Yields of the Photoadducts from the Photocycloaddition of Dienones 1 and 2 to Dienes

diene	IP (vertical)	% yield [2+2+2+2]	trans-4,5 [4 + 2]	cis-6,7 [4 + 2]	cis- or trans-4,5 [2 + 2]	cis-4,5 [4 + 2]
butadiene	9.03, 9.07[a]	27[b]	33	8	--	--
2,3-dimethylbutadiene	8.76, 8.72	12 (2)[c]	48	32	--	--
2-methylbutadiene	8.89, 8.85	22 (2)	40 (2)	17 (2)	5	--
1-acetoxybutadiene	8.4	++[d]	++ (2)	10	--	--
trans,trans-2,4-hexadiene	8.19	--	--	--	82	++
1-vinylcyclohexene	--	--	52	12	31	++
1,1'-bicyclohexenyl	--	--	--	--	--	20
2,4-dimethyl-1,3-pentadiene	--	13	24	22	--	--
1,3-cyclohexadiene	8.25, 8.30	--	--	--	44	14

[a] The ionization potentials are in electron volts (eV) and are from: (i) Beez, M.; Bicri, G.; Bock H.; Heilbronner, E. *Helv. Chim. Acta* 1973, *56*, 1028. (ii) Sustman, R.; Schubert, R. *Tetrahedron Lett.* 1972, 2739. (iii) Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973; p 198. The value for 1-acetoxybutadiene was interpolated from peak potential data reported in *Chem. Ber.* 1978, *111*, 1294. [b] The yields reported are isolated yields and are not based on recovered dienone. [c] The number in parentheses indicates the number of isomers. [d] These compounds were present but an exact yield determination was not possible.

the steroidal enones add olefins regiospecifically and do not generally yield products arising from hydrogen transfer.[3] Also in contrast to the simple cyclohexenones, steroidal enones phosphoresce.[4] However, when the chromophore in the steroidal enones was increased by an additional double bond to form the linear 3-keto-4,6-diene and the 7-keto-3,5-diene, substantial differences in the stereo- and regiospecificity of the reaction were found.[3a,5] Instead of the usual mixture of cis-4α,5α and trans-4α,5β [2 + 2] adducts being formed, only the trans-4α,5β adduct was formed, and no addition across the second double bond was observed. Also in contrast to the 3-keto-4-ene steroids, the 3-keto-4,6-dienes were reported neither to phosphoresce nor fluoresce.[6] The photocycloaddition reactions of steroidal enones occurred through their triplet state(s) since the additions were effectively quenched by dienes.[3c] However when this same dienic quenching was tried with the dienones, rapid cycloaddition to the diene occurred, and the structures were reported for the butadiene adducts.[7] The subject of this report is to discuss the scope of the cycloaddition reactions of 3-keto-4,6-dienic steroids to the varying types of Diels–Alder dienes and some aspects of the mechanism.

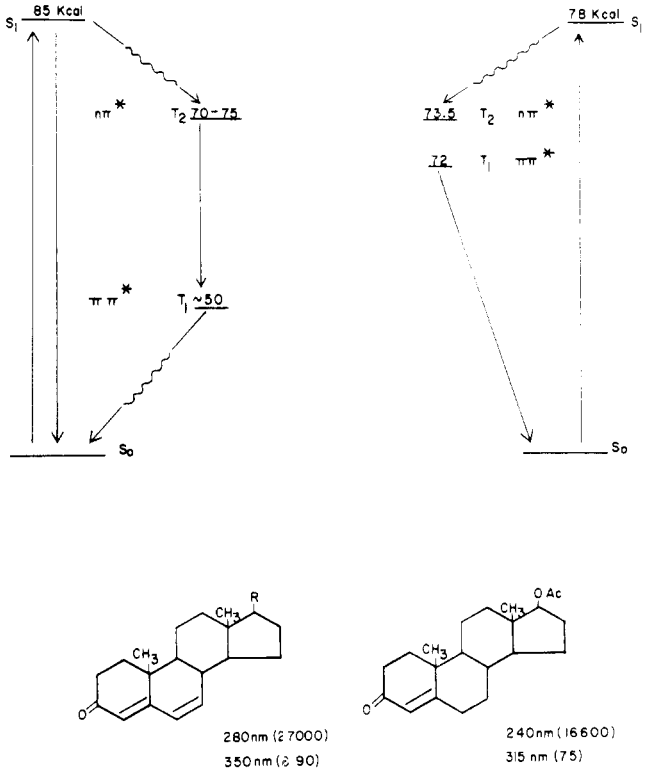

Figure 1. A comparison of the energy levels of the 3-keto-4,6-dienone and the 3-keto-4-ene (testosterone acetate) chromophores.

Results

The linear 3-keto-4,6-dienes absorb strongly in the ultraviolet. In methanol, the $\pi\pi^*$ band occurs at 282 nm with an intensity of ϵ 27 000.[8] Although optical rotatory dispersion (ORD) measurements indicate an $n\pi^*$ absorption at approximately 360 nm,[9] it is not resolved in methanol. It is, however, observed in benzene and occurs at 350 nm (ϵ 90). The dienone **2** fluoresces at 330 ± 5 nm for a singlet energy (S_1) of 85 kcal/mol (Figure 1).[10] This is close to that of the enone **3**, testosterone acetate (78 kcal/mol), which was determined by photoelectron spectroscopy.[4c]

(1) Presented in part at the 6th Great Lakes Regional Meeting, Houghton, Michigan, June, 1972, at the 6th International Congress on Photochemistry and Photobiology, Bochum, West Germany, August, 1972, and at the 2nd Rocky Mountain Regional Meeting of the American Chemical Society, Boulder, Colorado, June, 1978.

(2) (a) Corey, E. J.; Bass, J. D.; LeMahieu, R.; and Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570. (b) Eaton, P. E. *Acc. Chem. Res.* **1968**, *1*, 58. (c) DeMayo, P. *Ibid.* **1971**, *4*, 41. (d) Chapman, O. L.; Lenz, G. *Org. Photochem.* **1967**, *1*, 297.

(3) Steroid 3-keto-4-enes: (a) Rubin, M. B.; Maymon, T.; Glover, D. *Isr. J. Chem.* **1970**, *8*, 717. (b) Sunder-Plassman, P.; Nelson, P. H.; Boyle, P. H.; Cruz, A.; Iriarte, J.; Crabbé, P.; Zderic, J. A.; Edwards, J. A.; Fried, J. H. *J. Org. Chem.* **1969**, *34*, 3779. (c) Lenz, G. R. *Tetrahedron* **1972**, *28*, 2195. (d) Boyle, P.; Edwards, J. A.; Fried, J. H. *J. Org. Chem.* **1970**, *35*, 2560. For 3-keto-1-enes: (e) Boyle, P.; Edwards, J. A.; Fried, J. H. *J. Org. Chem.* **1970**, *35*, 2560. For 20-keto-16-enes: (f) Sunder-Plassman, P.; Nelson, P. H.; Boyle, P. H.; Cruz, A.; Iriarte, I.; Crabbé, P.; Zderic, J. A.; Edwards, J. A.; Fried, J. H. *J. Org. Chem.* **1969**, *34*, 3779. (g) Tökes, L.; Christensen, A.; Cruz, A.; Crabbé, P. *J. Org. Chem.* **1971**, *36*, 2381.

(4) (a) Kearns, D. R.; Marsh, G.; Schaffner, K. *J. Chem. Phys.* **1968**, *49*, 3316. (b) Marsh, G.; Kearns, D. R.; Schaffner, K. *Helv. Chim. Acta* **1968**, *51*, 1890. (c) Marsh, G.; Kearns, D. R.; Schaffner, K. *J. Am. Chem. Soc.* **1971**, *93*, 3129.

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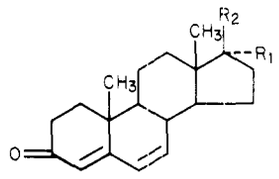
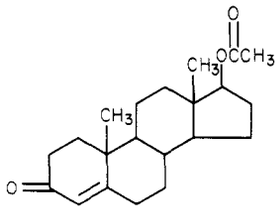
(9) Crabbé, P. "Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry"; Holden-Day: San Francisco, Calif., 1965; p 226.

(10) The fluorescence spectrum of dienone **2** was determined by Professor N. C. Yang of the University of Chicago, whom we thank.



1, R_1 = H; R_2 = O_2CCH_3

2, R_1,* R_2 = -$(CH_2)_2CO_2$-

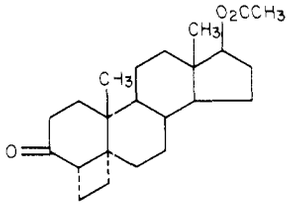


3

Since it is known that increasing conjugation has little effect on triplet $n\pi^*$ states,[11] this state for dienones may be estimated as occurring around 70–75 kcal/mol. The $n\pi^*$ triplet for the enone **3** occurs at 73.5 kcal/mol.[4b,c] Conversely, since the $\pi\pi^*$ triplet does decrease in energy upon extension of the conjugation,[11] the dienone $\pi\pi^*$ triplet should be much lower than the 72 kcal/mol observed for enone **3**. We estimate the $\pi\pi^*$ triplet to occur around 50 kcal/mol because of the ready, quenchable, addition to dienes shown in Table I, and on the results of Lillya, who determined a $\pi\pi^*$ triplet-state energy of 46–51 kcal/mol for *trans,trans*-3,5-heptadienone.[6] Therefore the major difference between dienones **1** and **2** and the enone **3** lies in the large splitting between the $n\pi^*$ and the $\pi\pi^*$ triplet states and any chemistry emanating from the triplet state should occur from the $\pi\pi^*$ state exclusively. This then eliminates the ambiguity of reactive triplet state(s) observed in enone **3**, where the $n\pi^*$ and $\pi\pi^*$ triplets are almost isoenergetic.[4]

Since the discovery that attempted quenching of the addition of dienones to olefins using piperylene resulted in rapid cycloaddition to this diene,[5b,7] the subsequent studies, enumerated here, on Diels–Alder dienes will be discussed in terms of their predominant configuration. Diels–Alder dienes are defined as those 1,3-conjugated dienes which undergo a concerted [4 + 2] cycloaddition with dienophiles and for flexible dienes are subdivided according to their predominant conformation. Non-Diels–Alder dienes are those 1,3-dienes which do not undergo this addition, e.g., *trans*-dienes or flexible dienes which exist exclusively in the *s*-trans conformation.

Butadiene. When 6-dehydrotestosterone acetate (**1**) was irradiated while passing a slow stream of butadiene through the solution, a rapid reaction ensued to form two major and two minor photoproducts (Scheme I). These adducts were conveniently separated by chromatography on silica. The first compound thus obtained was an adduct (**4**) of the dienone **1** and butadiene as indicated by its parent peak in the mass spectrum [*m/e* 382 (27%)]. However, in place of the original nine olefinic hydrogens in the dienone and butadiene, the NMR spectrum of **4** demonstrated the complete absence of any olefinic resonances. In fact, besides the 17α-hydrogen, the farthest downfield resonance occurred at δ 1.81 and was attributed to the proton attached to the carbon which is bonded to C5 of the steroid. The hydrogen is endo and in the deshielding cone of the C3 carbonyl group. This strongly deshielded aliphatic proton is even further deshielded to δ 2.83 in deuteriobenzene.[12] This assignment was subsequently shown to be correct by the absence of a deshielded proton in the 2,3-dimethylbutadiene adduct and its presence in only one of the isoprene adducts, as well as double resonance experiments on the ketone derived from the 1-acetoxybutadiene adduct. The infrared spectrum indicated a simple unconjugated cyclohexanone carbonyl group at 1720 cm^{-1}. The configuration of the newly formed bonds was determined to be 4α,5α,6α,7α by its ORD/CD spectra, which showed a weak positive Cotton effect which was virtually identical with *cis*-4α,5α-cyclobutane **10** derived



10

from testosterone acetate **3** and ethylene.[3c] Additionally, compound **4** could be saponified and reacetylated to regenerate the same compound. These experiments precluded a ladder compound having a 4α,5β,6β,7β configuration which could have been formed from a 4α,5β [2 + 2] adduct through a nondefined second ring closure. Had this occurred the observed Cotton effect would have been similar to that of the 4α,5β-trans-fused [2 + 2] adducts and been at least ten times stronger. Additionally, the orientation of unsymmetrical adducts eliminated this possibility, but at the time these experiments were performed, this was not known. On this experimental evidence, the adduct **4** was assigned the 4:4:4 ring system where butadiene has been added across both of the double bonds of the dienone to form a ladder compound. Additional evidence for this structure was later obtained from a derivative of the 1-acetoxybutadiene adduct.

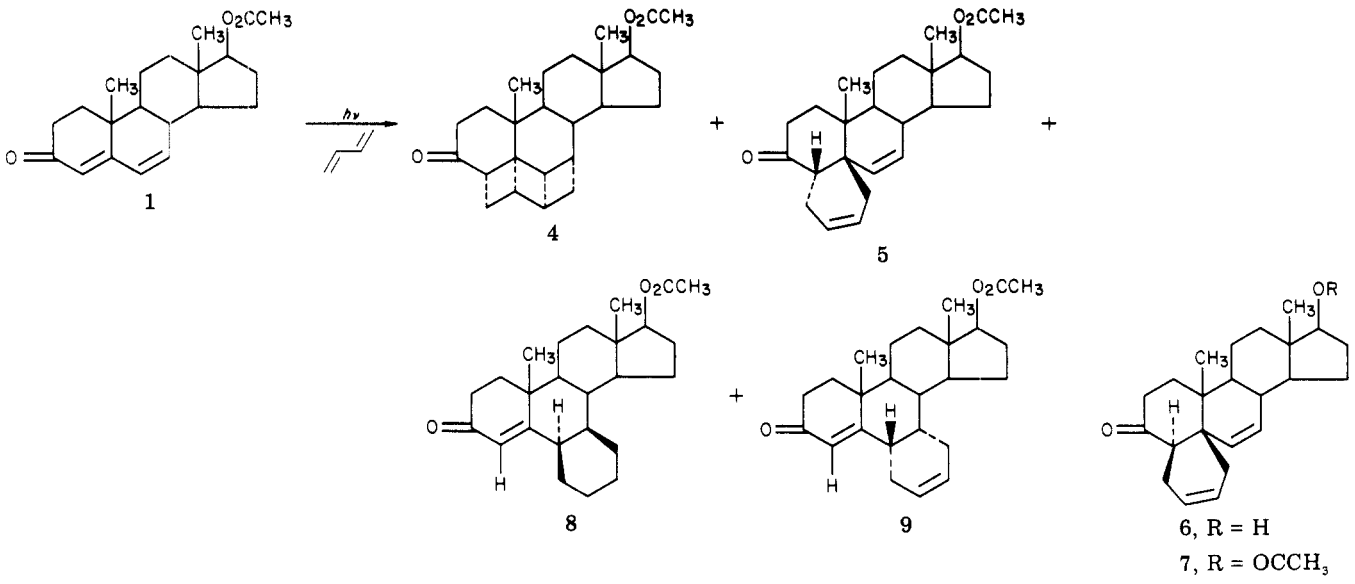
The second compound, **5**, was eluted in 33% yield and was identified as the trans-fused 4α,5β [4 + 2] Diels–Alder adduct because of the following observations. The 3-ketone appeared at normal position for saturated cyclohexanones[13] and the ultraviolet spectrum had only $n\pi^*$ absorption. The NMR spectrum showed the presence of four olefinic protons, appearing as a sharp two-proton singlet at δ 5.65 overlapped with a two-proton multiplet extending from δ 5.58 to 5.83. It was not possible to separate these resonances by recording the spectrum in deuteriobenzene or by running it at 100 MHz. Additionally, the 4β-hydrogen, which is coupled to the two cyclohexane protons of the newly formed ring, appeared as a quartet at δ 2.78. Similar observations of the 4β-hydrogen have occurred in steroidal trans-fused [2 + 2] adducts.[3,5] The trans-fused 4α,5β configuration was assigned from a consideration of both the ORD/CD spectra and epimerization to the thermodynamically more stable 4β,5β adduct. The ORD spectrum of the trans-fused [4 + 2] adduct **5** showed a strong positive Cotton effect with a molecular amplitude of a = +95 (Figure 2). The circular dichroism spectrum (CD), which was also positive, confirmed the 4α configuration. When compound **5** was treated with sodium methoxide in methanol concomitant epimerization and saponification of the 17β-acetate occurred to form the cis-fused 4β,5β [4 + 2] alcohol **6**. Acetylation then generated **7**, the cis-fused 4β,5β [4 + 2] epimer of compound **5**. This compound also occurred in small amounts in the irradiation mixture due to fortuitous epimerization of the trans isomer **5**. Had compound **5** been a primary adduct, it would have the 4α,5α configuration rather than the β.[5,20] Compound **7** also showed a four-proton olefinic multiplet centered at δ 5.60, but the quartet attributable to the 4β-hydrogen had merged in the methylene envelope when

(11) Evans, D. F. *J. Chem. Soc.* **1960**, 1735.

(12) Bhacca, N. S.; Williams, D. H. "Applications of NMR Spectroscopy in Organic Chemistry"; Holden-Day: San Francisco, Calif., 1964, p 159ff.

(13) Nakanishi, K. "Infrared Absorption Spectroscopy"; Holden-Day: San Francisco, Calif., 1962; p 42.

Scheme I



it epimerized into the 4α position. The ORD spectrum of **7** possessed an extraordinarily large negative Cotton effect with a molecule amplitude of $a = -213$. Equivalent chiroptical effects were obtained on the precursor alcohol **6**. These results confirmed the 4β,5β stereochemistry in the primary adduct **5**. The reasons for epimerization in these adducts have already been discussed.[14]

After the two major products were eluted, the minor products were obtained. The first of these was identified as a cis-fused 6,7 [4 + 2] Diels–Alder adduct (**9**) which was isolated in 4% yield. An ultraviolet absorption at 244 nm for a 3-keto-4-ene chromophore indicated that the dienone had added butadiene across the 6,7 positions.[15] The IR spectrum also indicated an enone grouping. However, the NMR spectrum was most instructive in not only assigning the structure of **9** as a [4 + 2] Diels–Alder adduct but also its stereochemistry. A broad two-proton singlet appeared at δ 5.60 and was assigned to the cyclohexene protons of the newly formed ring. Another olefinic proton appeared as a doublet at δ 5.77. The stereochemistry about the newly formed ring was determined to be 6α,7α by the observation that the 4-olefinic proton was a doublet (J = 1.5 Hz),[16] and a stable configuration about the newly formed ring was indicated when compound **9** was reobtained after saponification with sodium methoxide and subsequent acetylation.

Closely following adduct **9** was its highly crystalline isomer **8** (4% yield). Compound **8** was assigned the cis-6β,7β [4 + 2] Diels–Alder structure because of an enone chromophore in both its UV and IR spectra and three olefinic protons in its NMR spectrum with the 4-enone hydrogen appearing as a sharp singlet at δ 5.75.[16] The adduct **8** could also be reobtained after saponification with sodium methoxide and reacetylation. The yields of the butadiene adducts and all the other dienes studied are collected in Table I.

2,3-Dimethylbutadiene. This diene was originally studied to confirm the results obtained with butadiene. The advantages of this diene are due to the presence of the two methyl groups. Thus, with the ladder compound, 2,3-dimethylbutadiene will give rise to two additional tertiary aliphatic methyl groups and, with the [4 + 2] Diels–Alder adducts, the methyl groups remain olefinic. Additionally we were interested in the effect of a slightly more electron-rich diene to study possible effects of the electron-donating ability of the dienes.

Irradiation of dienone in the presence of 2,3-dimethylbutadiene led to a rapid reaction and generated several adducts which were separable by a mixture of chromatographic and chemical means (Scheme II). The 4,5 [4 + 2] Diels–Alder adducts were the major products (48%) and the highly crystalline trans-4α,5β [4 + 2] epimer **13** could be easily isolated by fractional crystallization. The two olefinic methyl groups in **13** appeared in its NMR spectrum as a broad singlet at δ 1.63. The ORD/CD spectra confirmed the stereochemistry of the adduct with a positive Cotton effect, which was converted into a negative Cotton effect upon epimerization and saponification to the 17β-hydroxy 4β,5β [4 + 2] adduct **14**. Subsequent acetylation yielded **15**, the epimer of **13**. The other major adduct, isolated in 32% yield, was the cis-6α,7α [4 + 2] adduct **16**. This compound was readily identified by the presence of two tertiary olefinic methyl groups and a doublet for the 4-olefinic proton in its NMR spectrum.[16]

The [2 + 2 + 2 + 2] ladder adduct **11** was isolated in 8% yield by chromatography. Again there were no NMR signals below δ 2.5 except the 17α proton. In addition to the two singlets for the angular methyl groups at C10 and C13, two new diene-derived tertiary methyl singlets occurred at δ 1.03 and 1.10. Since **11** was an oil and could not be induced to crystallize, it was saponified to the crystalline alcohol **12**. However, in contrast to all the other dienes studied, 2,3-dimethylbutadiene yielded a small amount of a second [2 + 2 + 2 + 2] adduct. This adduct **17** was isolated as a pure crystalline compound from a mixture with **15** by ruthenium tetraoxide oxidation[17] and subsequent flash chromatography.[18] Positive chiroptical effects indicated α addition to the steroid and the lack of unsaturation in **17** indicated that it was isomeric with the ladder compound **11**. The only structural possibility for **17** is a crossed addition made to form a [2 + 2 + 2 + 2] adduct containing a 5:4:5 ring system. This type of cycloaddition had previously been observed by Srinivasan

(14) Lenz, G. R. *J. Org. Chem.* **1979**, *44*, 1382.
(15) Fieser, L. F.; Fieser, M. "Steroids", Reinhold: New York, 1959; p 15ff.
(16) (a) Collins, D. J.; Hobbs, J. J.; Sternhell, S. *Aust. J. Chem.* **1963**, *16*, 1030. (b) Wittstruck, T. A.; Malhotra, S. K.; Ringold, H. J. *J. Am. Chem. Soc.* **1963**, *85*, 1699.
(17) Piatek, D. M.; Bhat, H. B.; Caspi, E. *J. Org. Chem.* **1969**, *34*, 112.
(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

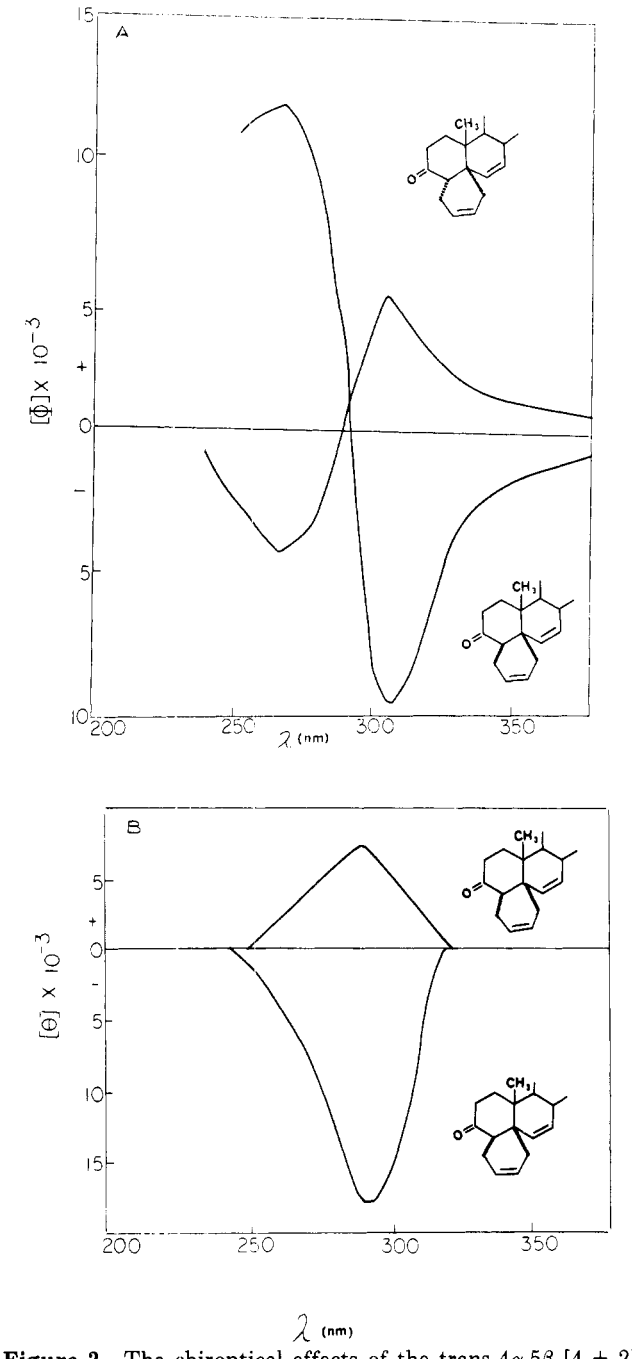
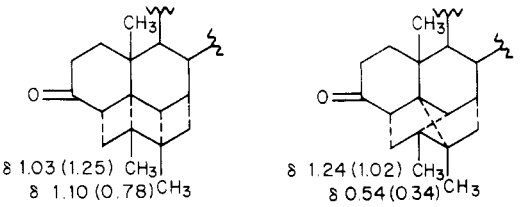


Figure 2. The chiroptical effects of the trans-4α,5β [4 + 2] butadiene adduct **5** and its 4β,5β [4 + 2] epimer **7**: (a) optical rotatory dispersion; (b) circular dichroism.

with 1,5-cyclooctadiene.[19] The NMR spectrum is also in accord with the crossed structure. Consideration of a Dreiding model of **17** showed that the hydrogens on the *endo*-methyl group sit directly under the 3-carbonyl group and 2.2 Å removed. Therefore these protons should be shielded and further shielded in deuteriobenzene. This is indeed the case; the observed chemical shifts are given next to methyl groups in the partial structures for **11** and **17**. The first number is the chemical shift in chloroform and the number in parentheses is the chemical shift in deuteriobenzene. The *endo*-methyl group in the ladder compound **11** is deshielded and undergoes a further moderate deshielding in deuteriobenzene while the *endo*-



11 **17**

methyl group in the alternate isomer **17** is strongly shielded and even more so in deuteriobenzene. The difference in chemical shifts for these two methyl groups amounts to δ 0.49 in deuteriochloroform and δ 0.91 in deuteriobenzene.

2-Methylbutadiene (Isoprene). Isoprene was studied to determine the effect of an internal methyl group on product distribution. Due to the unsymmetrical structure of this diene, this photocycloaddition was approached somewhat apprehensively. This turned out to be justified, since eventually eight separate compounds were isolated from this reaction (Scheme III).

The reaction mixture was separated mainly by chromatography and fractional crystallization. The first compound was isolated in 2.2% yield and identified as the ladder compound **18**, possessing an *endo*-methyl group since there were no downfield proton signals, while the new tertiary aliphatic methyl group resonated at δ 1.25, which shifted to δ 1.47 in deuteriobenzene. The alternative isomer **19** was isolated in 19.5% yield. In this isomer there was no appreciable shift for the *exo*-methyl group, while recording the NMR spectrum in deuteriobenzene shifted the endo proton out of the methylene envelope to δ 2.55. Both of these isomers possessed weak positive Cotton effects with identical molecular amplitudes of $a = +7$.

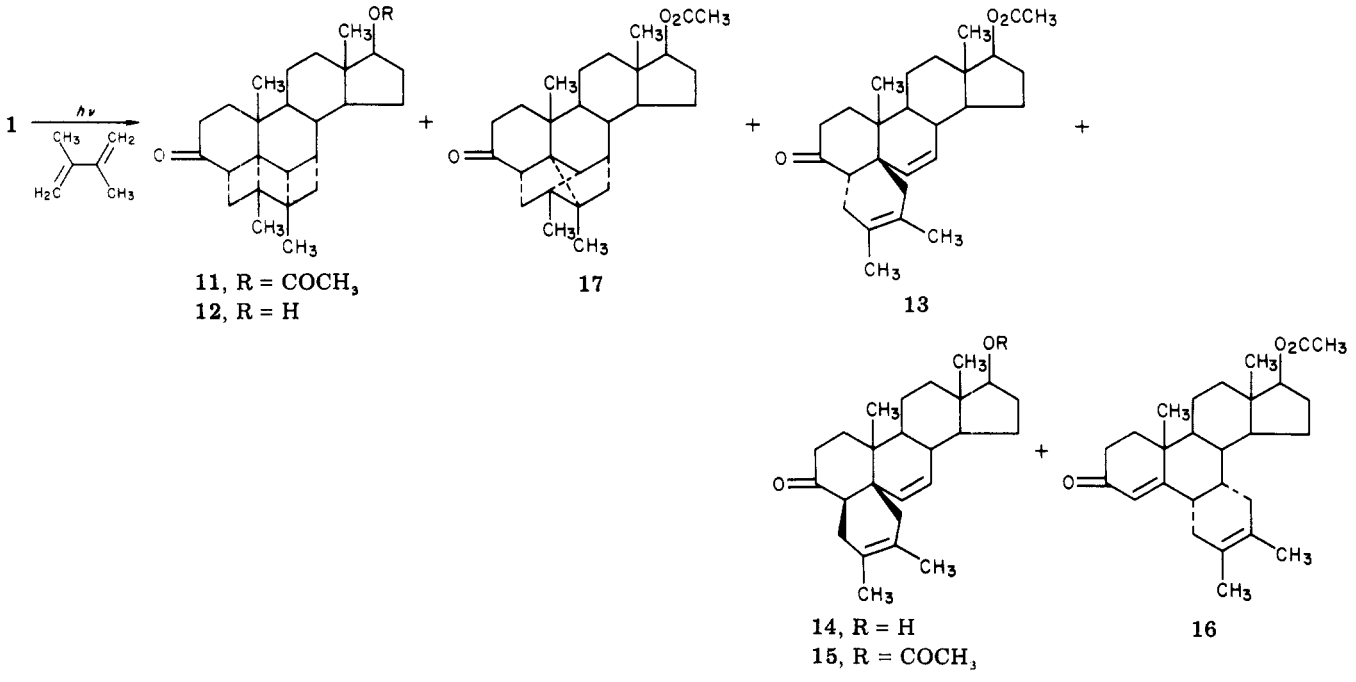
Perhaps the most unexpected adduct isolated in 5% yield in the isoprene series was the [2 + 2] adduct **20**. That the addition had occurred across the 4,5 double bond was evident from the absence of $\pi\pi^*$ absorption in the ultraviolet spectrum. The orientation, structure, and stereochemistry of the adduct were determined by a combination of NMR and ORD/CD spectroscopy. The NMR spectrum of **20** showed, besides the 6,7 double bond, the presence of an isopropenyl group with two olefinic protons and one olefinic methyl group. The position of attachment of the isopropylene group was determined to be that indicated when the tertiary allylic cyclobutyl proton was observed as a triplet at δ 3.43. The downfield position for this proton of vinyl-substituted cyclobutanes had previously been observed in this series.[20] The stereochemistry was determined by recovery of **20** from sodium methoxide solution and a weakly positive Cotton effect in the ORD with a molecular amplitude of $a = +2$. The [2 + 2] adduct **20** slowly degraded under both direct (Pyrex filter) and sensitized irradiation (acetone, Pyrex) and did not form the ladder compound **19**.

The two 4,5 [4 + 2] isomers **21** and **22** were separable by chromatography and isolated, each in 20% yield. These compounds were characterized as [4 + 2] adducts each by the presence of a vinylic methyl group and only three olefinic hydrogens in their NMR spectra. The structure for compound **21** was assigned because the cyclohexene olefinic proton was more deshielded and the methyl group less deshielded than its isomer **22**. The same observations held when the spectrum of the isomeric pair was run in deuteriobenzene. When the ORD and CD spectra were taken, however, both of these adducts showed strongly negative chiroptical effects indicating a 4β,5β stereochem-

(19) (a) Srinivasan, R. *J. Am. Chem. Soc.* **1963**, *85*, 3048. (b) Srinivasan, R. *Ibid.* **1963**, *85*, 819. (c) Baldwin, J. E.; Greeley, R. H. *Ibid.* **1964**, *86*, 3396. (d) Srinivasan, R. *Ibid.* **1964**, *86*, 3318.

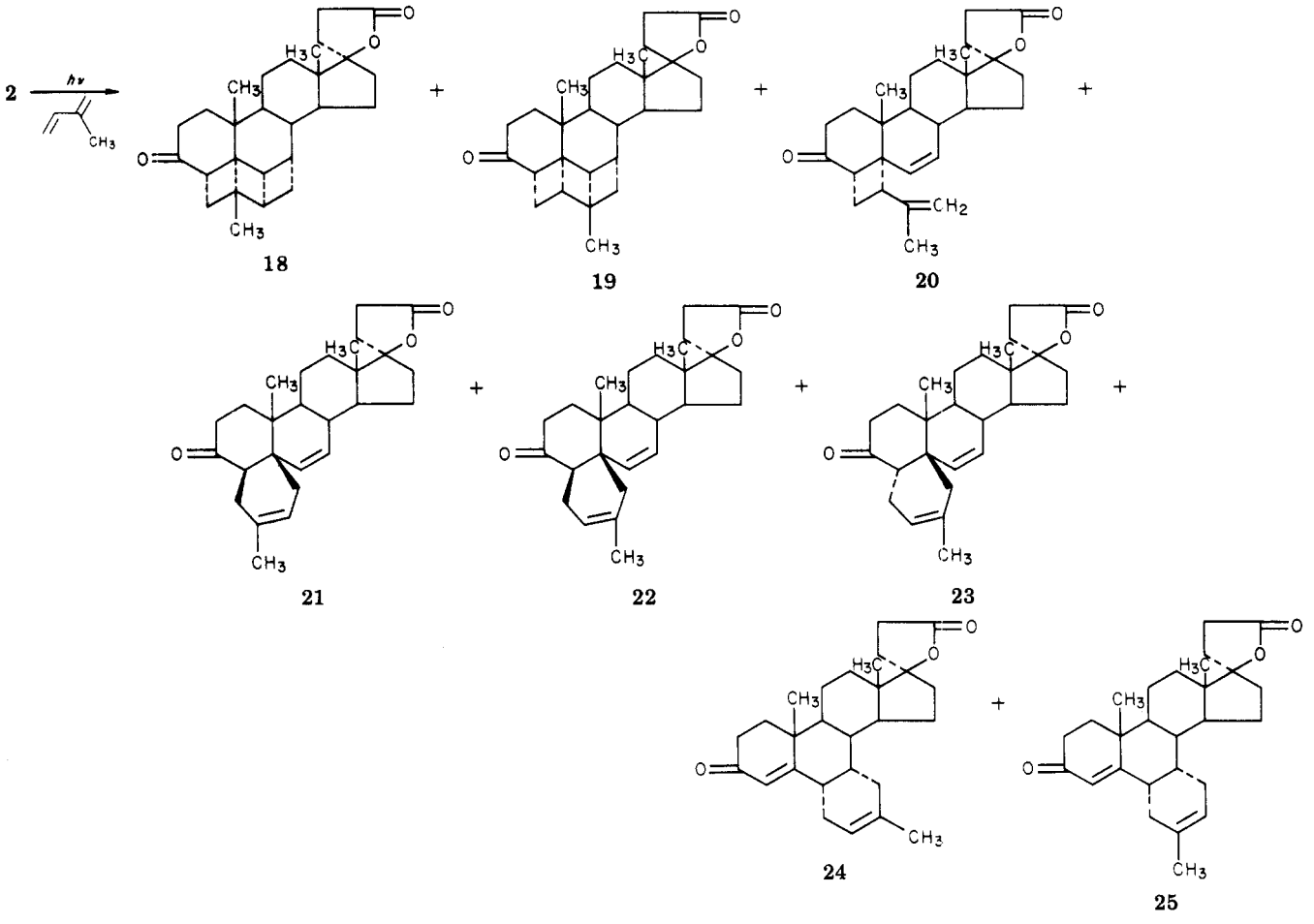
(20) Lenz, G. R. *Tetrahedron* **1975**, *31*, 1587.

Scheme II



11, R = $COCH_3$
12, R = H
17
13
14, R = H
15, R = $COCH_3$
16

Scheme III

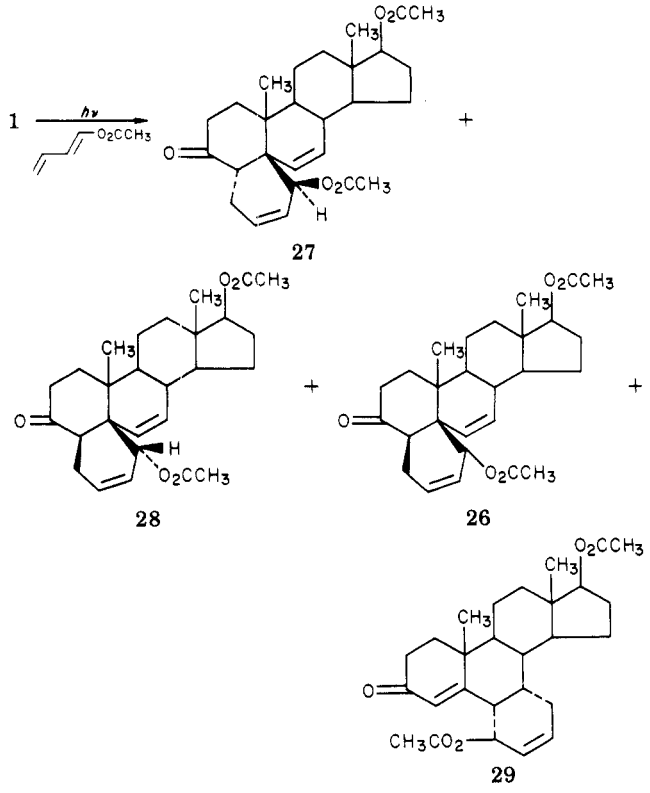


18
19
20
21
22
23
24
25

istry. In another experiment, it was possible to isolate one of the trans-4α,5β [4 + 2] isomers, **23**. Its structure was indicated by its epimerization into **21**. Repeated attempts at obtaining the ORD and CD spectra on *trans*-**22** resulted in obtaining weakly negative curves, indicating appreciable in situ epimerization to **21** had occurred. The trans [4 + 2] adducts are much less stable than the trans [2 + 2] adducts, epimerizing readily to the cis-4β,5β [4 + 2] adducts.

The 6,7 adducts **24** and **25** were isolated as a mixture and could not be separated. The integration of both the olefinic and methyl group resonances indicated that they existed as an equimolar mixture. These were identified as [4 + 2] adducts by the presence of one olefinic hydrogen

Scheme IV



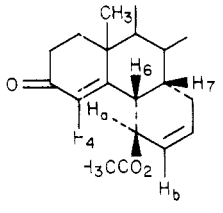
and a vinylic methyl group attributable to the newly formed ring. The stereochemistry of both isomers was determined to be 6α,7α by the appearance of the enone hydrogens as doublets.[16] The mixture of isomers was unaffected by sodium methoxide. Since there was no apparent way of determining which isomer was which, the position of the methyl groups was assigned arbitrarily in compounds **24** and **25**, and these assignments may be reversed.

1-Acetoxybutadiene. Irradiation of dienone 1 in the presence of 1-acetoxybutadiene[21-24] yielded a variety of adducts (Scheme IV). Although most of the chromatographic fractions of the 4,5 adducts were noncrystalline mixtures, some of the adducts could be isolated in small amounts by fractional crystallization.

The first isomer isolated from the irradiation was identified as a head-to-tail 4β,5β [4 + 2] adduct **26**. The ORD/CD spectra demonstrated that **26** had a 4β,5β ring junction as there was a strongly negative Cotton effect. The gross structure and diene orientation was determined by its NMR spectrum and subsequent chemical reactions. In the NMR spectrum of compound **26**, the four olefinic protons and the α-acetoxy proton all appeared between δ 5 and 6, thus demonstrating [4 + 2] cycloaddition. In this particular 4β,5β isomer, the 4α proton was resolved from the methylene envelope and appeared at δ 3.07, as a quartet, indicating coupling to two other vicinal protons.

The two epimeric trans-4α,5β [4 + 2] isomers **27** and **28** were also isolated in small amounts. The stereochemistry of both epimers was again determined by their chiroptical effects, and [4 + 2] addition was indicated by the presence of four vinyl and one α-acetoxy hydrogen. Head-to-tail addition was demonstrated by the appearance of the 4β-hydrogen as a doublet of doublets at δ 3.37 and 3.13 for compounds **27** and **28**, respectively. Both of the α-acetoxy protons appeared as doublets with secondary splitting. An inspection of models indicates that when the α-acetoxy proton is endo to the steroid A ring (dashed line), the dihedral angle is approximately 105°. When this proton is exo to the A ring (solid line), the dihedral angle is 10°. As a result, the exo proton should be coupled more strongly than the endo.[25] In the trans epimers **27** and **28**, the α-acetoxy protons appear at δ 4.07 and 5.12 with coupling constants of J = 4 and 9 Hz, respectively. Therefore, compound **27** was assigned the endo structure and its epimer **28** the exo structure.

Surprisingly there was only a single 6,7 adduct (**29**) formed in 10% yield. That it was a Diels–Alder [4 + 2] adduct was shown by the presence of three olefinic protons and an α-acetoxy hydrogen, as well as by the enone absorption at 241 nm. The appearance of the 4-enone hydrogen as a doublet indicated the 6α,7α stereochemistry.[16] The position of the acetoxyl group was determined by double resonance experiments at 90 MHz. A resonance occurred as a broad doublet, J = 4 Hz, at δ 2.62 which was assigned to the axial 6β-hydrogen. Irradiation at the 4 proton collapsed this broad signal to a doublet of doublets and the α-acetoxy proton appeared at δ 5.27 as a doublet of doublets. The major coupling was assigned to the olefinic proton and the minor one was assigned to coupling with the 6β-hydrogen. Irradiation of the 6β proton collapsed the α-acetoxy proton to a doublet and the 4-vinylic proton to a singlet, demonstrating that the acetoxy group was substituted on the methylene group attached to carbon 6 and, because of the small coupling constant, the dihedral angle was close to 90°. Inspection of models indicated a reason for the occurrance of only a single epimer. In the



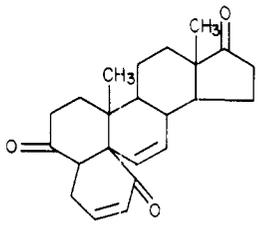
$J_{4,6}$ = 1.5 Hz
$J_{6,7}$ = 4.0 Hz
$J_{a,6}$ = 1.5 Hz
$J_{a,b}$ = 4.5 Hz

model with the endo α-acetoxy hydrogen, this proton is close to the C4 enone proton and forms a 115° dihedral angle with the 6β-hydrogen. In the alternative isomer where the α-acetoxy proton is exo, severe steric interactions occur between the acetoxy group and the A ring of the steroid. Also the dihedral angle of this epimer is 25°, which would lead to a coupling constant much larger than that observed.

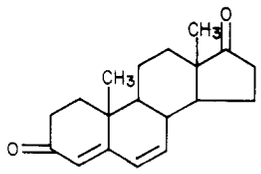
In order to separate the noncrystalline mixtures of the 4,5 isomers, which also contained some starting dienone 1, they were saponified and then oxidized to the ketones. Since attempted oxidations with dichlorodicyanobenzoquinone[26] and silver carbonate on Celite[27] were unsuccessful, the residue was oxidized with Jones reagent,[28] even though this resulted in extensive losses in material. The

(21) Bailey, W. J.; Barclay, R., Jr. *J. Org. Chem.* **1956**, *21*, 328.
(22) Sauer, J.; Langond, D.; Mielert, A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 268.
(23) Onischenko, A. "Diene Synthesis"; Israel Program for Scientific Translations: Jerusalem, 1964; p 215ff.
(24) Fonken, G. J. *Org. Photochem.* **1967**, *1*, 212.
(25) Smith, G. V.; Kriloff, H. *J. Am. Chem. Soc.* **1963**, *85*, 2017.
(26) Burstein, S. H.; Ringold, H. J. *J. Am. Chem. Soc.* **1964**, *86*, 4952.
(27) Fetizon, M.; Golfier, M. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1968**, *267*, 900.
(28) Bowdon, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39.

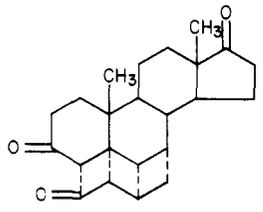
resultant mixture thus obtained was chromatographed and the three components were separated.



30



31



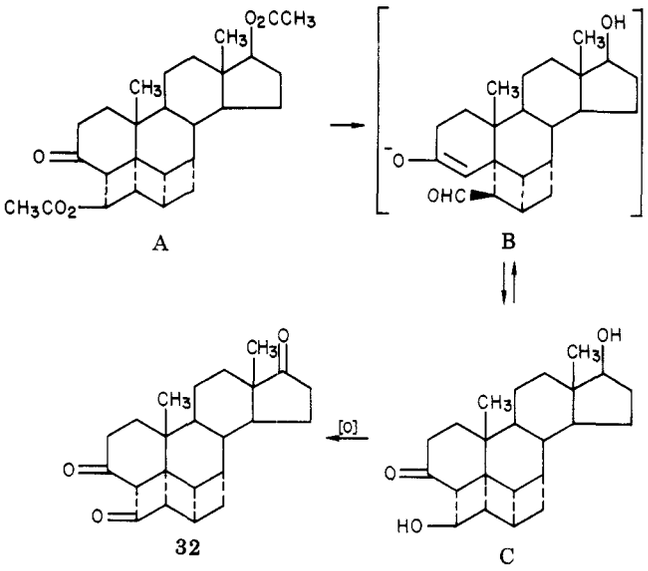
32

The first of these compounds, **30**, possessed a cyclopentanone carbonyl at 1745 cm^{-1}, a cyclohexanone carbonyl at 1725 cm^{-1}, and an α,β-unsaturated enone at 1680 and 1650 cm^{-1}. A simple cyclohexenone was indicated by a UV absorption at 222 nm. The NMR spectrum showed the 6,7 hydrogens as a singlet and the two cyclohexenone protons as multiplets at δ 5.87 and 6.87. The geminal allylic protons of the cyclohexenone appeared as multiplets at δ 2.75 and 3.33. Based on the presumption than **26**, **27**, and **28** served as precursors and also on the spectroscopic data, compound **30** was assigned the structure indicated. Indeed individual samples of **26** and **28** could be saponified and oxidized to compound **30**.

The second compound isolated (**31**) was identified as the product of oxidation of the saponified dienone 1, androsta-4,6-diene-3,17-dione, by comparison with an authentic sample.

The most interesting compound of this series was the keto ladder compound **32**. The IR spectrum of **32** indicated the presence of cyclobutanone, cyclopentanone, and cyclohexanone carbonyl groups. There was no $\pi\pi^*$ absorption in the UV. The NMR spectrum of compound **32** provided the key to the position of the cyclobutyl carbonyl group. In deuteriochloroform, the farthest downfield resonance occurred as a doublet (J = 2.5 Hz) at δ 3.27. This was assigned to the endo hydrogen on the carbon attached to carbon 5. Additionally, a sharp singlet appeared at δ 2.79 which was assigned to the 4β proton, which is α to two carbonyl groups and not coupled to any other protons. Europium shift and double resonance experiments determined the position of the exo ladder proton vicinal to the strongly deshielded endo hydrogen. The proton occurred as a quintet with all couplings being approximately 3 Hz. Due to the three carbonyl groups, further europium shift and double resonance studies allowed the assignment of the majority of the protons in ladder compound **32** (see Experimental Section). The above NMR results are clearly compatible only with the structure indicated, and not with the alternative where the cyclobutanone is attached to the steroid at C-7. If it were in this position, the strongly deshielded proton would not be a doublet, since it would be coupled to at least three other protons and would be expected to be a multiplet like the butadiene adduct **4**. There is also no hydrogen α to the downfield proton which is coupled to four other hydrogens, especially with a small coupling constant. Finally, the presence of a singlet for a proton α to a carbonyl group is clearly incompatible with a carbonyl group at C-7, since all the α protons are coupled to at least two other hydrogens.

Scheme V



The very fact that the cyclobutanone ladder compound **32** was isolated was puzzling at first, since β-acetoxycyclobutanones are known to fragment into keto aldehydes in high yield.[2c,29] Presumably the acetoxy ladder compound A, which we were not able to isolate, also fragments to form an aldehyde enolate B (Scheme V). Several observations may be made about enolate B. First, due to its method of formation, the aldehyde group will be exocyclic to the A ring of the steroid. Epimerization to the endo isomer, where the aldehyde group is under the A ring, is very unlikely due to the severe steric congestion and to the rigidity of the substituted B ring of the steroid. So it is very likely that the aldehyde will stay predominantly in the exo position. Second, in order to protonate the enolate to form the keto aldehyde, a proton has to approach from the shielded β face of the steroid, since the α face is blocked by the aldehyde. This is also an unfavorable situation. Therefore, due to the proximity of the aldehyde, the enolate can re-form the aldol product C, and then oxidation generates the keto ladder compound **32**.

***trans,trans*-2,4-Hexadiene.** This trans,trans diene is an effective Diels–Alder diene, readily undergoing thermal cycloadditions while the cis,trans isomer does not without prior isomerization or rearrangement.[30] But having terminal methyl groups, it is also a very good electron donor, so it was of more than passing interest to see the interplay of these effects on the photocycloaddition of the dienone **2** to this diene.

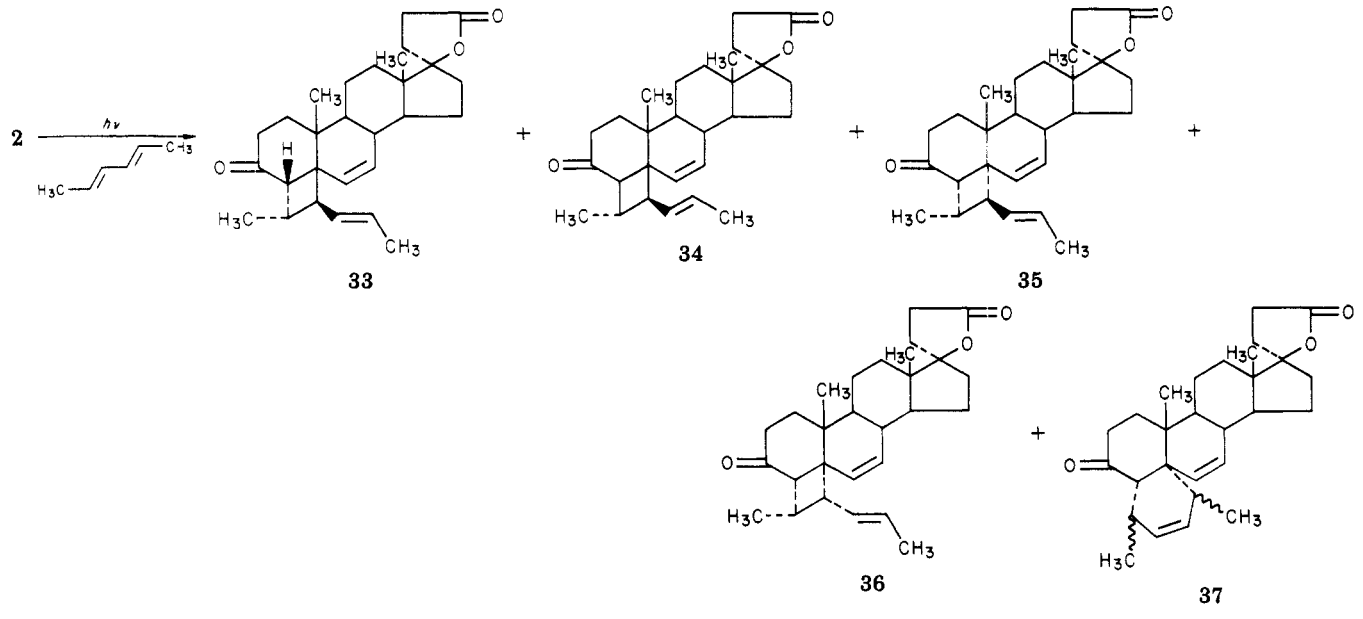
The photocycloaddition of dienone **2** to *trans,trans*-2,4-hexadiene yielded, by TLC, two groups of adducts (Scheme VI). The second slower moving group consisted of primarily one compound, **33**, which was easily isolated by fractional crystallization. This compound was identified as the trans-fused 4α,5β [2 + 2] adduct **33**. The cyclohexanone carbonyl group absorbed at 1720 cm^{-1}.[31] The NMR spectrum indicated the presence of two additional vinylic hydrogens, while there was one vinylic and one aliphatic secondary methyl group. These results are only compatible with a [2 + 2] adduct and exclude the [4 + 2] Diels–Alder adduct. The stereochemistry was proven by

(29) For reviews see: (a) Sammes, P. G. *Q. Rev., Chem. Soc.* **1970**, *24*, 37. (b) Sammes, P. G. *Synthesis* **1970**, 636.

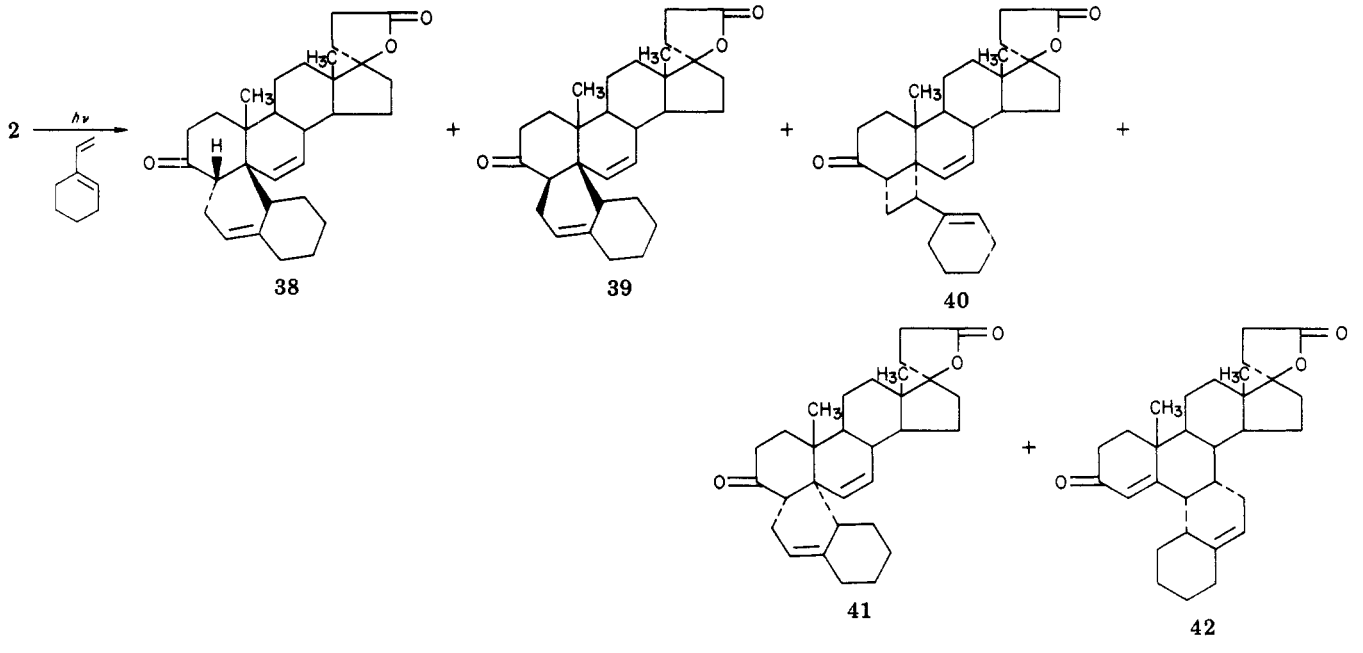
(30) Alder, K.; Vogt, W. *Justus Liebigs Ann. Chem.* **1951**, *571*, 137.

(31) Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570.

Scheme VI



Scheme VII



the very strong chiroptical effects and the sodium methoxide catalyzed epimerization to the 4β,5β [2 + 2] adduct **34**. The presence of an IR absorption at 970 cm^{-1} demonstrated that the propenyl group in **33** and **34** remained trans.[32] If a diradical were a discrete intermediate in the formation of the trans adduct, then the *trans*-crotyl radical would maintain its stereochemical integrity.[33] The structure indicated in **34** was based on the assumption of photocycloaddition to the trans,trans diene without isomerization and on the absence of a low-field resonance for a vinyl-substituted cyclobutyl proton. This absence can only be due to an endo aliphatic cyclobutyl methyl group.[20] The cis-4β,5β [2 + 2] compound **34** was identified as the minor component in the slower moving group. The combined yield of these compounds was 55%.

The faster group of compounds was obtained in 45% yield. We were not able to obtain these as pure crystalline compounds, but the structures were tentatively assigned from the physical spectra of their mixtures. The majority was a mixture of 4α,5α [2 + 2] adducts **35** and **36**. At 60 MHz, the position of the vinyl methyl group remained constant at 101 Hz while the secondary methyl group at 70 Hz (J = 6 Hz) in the initial chromatographic fractions diminished and a new doublet 3 Hz downfield grew at its expense. In the final fractions, two new doublets appeared which were 4 Hz downfield and 9.5 Hz upfield of the initial signal at 70 Hz. These were assigned to the 4α,5α [4 + 2] adduct. The 3-carbonyl group in **37** appeared at 1725 cm^{-1}, which is characteristic of all the [4 + 2] adducts (see the discussion for the vinylcyclohexene adducts), while all the cis [2 + 2] adducts appear at ~1700 cm^{-1}.[3,20] Because the stereochemistry of the secondary aliphatic methyl group is fixed upon initial bond formation, compounds **35** and **36** are epimeric about the vinyl-substituted cyclobutane carbon. The infrared spectra again indicated a trans dou-

(32) Nakanishi, K. "Infrared Absorption Spectroscopy"; Holden-Day: San Francisco, Calif., 1964; p 24.
(33) Schleyer, P. v. R.; Pople, J. A.; Hehre, W. J. *Tetrahedron* **1977**, *33*, 2497.

ble bond. All the fractions investigated had positive ORD and CD spectra. In agreement with the results for the non-Diels–Alder diene cycloadditions,[20] there was no evidence for any 6,7 adducts.

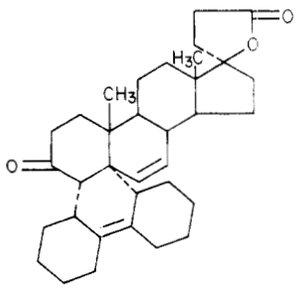
1-Vinylcyclohexene. Irradiation of dienone **2** in the presence of this Diels–Alder diene[34] resulted in the rapid formation of four products (Scheme VII). When the irradiation solvent was evaporated and dissolved in benzene, one of the products crystallized. Subsequent material isolated from column chromatography brought the yield of this product to 52%. This compound, **38**, was identified as the head-to-tail trans-fused 4α,5β [4 + 2] adduct on chemical and spectral evidence. Head-to-tail addition was indicated by the presence of a triplet for the 4β proton in its NMR spectrum. The trans adduct possessed a positive Cotton effect (a = +66). A molecular amplitude of this magnitude was indicative of a [4 + 2] adduct, since the trans [2 + 2] adducts have molecular amplitudes of several hundred.[5] Epimerization of **38** with sodium methoxide in methanol gave the 4β,5β [4 + 2] adduct **39** with a strongly negative Cotton effect (a = −168). A molecular amplitude of this magnitude is also characteristic of [4 + 2] adducts, since those of the [2 + 2] adducts are generally quite small.[3,5] A further differentiation between [2 + 2] and [4 + 2] addition in these compounds was furnished by the infrared frequencies of the carbonyl groups. In both the [2 + 2] and [4 + 2] trans isomers, the 3-carbonyl group frequency occurred between 1720 and 1725 cm^{-1}. However, in both the 4α,5α and 4β,5β [2 + 2] isomers of a wide variety of olefins and dienes, the 3-carbonyl absorption was between 1690 and 1700 cm^{-1}, while for the 4α,5α and 4β,5β [4 + 2] adducts this absorption is between 1720 and 1725 cm^{-1}.[3,5,20] Since the carbonyl frequency in **39** occurs at 1725 cm^{-1}, it is a [4 + 2] adduct, and, by inference, so is its precursor **38**.

The first compound isolated chromatographically, in 31% yield, was **40**. This compound was identified as the cis-4α,5α [2 + 2] adduct by its recovery with sodium methoxide solution and a weakly positive Cotton effect (a = +15). The cyclohexanone carbonyl group also appeared at 1705 cm^{-1}. Additionally, the tertiary vinyl-substituted cyclobutyl hydrogen appeared significantly downfield at δ 3.28 as a multiplet and is characteristic of both epimers of this type of vinyl-substituted steroidal cyclobutane.[20]

A small amount of an additional compound **41**, intermediate in polarity between compounds **38** and **40**, was isolated by preparative TLC. This was identified as the cis-4α,5α [4 + 2] adduct by its carbonyl absorption at 1725 cm^{-1}, its stability to sodium methoxide, and a positive Cotton effect (a = +103) in its ORD spectrum. The NMR spectrum showed three olefinic protons and the absence of any downfield resonances characteristic of vinylcyclobutanes.[20]

The final compound isolated, in 12% yield, was the cis-6α,7α [4 + 2] adduct **42**. The structure was assigned by analogy with the 1-acetoxybutadiene adduct **29** and the enone absorption in the UV spectrum, as well as the allylic coupling between the enone hydrogen and the pseudo-axial 6β-hydrogen.[16]

1,1′-Bicyclohexenyl. Irradiation of the dienone **2** in the presence of this diene[35] led to a slower reaction than with the other dienes and substantial steroidal degradation occurred. A single adduct (**43**) was isolated in 20% yield. This product was easily identified as a 4,5 [4 + 2] adduct by the absence of ππ* absorption in the UV spectrum, and

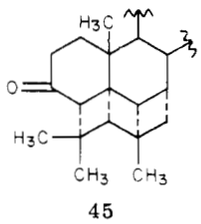


43

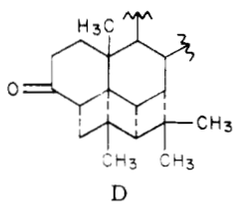
the presence of only the 6,7 olefinic protons. The ORD and CD spectra indicated 4α substitution with a molecular amplitude of a = +97. However, repeated and prolonged treatment with refluxing sodium methoxide solution failed to cause epimerization and compound **43** was recovered, thus proving that adduct **43** was a cis-fused 4α,5α [4 + 2] Diels–Alder adduct, in contrast to all the others studied, with the exception of the small amount of cis [4 + 2] adduct **41** isolated from the vinylcyclohexene irradiation.

2,4-Dimethyl-1,3-pentadiene. This particular diene is one of the few available dienes that exists primarily in the s-cis conformation,[36] and is among the most reactive Diels–Alder dienes.[37] When the dienone **2** was irradiated in the presence of the diene, a rapid reaction occurred yielding six products (Scheme VIII). Chromatography separated all but the 6,7 adducts cleanly. The first compound eluted in 9% yield was identified as a dienone by its characteristic UV absorption at 291 nm and the typical dienone IR bands at 1670 and 1625 cm^{-1}.[38] The appearance of the usual doublet of doublets for the 6,7 olefinic protons indicated that the dienone **2** had been substituted at carbon 4. The remainder of the structure was also determined from its NMR spectrum by the appearance of two geminal olefinic protons at δ 4.95 and a vinyl methyl group at δ 1.42. An allylic methylene group resonated at δ 3.23. The remaining two methyl groups of the diene were observed as sharp singlets, indicating that these two dienic methyl groups had become tertiary and aliphatic. The only structure consistent with these observations is **44**, where the 4-carbon of the dienone **2** had added to the diene at its more substituted end and undergone hydrogen transfer.

The second compound isolated in 13% yield was found to be the ladder compound **45** based on the absence of any olefinic protons and the presence of five tertiary aliphatic methyl groups in its NMR spectrum. Although the structure of adduct **45** could be assigned as indicated by analogy to the 1-acetoxybutadiene derived ladder compound **32**, more direct evidence was available from solvent induced NMR shifts. In all the ladder compounds studied the endo substituent on the carbon atom attached to carbon 5 of the steroid was shifted significantly downfield in deuteriobenzene compared to their chemical shift in deuteriochloroform. If the structure of **45** is considered versus its isomer D, it can be predicted that in compound **45** the



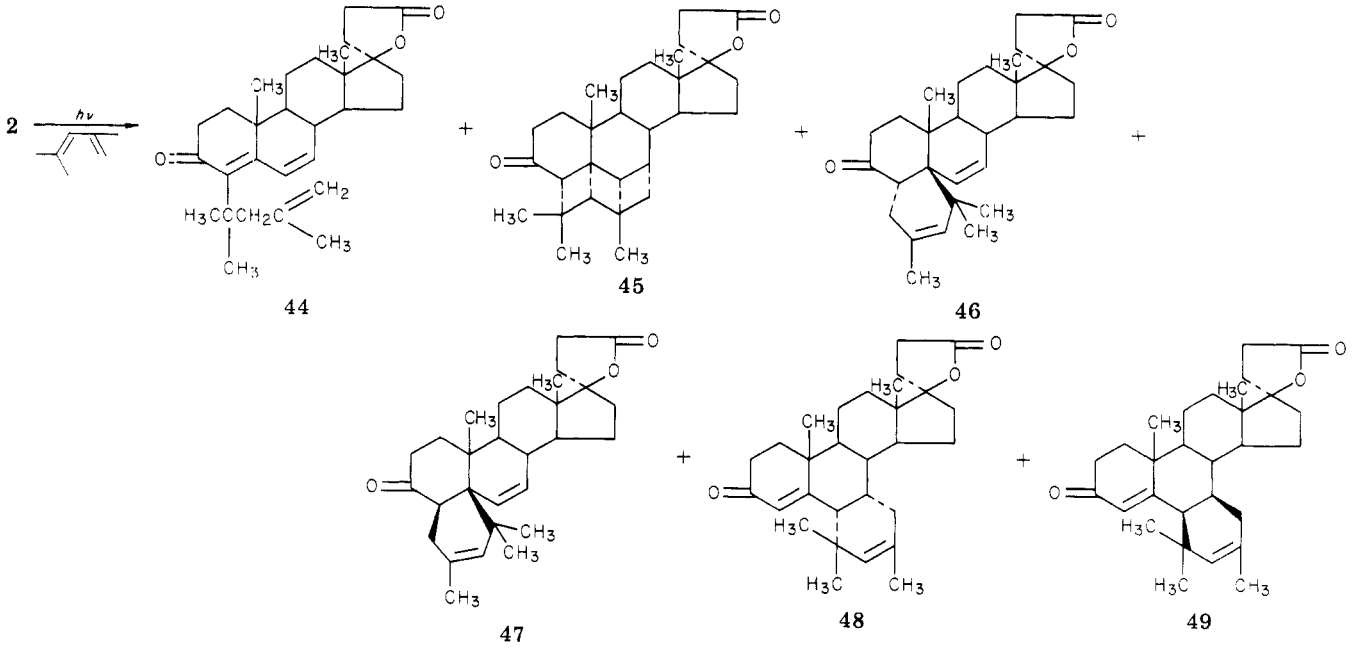
45



D

(34) Nazarov, I. N.; Kuznetsova, A. I.; Kuznetsov, N. V. *Zh. Obshch. Khim.* **1955**, *25*, 38.
(35) Bergmann, F.; Eschinazi, H. E. *J. Am. Chem. Soc.* **1943**, *65*, 1405.
(36) Brande, E. A.; Waight, E. S. *Prog. Stereochem.* **1954**, *1*, 136.
(37) Onishchenko, A. S. "Diene Synthesis"; Israel Program for Scientific Translations, Jerusalem, 1964, pp 8–16.
(38) Nakanishi, K. "Infrared Absorption Spectroscopy"; Holden-Day: San Francisco, Calif., 1964, p 42.

Scheme VIII

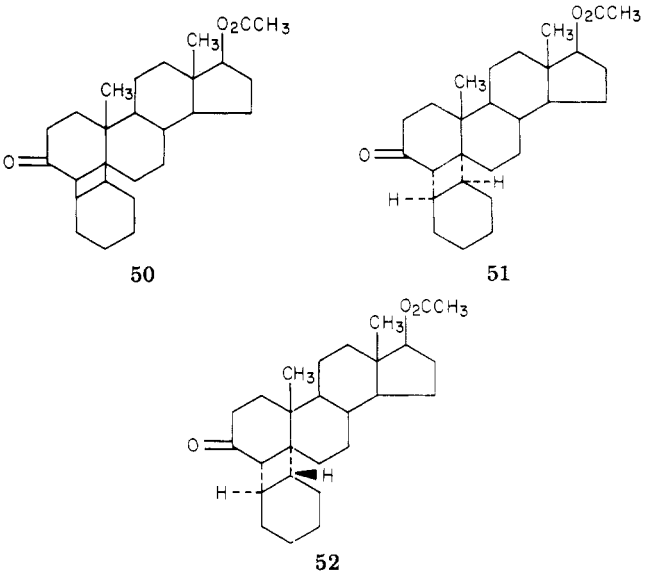


endo hydrogen will be shifted downfield, although not as strongly due to shielding by the geminal *endo*-methyl group, while the 4β-hydrogen should appear as a singlet. On the other hand, in the isomer D, the 4β-hydrogen should appear as a multiplet and the *endo*-methyl group should be deshielded. When the spectrum was recorded in deuteriobenzene, two singlets appeared at δ 2.38 and 2.27 which were assigned to an endo hydrogen and the 4β proton. Additionally, by comparing the methyl chemical shifts of adduct **45** in both solvents with those of the butadiene (**4**) and isoprene (**18** and **19**) ladder compounds, it was possible to demonstrate that the largest downfield methyl shift in **45** was δ 0.02, which was less than one-tenth as great as that observed with isoprene adduct **18**. Thus the NMR results are compatible only with the head-to-head adduct **45**.

The [4 + 2] Diels–Alder adduct **46** was next isolated in 24% yield. The 4α,5β-trans stereochemistry was indicated by its positive chiroptical effects and subsequent epimerization to the 4β,5β-cis [4 + 2] adduct **47**. Head-to-tail addition was indicated by the appearance of the 4β-hydrogen as a doublet of doublets in the NMR spectrum at δ 3.12.

The 6,7 adducts were the last compounds eluted from the column and were isolated as an equimolar mixture in 22% yield. It was possible to isolate the 6β,7β isomer **49** cleanly by fractional crystallization. The 4-enone proton appeared as a sharp singlet and the remainder of the structure was assigned by analogy to adduct **29**. The other isomer (**48**) we were not able to isolate either by fractional crystallization or by chromatography. The NMR spectrum clearly indicated its presence with the enone hydrogen appearing as a doublet at δ 6.15 and an olefinic and two additional tertiary aliphatic groups. Again the mode of addition was assigned by analogy to adduct **29**. Both the 6α,7α and 6β,7β adducts **48** and **49** were stable to prolonged refluxing in sodium methoxide solution.

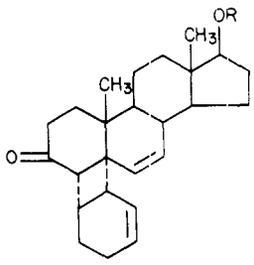
1,3-Cyclohexadiene. Because of the lack of ready availability of other cyclic 1,3-dienes, 1,3-cyclohexadiene was the only cis diene studied. Because of the inability to readily differentiate 1,2 versus 1,4 addition in this series by the usual physical methods, the adducts were eventually hydrogenated and compared to the adducts of testosterone acetate (**3**) with cyclohexene. The addition of enone **3** to cyclohexene generated the 4β,5β adduct **50**, presumably



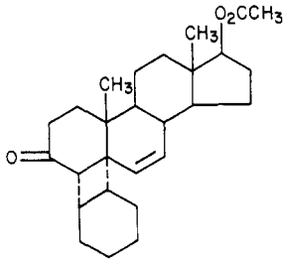
by fortuitous epimerization of the trans-4α,5β adduct, and the two cis-fused 4α,5α adducts, **51** and **52**.[3c] Since McCullough has shown, by X-ray, that cis addition of enones to cyclic olefins yields the anti isomer,[39] and if we assume a common diradical intermediate for **51** and **52**, this would lead to the stereochemistry indicated. On the other hand, the trans isomer leads to the syn compound upon epimerization.[39]

When dienone **1** was irradiated in the presence of 1,3-cyclohexadiene, only two compounds were formed. When the irradiation solution was concentrated, one of these compounds, **53**, crystallized. This compound was identified as a 4α,5α adduct by the disappearance of dienone absorptions in the IR and UV spectra. The chiroptical effects indicated the presence of a 4α,5α ring fusion. This, together with the hydrolysis to the alcohol **54** and subsequent reacetylation to adduct **53**, confirmed the stereo-

(39) Bowman, R. M.; Calvo, C.; McCullough, J. J.; Rasmussen, P. W.; Snyder, F. F. *J. Org. Chem.* **1972**, *37*, 2084.



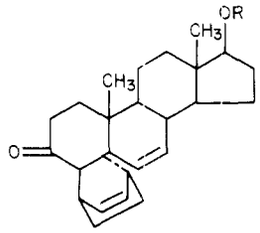
53, R = CH_3CO
54, R = H



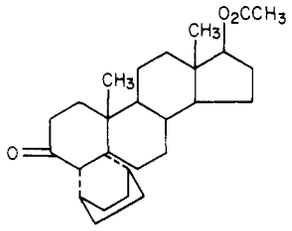
55

chemistry. Hydrogenation at room temperature smoothly consumed 1 equiv of hydrogen to yield the dihydro derivative **55**. The chracteristic doublet of doublets for the 6,7-olefinic hydrogens indicated the structure. Hydrogen at 60 °C and 60 psi gave the totally hydrogenated adduct **51** which was identical in all respects with the same compound isolated from the photocycloaddition of testosterone acetate to cyclohexene.

Since the residue after crystallization of **53** could not be separated by chromatography, it was saponified and then separated. After separation of alcohol **54**, the other compound (**56**) was isolated in 14% yield. Since it was an oil



56, R = H
57, R = CH_3CO



58

and could not be induced to crystallize, it was reacetylated to give the crystalline initial adduct **57**, which possessed positive chiroptical effects. Compound **57** was hydrogenated to the completely saturated adduct **58**, which was not identical with any of the testosterone acetate–cyclohexene adducts. As a result, adduct **56** was assigned the cis-4α,5α [4 + 2] structure. Again assuming a common diradical intermediate for both **53** and **56**, the double bond in the bicyclo ring system would be endo.

Quenching and Related Studies. Since the triplet energy of the dienones is lower than the usually employed dienic quenchers, quenching experiments were performed using Ullman's quencher, 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide.[40] This quencher has been reported to have an effective triplet energy of 35.6–42.4 kcal/mol, which is significantly below the dienone's triplets. Quenching studies were done with dienone **2**, and 2,3-dimethylbutadiene, since this diene is a liquid, gave only two predominant products, the 4,5-trans [4 + 2] and 6,7-cis [4 + 2] adducts, and these were stable to gas chromatography. The results are shown in Figure 3. The photocycloaddition to form both adducts is strongly quenched, but differential quenching is observed for the two adducts. The photo-Diels–Alder adduct across the 4,5 double bond is strongly quenched with a Stern–Volmer slope of 412 M^{-1} while the cis photo-Diels-Alder adduct across the 6,7 double bond is less effectively quenched, with a slope of 134 M^{-1}.

Since both [2 + 2 + 2 + 2] adducts are formed in low yields vis-a-vis the major adducts, quantitative quenching results were not feasible. Qualitative results were obtained,

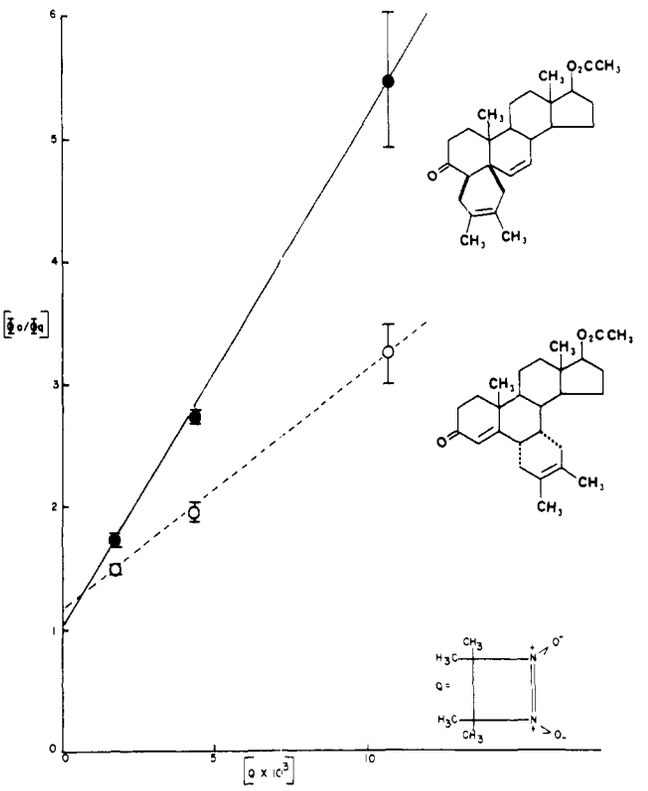


Figure 3. Stern–Volmer plot of the quenching, by 3,3,4,4-tetramethyl-1,2-diazetidine 1,2-dioxide, of the photocycloaddition of the dienone (0.050 M) to 2,3-dimethylbutadiene, 1.10 M in ethyl acetate.

however, by loading the irradiation solution with Ullman's quencher. At 0.04 M quencher, the effective solubility in the ethyl acetate–diene irradiation solution, the majority of [4 + 2] photocycloaddition is quenched. Since the concentration of diene was equivalent to the preparative runs, [2 + 2 + 2 + 2] cycloaddition should have occurred if the reaction occurred through the singlet excited state of the dienone. Under these conditions, formation of either the ladder compound or the alternative isomer was not observed. The results of these quenching experiments indicate that the formation of the cis and trans [4 + 2] adducts, as well as both [2 + 2 + 2 + 2] adducts, occurs through the triplet excited state of the dienone.

Since the differential quenching observed was indicative of an exiplex mediated reaction, the solvent dependence of the photocycloaddition of dienone **2** to 2,3-dimethylbutadiene was studied.[41] However the results were equivocal, and no meaningful results were obtained.

The linear dienones have been reported to neither fluoresce nor phosphoresce.[6] However, the dienone **2** does have a weak fluorescence at 330 ± 5 nm in 1,1,2-trifluoroethane with a quantum yield of $\Phi_f = (8 \pm 2) \times 10^{-4}$ and is on the same order as that observed for acetone.[42,43] The fluorescence of dienone **2** is quenched by *trans,trans*-2,4-hexadiene with a Stern–Volmer slope of $k_q\tau = \sim 0.3$.[43] Quenching studies of dienone **2** with other dienes were not possible due to interference of the dienes with the fluorescence measurements.

(40) Ullman, E. F.; Singh, P. *J. Am. Chem. Soc.* **1972**, *94*, 5077.

(41) (a) Lewis, F. D.; Hirsch, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 5914. (b) Lewis, F. D.; Hoyle, C. E. *Ibid.* **1976**, *98*, 4338. (c) Lewis, F. D.; Ho, T-I. *Ibid.* **1977**, *99*, 7991. (d) Lewis, F. D.; Hoyle, C. E. *Ibid.* **1977**, *99*, 3779.

(42) Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973; p 3.

(43) These experiments were performed by Professor N. C. Yang, University of Chicago, whom we thank.

The possible wavelength dependence on the photocycloaddition of dienone **2** to 2,3-dimethylbutadiene was also investigated. The $n\pi^*$ and $\pi\pi^*$ bands in the dienone are well resolved in ethyl acetate and occur at 350 (ϵ 90) and 282 nm (ϵ 27 000), respectively. Therefore, irradiation at 350 nm should selectively excite the $n\pi^*$ band. Since there is a minimum in the ultraviolet absorption spectrum at 320–325 nm, irradiation at 300 nm should predominantly excite the $\pi\pi^*$ band. Irradiation at a lower wavelength is not feasible because of the diene absorption. No wavelength dependence was observed and, additionally, preparative runs at different wavelengths and isolation of products also did not shown any wavelength dependence for the [2 + 2 + 2 + 2] adducts, as well as the cis and trans [4 + 2] adducts. Schaffner and Jeger have observed similar results in the hydrogen abstraction reactions of dienones.[44]

There were no charge-transfer interactions observed in the UV and visible spectra of the dienone–diene solutions, nor was there any thermal reaction between the dienones and dienes.

Discussion

The photocycloaddition of dienones to dienes is unique in giving [2 + 2 + 2 + 2] addition. From the range of dienes studied several observations can be made. The reaction is general above a certain ionization potential, is not dependent on the predominant diene configuration, and occurs through the dienone triplet state. The cycloaddition is stereospecific across the α face of the steroid, since β addition is impossible because of the 10-methyl group. Dienes with terminal substituents form only head-to-head adducts, while internal substituents yield mixtures. There are definite steric effects on the cycloaddition when there are internal substituents on the diene. For instance, the methyl group in isoprene allows formation of both possible [2 + 2 + 2 + 2] ladder compounds. The unequal amounts of these isomers which are formed (19/18 = 9) are probably due to a steric effect. The *endo*-methyl group in 18 experiences strong steric interactions with the steroid A-ring substituents, especially the axial 1α-hydrogen. In the 2,3-dimethylbutadiene adduct **11**, the same situation exists that occurs in isoprene except that there is no way of minimizing these steric interactions. Presumably for this reason, the alternative cycloaddition mode becomes competitive and approximately an equivalent amount of the more stable 5-4-5 ring [2 + 2 + 2 + 2] adduct **17** is formed.

The [2 + 2 + 2 + 2] cycloaddition is a function of ionization potential (Table I). Above an ionization potential of approximately 8.4 eV where the dienes become poorer electron donors, the cycloaddition occurs. This type of behavior and the maximal π overlap necessary to generate these adducts is reminiscent of an exiplex-mediated cycloaddition. This cycloaddition is also somewhat analogous to the [4 + 4] cycloaddition of aromatic hydrocarbons to dienes which occurs through singlet exiplexes,[45,46] although intersystem crossing to the triplet has been demonstrated.[47] Triplet exiplexes have also been implicated as intermediates in other cycloaddition reactions, including those of enones.[41a,48] If the [2 + 2 + 2 + 2] adducts are formed through an exiplex, then an explanation of the ionization potential dependence is available. As the dienes become better electron donors, charge transfer quenching quickly becomes competitive with cycloaddition.[49] There may be some evidence for this occurring. In the photocycloaddition of dienone **2** to 2,4-dimethyl-1,3-pentadiene, the only example of hydrogen transfer was observed. The structure of this adduct (**44**) indicates that it could be formed through the same intermediate as the ladder compounds and is not related to the trans [4 + 2] additions across the α,β dienone bond. The structure of **44** also indicates that it is formed through electron transfer to form a radical anion–radical cation pair, followed by coupling and subsequent hydrogen transfer.

A [2 + 2 + 2 + 2] cycloaddition is photochemically allowed to occur suprafacially between an even number of components.[50] An alternative mode of formation is an initial [4 + 4] cycloaddition followed by an undefined [2 + 2] addition. But if the [4 + 4] adduct were formed, a molecular model indicates that it is extremely rigid and the perpendicular distance between the parallel bonds is only 1.65 Å compared to an ordinary single bond of 1.54 Å.[51] The π orbitals, in this simple model, also completely overlap.[60] Since the symmetry is correct for the [2 + 2 + 2 + 2] cycloaddition, it is difficult to see how a [4 + 4] intermediate could have a discrete existance since the internal π orbitals would also be starting to overlap at approximately the same rate as bond formation was occurring at the terminal ends. An attempt to generate the [4 + 4] adduct by ring opening of the ladder adduct **11** with rhodium chloride–norbornadiene complex was unsuccessful.[52] Thus the formation of the ladder compounds is probably a true triplet [2 + 2 + 2 + 2] photocycloaddition. Initial [2 + 2] photocycloaddition across the α,β dienone double bond would give the wrong structure for the unsymmetrical ladder adducts, while initial [2 + 2] addition of olefins or dienes across the γ,δ double bond has not been observed.[5,20] If it were formed, the initial 6,7 [2 + 2] adduct should have been detected since the resultant chromophore could be the same as the enone **3**, which has a weaker and lower wavelength chromophore than the dienones and whose triplet is quenched by dienes.[3] Analogous examples with [2 + 2] addition across the α,β double bond with non-Diels–Alder dienes demonstrated that both possible epimers were formed and the less hindered form strongly predominated. This less hindered isomer would have the wrong stereochemistry to form the ladder compounds.

The photo-Diels–Alder reaction across the α,β double bond of the steroid dienone with various dienes to form trans [4 + 2] head-to-tail adducts is photochemically allowed.[53] This cycloaddition, like all the other non [2 + 2] additions in dienone–diene photochemistry, is a function of diene ionization potential (Table I). The reaction is general in forming trans [4 + 2] adducts with electron-poor

(44) (a) Karvas, M.; Martl, F.; Wehrli, H.; Schaffner, K.; Jeger, O. *Helv. Chim. Acta* **1974**, *57*, 851. (b) Gloor, J.; Schaffner, K. *Ibid.* **1974**, *57*, 1815. (c) Nobs, F.; Burger, U.; Schaffner, K. *Ibid.* **1977**, *60*, 1607. (d) Schaffner, K.; Jeger, O. *Tetrahedron* **1974**, *30*, 1891.

(45) (a) Yang, N. C.; Libman, J. *J. Am. Chem. Soc.* **1972**, *94*, 1405. (b) Kaupp, G. *Angew. Chem.* **1972**, *84*, 718.

(46) (a) Yang, N. C.; Shold, D. M.; McVey, J. K. *J. Am. Chem. Soc.* **1975**, *97*, 5004. (b) Yang, N. C.; Srinivaschar, K.; Kim, B.; Libman, J. *Ibid.* **1975**, *97*, 5006.

(47) (a) Saltiel, J.; Townsend, D. E.; Metts, L. L.; Wrighton, M.; Mueller, W.; Rosanske, R. *J. Chem. Soc., Chem. Commun.* **1978**, 588. (b) See also Farid, S.; Doty, J. C.; Williams, J. L. R. *Ibid.* **1972**, 711.

(48) (a) Caldwell, R. A.; Ghali, N. I.; Chien, C.-K.; DeMarco, D.; Smith, L. *J. Am. Chem. Soc.* **1978**, *100*, 2857. (b) Caldwell, R. A. *Ibid.* **1973**, *95*, 1690. (c) Farid, S.; Hartman, S. E.; Doty, J. C.; Williams, J. L. R. *Ibid.* **1975**, *97*, 3697.

(49) (a) Evans, T. R. *J. Am. Chem. Soc.* **1971**, *93*, 2081. (b) Guttenplan, J. B.; Cohen, S. G. *Ibid.* **1972**, *94*, 4040. (c) Wagner, P. J.; Leavitt, R. A. *Ibid.* **1973**, *95*, 3669. (d) Wagner, P. J.; Puchulski, A. E. *Ibid.* **1978**, *100*, 5948.

(50) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim, West Germany, 1971; p 112.

(51) Gordon, A. J.; Ford, R. A. "The Chemists Companion"; Wiley: New York, 1972; p 107.

(52) Eaton, P. E.; Patterson, D. R. *J. Am. Chem. Soc.* **1978**, *100*, 2573.

(53) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Wiley: New York, 1972; p 107.

dienes above an ionization potential of approximately 8.4 eV. As the dienes become more electron rich, cis and trans [2 + 2] adducts which are products formally derived from a diradical are formed and become the exclusive products with the normally very reactive Diels–Alder diene, 1,3-cyclohexadiene (IP = 8.25 eV). Vinylcyclohexene represents the transition where the trans [4 + 2] adduct is formed as well as the cis [2 + 2] and cis [4 + 2] adducts are formed, but unfortunately its ionization potential is unknown.

It was possible to differentiate between a photochemical [4 + 2] cycloaddition and a thermal [4 + 2] cycloaddition from a photochemically formed ground state transoid dienone[54-58] using both physical and chemical tests. In most of the systems where a transoid enone has been implicated, the energy of the triplet state is much higher than the dienes used as traps and internal conversion from the triplet to the transoid ground state is much faster than intermolecular energy transfer.[2b,55] Experimentally, transoid enones also possess enhanced stability at low temperatures, undergo facile addition of hydroxylic solvents and stereospecifically form trans [4 + 2] adducts with dienes such as furan, cyclopentadiene, and cyclohexadiene. In contrast, the photo-Diels–Alder [4 + 2] cycloaddition of dienone 1 to 2,3-dimethylbutadiene is readily quenched (Figure 3), indicating a triplet reaction. Attempted trapping of a transoid dienone at −78 °C with butadiene was unsuccessful.[59] Irradiation of dienone 1 in alcohols did not result in the formation of alcohol adducts, and addition of 2,3-dimethylbutadiene yielded the same adducts as in ethyl acetate. Cyclohexadiene and the other cis dienes have generally been used as traps for transoid enones since they possess the requisite cis configuration necessary to undergo [4 + 2] cycloaddition with the short-lived transoid enones. Dienone 1 undergoes predominantly cis [2 + 2] addition with cyclohexadiene and no trans [4 + 2] adducts were observed. No cycloaddition at all was observed with either furan or 2,5-dimethylfuran. Based on the facile quenching of the cycloaddition and the dienone's chemical behavior, the observed triplet [4s + 2a] cycloaddition is therefore a concerted photo-Diels–Alder reaction.[53]

Shaik and Epiotis have calculated the qualitative potential energy surfaces for $\pi\pi^*$ triplet [4 + 2] photoreactions and determined stereoselection rules for spin inversion.[60] Their calculations have indicated that there is a hole in the triplet, but not the singlet, potential energy surface, which is dependent on spin orbital coupling and which allows access to ground-state singlet poducts. The efficiency of the triplet–singlet ground-state transition is a function of the energy gap between the donor and acceptor components of the reaction and, as such, shows a strong correlation with ionization potential and electron affinity, respectively. The stereoselectivity predictions for the triplet [4 + 2] cycloadditions indicate that [4s + 2a] addition is expected for reaction pairs which are predominantly donor–donor or acceptor–acceptor. As the reaction pair becomes a better donor–acceptor pair, diradical formation is predicted to occur and finally for the best donor–acceptor pairs, predominant [4s + 2s] addition is expected. Comparison of the experimental results of diene additions across the α,β bond of the dienone with the theoretical predictions shows excellent agreement. With the poor donor, electron-poor dienes, exclusive [4s + 2a] cycloaddition to form trans photo-Diels–Alder adducts is observed. As the ionization potential of the dienes is lowered and they become better donors, a smooth transition is observed to form cis and trans [2 + 2] and cis [4 + 2] adducts which can be derived from an intermediate diradical. The range of ionization potential of the dienes studied is not low enough to attain exclusive cis [4 + 2] addition.

The cis [4 + 2] cycloaddition of dienes across the γ,δ double bond of the dienone is also a function of diene ionization potential and the cycloaddition is readily quenched. The differential quenching observed versus the trans [4 + 2] cycloaddition indicates that the addition could occur through prior exiplex formation. According to orbital symmetry rules, the cis [4 + 2] is forbidden yet it is unlikely that the reaction occurs through a diradical or zwitterionic intermediate. Olefins which cover the ionization potential range of the dienes which undergo the cis [4 + 2] addition do not yield any adducts across the γ,δ dienone double bond,[5] nor are [2 + 2] adducts across the terminal dienone double bond observed with any of the dienes investigated in this work or with *s*-trans dienes, whose structure prevents them from attaining the *s*-cis conformation.[20] Calculations on the cis [4 + 2] photocycloaddition indicate that it should occur through an exiplex and correlates directly with ground-state product.[61] However, a good donor–acceptor pair is necessary for cis addition to occur,[60,61] and the exact opposite is observed with electron-poor dienes adding and electron-rich dienes being nonreactive, possibly due to charge-transfer quenching.[49] It may be that the donor–acceptor designations are reversed in this case, since, based on the dienone–maleic anhydride irradiations,[5c] the terminal double bond of the dienone can function as a donor. As the diene ionization potential increases, they become poorer donors and fair acceptors. This reversal would lead to cis [4 + 2] addition. However, this is speculative and the details of the cis photo-Diels–Alder reaction across the terminal dienone double bond remain poorly understood.

Experimental Section

General. Melting points were determined on a Thomas-Hoover Unimelt capillary apparatus and are uncorrected. IR spectra were run in potassium bromide unless otherwise stated. Ultraviolet spectra were run in methanol and were not recorded if only n → π^* absorption was observed. NMR spectra were recorded on Varian A-60, T-60, FT-80, XL-100, and EM-390 spectrometers and were run in deuteriochloroform using tetramethylsilane as an internal standard. Other solvents are reported later in the Experimental Section. The NMR results are reported in chemical shifts (δ), followed by the signal shape: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. The multiplicity is followed by the coupling constant where applicable and the integrated signal intensity. ORD/CD curves were run on a Jasco ORD/UV-5 spectrometer and were run in methanol unless otherwise stated. GLC analyses were run on a Perkin-Elmer 900 gas chromatograph. Microanalyses were determined by the Searle Laboratories Microanalytical Department under the supervision of Mr. E. Zielinski. Mass spectra were run on an AEI MS-30. Optical rotations were determined in chloroform on a Perkin-Elmer Model 141 polarimeter.

6-Dehydrotestosterone Acetate (1) was prepared by acetylation of 6-dehydrotestosterone (Organon) with five parts of pyridine and four parts of acetic anhydride using 4-(*N*,*N*-di-

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methylamino)pyridine[62] as a catalyst.

The Photocycloaddition of 6-Dehydrotestosterone Acetate (1) to Butadiene. A solution of 10.0 g of 6-dehydrotestosterone acetate (1, 30.5 mmol) in 300 mL of ethyl acetate was irradiated with a 450-W medium-pressure mercury arc (Pyrex filter) while passing a stream of butadiene through the solution. After 8 h, TLC (1:4 ethyl acetate–benzene) indicated consumption of starting dienone and formation of five adducts. The solvent was removed on a rotary evaporator and the residue was chromatographed on 1 kg of Mallickrodt CC-7 silica with ethyl acetate–benzene (2:98) to give 3.15 g (8.25 mmol, 27%) of the ladder compound **4**: mp 181–182 °C (ether–petroleum ether); IR 1740, 1715, 1250 cm^{-1}; NMR δ 2.52 (t, 1 H), 1.81 (br s, 1 H, C5′ H), 1.37 (s, 3 H, OAc), 1.08 (s, 3 H), 0.82 (s, 3 H); NMR (C_6D_6) δ 4.73 (t, 1 H), 2.83 (br s, 1 H, C5′ H), 1.76 (s, 3 H), 0.78 (s, 6 H); $[\Phi]_{317}$ +2598°, $[\Phi]_{283}$ +1108°; a = +23; $[\theta]_{297}$ +2316°; MS m/e 382 (27%, parent).

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.45; H, 9.09.

The ladder compound **4** could be saponified with sodium methoxide in methanol and reacetylated to regenerate starting material in almost quantitative yield.

Continued elution gave 4.387 g (11.5 mmol, 33%) of the 4α,5β [4 + 2] adduct **5**: 223–225 °C (ether); IR 1730, 1720, 1250 cm^{-1}; NMR δ 5.58–5.83 (m, 2 H), 5.65 (s, 2 H), 4.58 (t, 1 H, C17α H), 2.78 (q, 1 H, C4β H), 2.03 (s, 3 H, OAc), 0.92 (s, 3 H), 0.82 (s, 3 H); $[\Phi]_{304}$ +4900°, $[\Phi]_{289}$ 0°, $[\Phi]_{268}$ −4600°, a = +95; $[\theta]_{290}$ +7550°.

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.36; H, 9.02.

Elution with ethyl acetate–benzene (5:95) gave 0.47 g (1.23 mmol, 4%) of the 6α,7α [4 + 2] adduct **9**: mp 133–135 °C (methanol–water); IR 3020, 1735, 1675, 1610, 1245 cm^{-1}; UV 244 nm (ϵ 12 500); NMR δ 5.77 (d, J = 1.5 Hz, 1 H, C4 H), 5.60 (br s, 2 H), 4.63 (t, 1 H, C17α H), 2.05 (s, 3 H, OAc), 1.23 (s, 3 H), 0.87 (s, 3 H).

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.12; H, 8.78.

Compound **9** could be saponified with sodium methoxide and reacetylated to regenerate starting material.

Closely following **9** came 0.48 g (1.26 mmol, 4%) of the 6β,7β [4 + 2] adduct **8**: 225–226 °C (ethyl acetate); IR 3020, 1735, 1680 (sh), 1670, 1610, 1250 cm^{-1}; NMR δ 5.75 (sharp s, 1 H, C4 H), 5.63 (m, 2 H), 4.63 (t, 1 H, 17α H), 2.02 (s, 3 H, OAc), 1.33 (s, 3 H), 0.83 (s, 3 H); NMR (C_6D_6) δ 5.80 (s, 1 H), 5.55 (m, 2 H), 4.70 (t, 1 H), 1.77 (s, 3 H), 0.93 (s, 3 H), 0.75 (s, 3 H).

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.42; H, 9.05.

Continued elution returned 0.26 g of dienone.

Epimerization of the Trans-4α,5β [4 + 2] Adduct 5. A solution of 500 mg of **5** in 100 mL of methanol was reacted with 1 g of sodium methoxide for 18 h. The solution was poured into 500 mL of water and extracted three times with 125 mL of methylene chloride. The combined organics were dried with sodium sulfate and removed under reduced pressure. The residue was taken up in ether and 313 mg of 4β,5β [4 + 2] adduct **6** crystallized upon addition of petroleum ether: mp 169–170 °C; IR 3520, 3030, 1720 cm^{-1}; NMR δ 6.40–6.85 (m, 4 H), 3.70 (t, 1 H), 0.85 (s, 3 H), 0.81 (s, 3 H); $[\Phi]_{306}$ −10 500°, $[\Phi]_{292}$ 0°, $[\Phi]_{266}$ +13 200°; a = −237; $[\theta]_{294}$ −16 250°.

Anal. Calcd for $C_{23}H_{32}O_2$: C, 81.13; H, 9.47. Found: C, 81.13; H, 9.60.

The mother liquors from the above crystallization were evaporated and the solid residue, which was essentially pure **6**, and 147 mg of crystalline **6** were dissolved in 5 mL of pyridine and 3 mL of acetic anhydride and a few crystals of 4-(*N*,*N*-dimethylamino)pyridine were added. The solution was stored in a steam cabinet for 3 days and then poured into water. The aqueous solution was extracted with chloroform and the organics, in turn, were washed with water, dilute hydrochloric acid, and dilute sodium bicarbonate. The chloroform solution was dried with sodium sulfate and evaporated. The residue was found to be soluble in petroleum ether and was crystallized from methanol–water to give **7**: mp 127–129 °C; IR 1740, 1720 cm^{-1}; NMR δ 5.60 (m, 4 H), 2.05 (s, 3 H, 17β-OAc), 0.87 (s, 6 H); $[\Phi]_{307}$ −9700°, $[\Phi]_{292}$ 0°, $[\Phi]_{266}$ +11 650°; a = −213; $[\theta]_{294}$ −18 300°.

Anal. Calcd for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.47; H, 8.90.

Photocycloaddition of 1 to 2,3-Dimethylbutadiene. 6-Dehydrotestosterone acetate (1, 5.0 g, 14.6 mmol) was dissolved in 165 mL of ethyl acetate and 25 mL of 2,3-dimethylbutadiene (Chemical Samples, 99%) was added. After irradiation for 80 min, the solvent was removed on a rotary evaporator and the residue chromatographed on 1500 g of CC-7 silica. Elution with ethyl acetate–benzene (5:95) gave 0.48 g (1.2 mmol, 8%) of **11** as a noncrystallizable oil: IR 1730 (17β-OAc), 1700 cm^{-1} (3-C=O); NMR δ 4.64 (t, 17α-H), 2.03 (s, 3 H, OAc), 1.10 (s, 6 H, CH_3), 1.03 (s, 3 H, CH_3), 0.84 (s, 3 H, CH_3).

Since **11** was an oil it was saponified with sodium methoxide in methanol to give the 17β-alcohol **12**: mp 138–140 °C (ethanol–water); IR 1700 cm^{-1} (C=O); NMR δ 3.66 (t, 17α-H), 1.07 (s, 6 H, CH_3), 1.03 (s, 3 H, CH_3), 0.77 (s, 3 H, CH_3); NMR (C_6D_6) δ 3.50 (t, 17α-H), 1.25 (s, 3 H, CH_3), 1.08 (s, 3 H, CH_3), 0.78 (s, 6 H, CH_3); ORD/CD $[\Phi]_{316}$ +2490°, $[\Phi]_{283}$ +845°, a = +16; $[\theta]_{295}$ +2170°, a = +26; mass spectrum m/e (rel intensity) 368 (parent, 21), 287 (100, P − 2,3-dimethylbutadiene + H).

Anal. Calcd for $C_{25}H_{38}O_2$: C, 81.47; H, 9.85. Found: C, 81.49; H, 9.96.

Compound **12** could be acetylated using acetic anhydride–pyridine to regenerate **11** as an oil.

Continued elution yielded 5.03 g of a mixture of [4 + 2] adducts from which 1.06 g (2.6 mmol, 18%) of the trans [4 + 2] adduct **13** could be crystallized using ether: mp 206–208 °C; IR 1740 (-OAc), 1725 cm^{-1} (3-C=O); NMR δ 5.58 (s, 2 H, C6,7 vinyl H), 4.60 (t, 17α-H), 2.78 (q, 1 H C4 H), 2.00 (s, 3 H, OAc), 1.63 (br s, 6 H, vinyl CH_3), 0.92 (s, 3 H, CH_3), 0.80 (s, 3 H, CH_3); NMR (C_6D_6) δ 5.76 (s, 2 H), 4.58 (t, 1 H), 1.75 (s, 3 H, OAc), 1.60 (br s, 6 H, vinyl CH_3), 0.73 (s, 6 H, C18,19 CH_3); ORD/CD $[\Phi]_{305}$ +3634°, $[\Phi]_{286}$ 0°, $[\Phi]_{273}$ −1100°, a = +47; $[\theta]_{290}$ +4627°, a_{calcd} = +56.

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 78.82; H, 9.56.

The remainder of the [4 + 2] adducts, 1.83 g (4.4 mmol, 30%), was saponified and epimerized to the 4β,5β [4 + 2] 17β-alcohol **14**: mp 152–154 °C (methanol–water); IR 3550 (17β-OH), 1705 cm^{-1} (3-C=O); NMR δ 5.53 (s, 2 H, C6,7 vinyl H), 3.68 (t, 1 H, 17α-H), 1.67 (br s, 3 H, vinyl CH_3), 1.58 (br s, 3 H, vinyl CH_3), 0.87 (s, 3 H, CH_3), 0.83 (s, 3 H, CH_3); ORD/CD $[\Phi]_{306}$ −1327°, $[\Phi]_{297}$ 0°, $[\Phi]_{269}$ +4828°, a = −62; $[\theta]_{293}$ −4293°, a_{calcd} = −52.

Anal. Calcd for $C_{25}H_{36}O_2$: C, 81.47; H, 9.85. Found: C, 81.13; H, 10.08.

A 900-mg portion of **13** was treated with 500 mg of sodium methoxide in 50 mL of methanol. After 8 h, the majority of the solvent was removed on a rotary evaporator and dilute hydrochloric acid was added to the residue. The aqueous solution was extracted with chloroform and discarded. The organic layer was dried with sodium sulfate and evaporated. The residue was taken up in 5 mL of pyridine and 4 mL of acetic anhydride plus a few milligrams of 4-(dimethylamino)pyridine. After 18 h, the excess acetylating mixture was destroyed with ethanol and upon watering out 678 mg of **15** was obtained: mp 162–166 °C; IR 1740 (OAc), 1725 (3-C=O), 1245 cm^{-1} (OAc); NMR δ 5.53 (s, 2 H, C6,7 vinyl H), 2.05 (s, 3 H, 17β-OAc), 1.68 (br s, 3 H, vinyl CH_3), 1.57 (br s, 3 H, vinyl CH_3), 0.87 (s, 6 H, C18,19 CH_3); ORD/CD $[\Phi]_{306}$ −8400°, $[\Phi]_{294}$ 0°, $[\Phi]_{260}$ +14 000°; a = −224; $[\theta]_{293}$ −18 700°.

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 78.91; H, 9.38.

A small overlap fraction at the end of the [4 + 2] adducts was determined by NMR to contain an additional compound which was subsequently identified as the alternate adduct **17**. This compound and the cis [4 + 2] adduct **15** were barely separable in several TLC systems, and saponification to the 17β-alcohol did not improve the separation. After reacetylation, the fraction weighed 480 mg and, by NMR weak integration of the tertiary methyl groups, consisted of an equimolar mixture of the alternate [2 + 2 + 2 + 2] adduct **17** and the cis [4 + 2] adduct **15**. Separation was effected by dissolving the mixture in 20 mL of acetone and adding it dropwise to a yellow solution of ruthenium tetroxide, which was formed by stirring 100 mg of ruthenium dioxide in 50 mL of acetone and adding 400 mg of sodium periodate in the minimum amount of water.[17] Two subsequent additions of sodium

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periodate were made by hourly intervals and, after 3 h, the mixture was filtered through filter aid and the solution was evaporated. The dark residue was taken up in ethyl acetate–methylene chloride (5:95) and flash chromatographed[18] to yield 180 mg of the alternate isomer **17**: mp 151–157 °C (methanol); IR 1735, 1700 cm^{-1}; NMR δ 4.61 (t, 1 H, 17α-H), 2.03 (s, 3 H, OAc), 1.24 (s, 3 H), 1.08 (s, 3 H), 0.78 (s, 3 H), 0.54 (s, 3 H); NMR (C_6D_6) δ 4.73 (t, 1 H), 1.73 (s, 3 H, OAc), 1.02 (s, 3 H), 0.93 (s, 3 H), 0.74 (s, 3 H), 0.34 (s, 3 H); $[\alpha]^{25}_{589}$ +41° (c 0.114, $CHCl_3$), $[\alpha]^{25}_{365}$ +193°; ORD/CD $[\Phi]_{308}$ +2020°, $[\Phi]_{274}$ +545°; a = +15; $[\theta]_{288}$ +2100°.

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 79.04; H, 9.44.

Elution with ethyl acetate–benzene (1:9) yielded 1.89 g (4.7 mmol, 32%) of the 6,7 [4 + 2] adduct **16**: mp 191–194 °C (ether–petroleum ether); UV 243 nm (ϵ 13 500); IR 1735 (OAc), 1670, 1610 cm^{-1} (enone); NMR δ 5.60 (d, J = 1.5 Hz, 1 H, C4 vinyl H), 2.05 (s, 3 H, 17β-OAc), 1.67 (br s, 3 H, vinyl CH_3), 1.57 (br s, 3 H, vinyl CH_3), 1.22 (s, 3 H, C19 CH_3), 0.87 (s, 3 H, C18 CH_3).

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 78.54; H, 9.17.

Continual elution retained 0.25 g (0.75 mmol, 5.2%) of starting dienone **1**.

The Photocycloaddition of Dienone 2 to 2-Methylbutadiene (Isoprene). Dienone **2** (10.0 g, 29.4 mmol) was dissolved in 145 mL of toluene and 50 mL of 2-methyl-1,3-butadiene (isoprene, Aldrich, 99%) was added. Argon was bubbled through the reaction mixture for 0.5 h prior to the irradiation and during the irradiation. The solution was irradiated, through Pyrex, for 5 h with a 450-W medium-pressure mercury arc. The solvent was removed under reduced pressure and the residue was chromatographed on 1600 g of E. Merck silica (1-L fractions). Elution with ethyl acetate–petroleum ether (1:4) gave 266 mg (2.2%) of the ladder compound **18**: mp 205–206 °C (methanol); IR ν 1780, 1710 cm^{-1}; NMR δ 1.25 (s, 3 H, ladder CH_3), 1.06 (s, 3 H, C19), 0.97 (s, 3 H, C18); NMR (C_6D_6) δ 1.47 (s, 3 H, ladder CH_3), 0.85 (s, 3 H, C18), 0.77 (s, 3 H, C19); $[\alpha]_D$ +54.7 ± 3.4° (c 0.090, $CHCl_3$), $[\alpha]^{25}_{365}$ +278.2 ± 3.4°; $[\Phi]_{315}$ +1450°, $[\Phi]_{292}$ +755°, a = +7; $[\theta]_{302}$ +938°, a_{calcd} = +11; MS m/e (relative intensity) 408 (parent, 62.6), 341 (6, P – 2-methylbutadiene – H), 335 (44, P – spirolactone + H).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.26; H, 8.59.

Elution with ethyl acetate–petroleum ether (3:7) gave 621 mg (1.5 mmol, 5%) of the [2 + 2] adduct **20**: mp 135 °C softens, 155 °C melts (methanol–water); IR ν 1780, 1710 cm^{-1}; NMR δ 5.65 (br s, 2 H, C6,7), 4.95 (s, secondary splitting to q, 1 H, vinyl H), 4.80 (br s, 1 H, vinyl H), 3.43 (t, J = 8 Hz, 1 H), 1.75 (br s, 3 H, vinyl CH_3), 0.98 (s, 3 H, C18), 0.77 (s, 3 H, C19); NMR (C_6D_6) δ 5.45 (m, 2 H, C6,7), 4.93 (br s, split to q, 1 H), 4.74 (br s, 1 H), 3.17 (t, J = 8 Hz, 1 H), 1.63 (br s, 3 H), 0.82 (s, 3 H), 0.60 (s, 3 H); $[\alpha]^{25}_D$ +57.0 ± 2.0° (c 0.100, $CHCl_3$); $[\Phi]_{295}$ +1940°, $[\Phi]_{280}$ +1756°, a = +2; $[\theta]_{289}$ +970°, a_{calcd} = +12.

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.25; H, 9.10.

Closely following the [2 + 2] adduct **20**, the second ladder compound (**19**) was eluted (2.34 g, 5.8 mmol, 19.5%): mp 244.5–251 °C (methanol–water); IR ν 1775, 1710 cm^{-1}; NMR δ 1.23 (s, 3 H, ladder CH_3), 1.08 (s, 3 H, C19), 0.98 (s, 3 H, C18); NMR (C_6D_6) δ 2.55 (s with secondary splitting, 1 H, C5′ ladder H), 1.23 (s, 3 H, ladder CH_3), 0.85 (s, 3 H, C18), 0.75 (s, 3 H, C19); $[\alpha]^{25}_D$ +78.1 ± 2.3° (c 0 128, $CHCl_3$); $[\alpha]^{25}_{365}$ +292.2 ± 2.3°; $[\Phi]_{315}$ +1450°, $[\Phi]_{292}$ +755°; a = +7; $[\theta]_{302}$ +940°, a_{calcd} = +11; MS m/e (relative intensity) 408 (parent, 22%), 341 (100, P – 2-methylbutadiene – H), 335 (14.5, P – spirolactone + H).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.49; H, 8.90.

After an intermediate fraction (184 mg), 1.259 g of the 4β,5β [4 + 2] adduct **21** was eluted. The following two fractions contained 0.984 g of **20** and 1.366 g of **21** as a mixture (5.8 mmol, 19.5%) (measured by NMR integration of the methyl peaks). Compound **21** shows: mp 209–211 °C (methanol–water); IR ν 1775, 1720 cm^{-1}; NMR δ 5.56 (s, 2 H, C6,7), 5.45 (m, 1 H, vinyl H), 1.64 (br s, 3 H, vinyl CH_3), 1.02 (s, 3 H, C18), 0.88 (s, 3 H, C19); NMR (C_6D_6) δ 5.66 (dd, J = 11, 1 Hz, 1 H), 5.49 (m, 1 H), 5.33 (dd, J = 10, 1 Hz, 1 H), 1.61 (br s with secondary splitting, 3 H), 0.86 (s, 3 H), 0.66 (s, 3 H); $[\alpha]^{25}_D$ –40.8 ± 2.4° (c 0.128, $CHCl_3$); $[\Phi]_{308}$ –8500°, $[\Phi]_{294}$ 0°, $[\Phi]_{266}$ +11 275°, a = –198; $[\theta]_{294}$ –14 460°, a_{calcd} = –176.

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.27; H, 8.95.

The two intermediate fractions mentioned above also contained 0.984 g of **22** as a mixture which was followed by 1.46 g of the pure isomeric 4β,5β [4 + 2] adduct **22** (6.0 mmol, 20%): mp 255–260 °C softens, 269–270 °C melts (ether); IR ν 1780, 1717 cm^{-1}; NMR δ 5.57 (d, 2 H), 5.25 (m, 1 H, vinyl H), 1.74 (br s, 3 H, vinyl CH_3), 1.02 (s, 3 H, C18), 0.87 (s, 3 H, C19); NMR (C_6D_6) δ 5.69 (dd, J = 10, 1 Hz, 1 H), 5.35 (d, J = 10 Hz, 1 H), 5.23 (m, 1 H), 1.77 (s, 3 H), 0.85 (s, 3 H), 0.62 (s, 3 H); $[\alpha]^{25}_D$ –46.0 ± 3.0° (c 0.100, $CHCl_3$); $[\Phi]_{306}$ –9315°, $[\Phi]_{293}$ 0°, $[\Phi]_{265}$ +12 910°, a = –222; $[\theta]_{294}$ = 16 835°, a_{calcd} = –205.

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.49; H, 8.90.

In another experiment, run under identical conditions, it was possible to isolate, after **22**, 1.008 g (2.45 mmol, 8%) of the trans-4α,5β [4 + 2] adduct **23**: mp 175.5–179 °C (ethyl acetate–petroleum ether); IR ν 1780, 1725 cm^{-1}; NMR δ 5.60 (m, 3 H), 1.68 (br s, 3 H, vinyl CH_3), 0.97 (s, 6 H, C18,19); NMR (C_6D_6) δ 5.50 (m, 3 H), 1.62 (br s, 3 H), 0.80 (s, 3 H), 0.67 (s, 3 H); $[\alpha]^{25}_D$ 2.0 ± 2.0° (c 0.100, $CHCl_3$). The ORD/CD curves of **23** gave a curve showing weakly negative effects, indicating appreciable epimerization to **21** had occurred.

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.27; H, 8.87.

Isomerization of **23** with sodium methoxide in methanol overnight at room temperature gave, after acidification with dilute hydrochloric acid, a clean conversion to **21**.

Elution with ethyl acetate–petroleum ether (1:1) gave 2.003 g (4.9 mmol, 17%) of a mixture of the two isomeric 6α,7α [4 + 2] adducts in approximately equal amounts: these two isomers could not be separated by chromatography. They were recovered unchanged from sodium methoxide in methanol, indicating that they were not a mixture of cis–trans isomers. The isomers **24** and **25** exhibit: mp 205–220 °C (methylene chloride–ethyl acetate); IR ν 1775, 1665, 1610 cm^{-1}; UV 241 nm (ϵ 14 000); NMR δ 5.75 (d, $J \simeq$ 1.5 Hz, 1 H, C4), 4.77 (d, $J \simeq$ 1.5 Hz, 1 H, C4), 4.50 (br s, 1 H, vinyl H), 1.70 (br s, 3 H, vinyl CH_3), 1.62 (br s, 3 H, vinyl CH_3), 1.25 (s, 3 H, C19), 1.02 (s, 3 H, C18); NMR (C_6D_6) δ 5.92 (d, $J \simeq$ 1.5 Hz, 1 H), 5.75 (d, $J \simeq$ 1.5 Hz, 1 H), 5.25 (br s, 1 H, vinyl H), 1.60 (br s, 3 H, vinyl CH_3), 0.85 (s, 3 H), 0.82 (s, 3 H).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.44; H, 8.87.

Further elution gave 0.381 g of starting dienone **2**.

Attempted Ring Closure of 19. **20** (618 mg) was dissolved in 145 mL of toluene and 45 mL of isoprene and irradiated, under argon, with a 200-W lamp. After 5 h there was no evidence for the formation of **19** and most of **20** was recovered.

The Addition of Δ^6-Testosterone Acetate to 1-Acetoxybutadiene. A solution of 10.0 g (30.5 mmol) of 6-dehydrotestosterone acetate (**1**) in 170 mL of toluene and 20 g of 1-acetoxybutadiene[21] was irradiated, under argon, with a 450-W medium-pressure mercury arc (Pyrex) for 5 h. The volatiles were removed under reduced pressure and the residue was chromatographed on 1.6 kg of E. Merck silica. Elution with ethyl acetate–petroleum ether (1:4) gave 18 fractions as mixtures from which small amounts of pure compounds could be isolated. Fraction 4 gave 104 mg of pure 4β,5β [4 + 2] adduct **26**: mp 234–237 °C (ether); IR ν 1735 cm^{-1}; NMR δ 5.00–6.08 (m, 5 H), 4.72 (t, 1 H, 17α-H), 3.07 (distorted q, 1 H, 4α-H), 2.07 (s, 3 H, OAc), 1.98 (s, 3 H, OAc), 0.88 (s, 6 H, 18,19-CH_3); $[\Phi]_{314}$ (sh) –9760°, $[\Phi]_{306}$ –10 400°, $[\Phi]_{290}$ 0°, $[\Phi]_{269}$ +6720°, $[\Phi]_{245}$ +4320°, $[\Phi]_{236}$ +7840°; a = –171; $[\theta]_{294}$ –14 080°.

Anal. Calcd for $C_{27}H_{36}O_5$: C, 73.60; H, 8.24. Found: C, 73.52; H, 8.17.

Fraction 10 gave 147 mg of one of the trans-4α,5β [4 + 2] epimers (**27**): mp 206–207 °C (ether); IR ν 1740 cm^{-1}; NMR δ 6.00 (br s, 2 H, cyclohexene H), 5.82 (dd, J = 10, 1 Hz, 6-H); 5.40 (dd, J = 10, 2.5 Hz, 7-H), 4.87 (d, with secondary splitting, J = 4 Hz, 1 H, α-acetoxy H), 4.78 (t, 17α-H), 3.37 (q, J = 9, 7 Hz, 4β-H), 2.13 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 0.95 (s, 3 H), 0.82 (s, 3 H); $[\Phi]_{304}$ +6600°, $[\Phi]_{271}$ +352°; a = +62; $[\theta]_{289}$ +6424°.

Anal. Calcd for $C_{27}H_{36}O_5$: C, 73.60; H, 8.24. Found: C, 73.47; H, 8.17.

Trituration of fraction 12 with ether gave 216 mg of the other trans-4α,5β [4 + 2] epimer (**28**): mp 209–211 °C; IR ν 1740, 1730, 1715 cm^{-1}; NMR δ 5.5–6.15 (m, 4 H), 5.12 (d, with secondary splitting, J = 9 Hz, 1 H, α-acetoxy H), 4.58 (t, 1 H, 17α-H), 3.13 (q, J = 8, 7 Hz, 1 H, 4β-H), 2.03 (s, 6 H, OAc), 0.97 (s, 3 H), 0.80 (s, 3 H); $[\Phi]_{317}$ +3696°, $[\Phi]_{300}$ 0°, $[\Phi]_{275}$ −4488°; a = +82; $[\theta]_{299}$ +6512°.

Anal. Calcd for $C_{27}H_{36}O_5$: C, 73.60; H, 8.24. Found: C, 73.18; H, 8.10.

Fractions 15–18 returned 356 mg of starting dienone **1**.

Elution with ethyl acetate–petroleum ether (3:7) gave 1.37 g (3.1 mmol, 10%) of the 6α,7α [4 + 2] adduct **29**: mp 153–155 °C (methanol–water); IR ν 1740, 1685, 1615 cm^{-1}; UV 241 nm (ε 14 000); NMR δ 5.75–6.10 (m, 2 H, cyclohexene H), 5.67 (d, J = 1.5 Hz, 1 H, C4 H), 5.27 (dd, J = 4.5, 1.5 Hz, 1 H, α-acetoxy H), 4.63 (t, 1 H, 17α-H), 2.62 (d, with secondary splitting, J = 4 Hz, 1 H, 6β-H).

Anal. Calcd for $C_{27}H_{36}O_5$: C, 73.60; H, 8.24. Found: C, 73.26; H, 8.14.

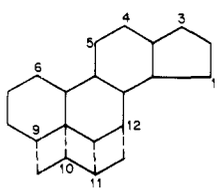
The noncrystalline mixture (4.25 g) of [4 + 2] isomers, containing some starting dienone **1**, was saponified in 100 mL of methanol and 10 mL of water which contained 4 g of sodium hydroxide. After 18 h, the mixture was acidified with concentrated hydrochloric acid and extracted with $CHCl_3$. The chloroform was dried with sodium sulfate and evaporated. After attempted oxidations with dichlorodicyanobenzoquinone[26] and freshly prepared Fetizon's reagent[27] failed, the mixture was oxidized with excess Jones reagent[28] and, after 15 min, quenched with 2-propanol and poured into water. The aqueous solution, after evaporation of the majority of the acetone, was extracted with chloroform. The chloroform extract was dried with sodium sulfate and evaporated. Addition of methanol to the residue caused partial crystallization to yield 209 mg of **30**: mp 236–238 °C; IR ν 1745, 1725, 1680, 1650 cm^{-1}; UV 222 nm (ε 9000); NMR δ 6.87 (m, 1 H, cyclohexenone H), 5.78 (m, 1 H, cyclohexenone H), 5.83 (s, 2 H, C6,7 H), 3.33 (d, with secondary splitting, J = 5 Hz, 1 H), 2.75 (d, with secondary splitting, J = 5 Hz, 1 H), 1.40 (s, 3 H), 0.95 (s, 3 H).

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.37; H, 8.01. Found: C, 78.60; H, 8.26.

The residue from the above crystallization was chromatographed on 500 g of E. Merck silica. Elution with ethyl acetate–petroleum ether (15:85) gave 1.07 g of 6-dehydroandrostenedione (**31**), identified by comparison with an authentic sample prepared by Jones oxidation of 6-dehydrotestosterone. This was followed by an additional 0.121 g of **30**. Elution with ethyl acetate–petroleum ether (1:3) gave 0.232 g of the ladder compound **32**: mp 291–294 °C (ethyl acetate–petroleum ether); IR ν 1775, 1740, 1710 cm^{-1}; NMR δ 3.31 (d, J = 2.9 Hz, 1 H), 2.79 (s, 1 H, 4β-H), 1.15 (s, 3 H), 0.90 (s, 3 H); NMR (C_6D_6) δ 3.33 (d, J = 2.5 Hz, 1 H), 2.19 (s, 1 H, 4β-H), 0.56 (s, 6 H).

Anal. Calcd for $C_{23}H_{28}O_3$: C, 78.37; H, 8.01. Found: C, 78.33; H, 8.13.

The results of a 100-MHz ^{1}H NMR study in hexadeuteriobenzene and deuteriochloroform on **32**, together with europium shifts [tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)europium] and decoupling experiments, yielded chemical shifts for most of the protons and many of the coupling constants. Standard steroid numbering is used with the ladder carbon attached to C5 being C20 and that attached to C7 being C23. Chemical Abstracts numbering, courtesy of Dr. Kurt Loening, as indicated, is also given. The results are collected in Table II.



The spectrum shows a singlet at 279 Hz in $CDCl_3$ and 219 Hz in C_6D_6. From its chemical shift and rate of shift with europium, this signal is α to a carbonyl and is assigned to C4 H. A one-proton doublet at 331 Hz in $CDCl_3$ and 355 Hz in C_6D_6 is the proton most shifted with europium and is assigned to C21 H. In deuteriobenzene, it was shown that this proton was coupled to a proton at 238 Hz, which is a pentet. The couplings are all small (~3 Hz). In deuteriochloroform, this proton was identified at 281 Hz. Therefore C21 H is coupled to C22 H which, in turn, is coupled to three other protons at C6β H, C23α H, and C23β H. None of these couplings are geminal or axial,axial and thus are small. In the europium study, the proton at C22 moves at about the same rate as another proton. The width at half-height is relatively narrow, and from changes in the shapes of the signals as the difference in chemical shift between them decreases these two protons are coupled. This other proton is assigned to the 6β-H which is coupled to the 7β-H and 22-H. The 6β- and 22β-H are approximately the same distance from the cyclobutyl carbonyl and thus would be expected to have similar shifts with europium.

Generally, it appears that europium complexes most strongly with the cyclobutanone carbonyl and least with the 3-ketone.

Table II. ^{1}H NMR Results for the Cyclobutanone Ladder Compound 32

steroid proton	C.A. proton	chemical shift, δ	coupling constant, Hz[a]
2α	6α	2.50	$J_{2\alpha,2\beta}$ = 14.5 $J_{2\alpha,1\alpha} \simeq 3.5$ $J_{2\alpha,1\beta} \simeq 3.5$
2β	6β	2.61	$J_{2\beta,1\alpha} \simeq 6$ $J_{2\beta,1\beta} \simeq 2$–3
4β	9β	2.79	
6β	11αβ	2.53	$J_{6\beta,7\beta} \simeq 3$ $J_{6\beta,22} \simeq 3$
7β	12β	2.61	$J_{7\beta,23\alpha} \simeq 3$ $J_{7\beta,23\beta} \simeq 5$
12β	4β	1.95	$J_{12\alpha,12\beta} \simeq 13$ $J_{12\alpha,11\alpha} \simeq 3$ $J_{12\alpha,11\beta} \simeq 3$
16α,β	1	2.58	$J_{16,15\alpha}$ = 6.5, 7
21	10	3.31	$J_{21,22}$ = 2.9
22	11	2.81	$J_{22,23\alpha} \simeq 3$ $J_{22,23\beta} \simeq 3$
23α	11bα	1.70	$J_{23\alpha,23\beta}$ = 14
23β	11bβ	1.53	

[a] Standard steroid numbering is given for the coupling constants (J).

Photocycloaddition of Dienone 2 to *trans,trans*-2,4-Hexadiene. A solution of 10.0 g (29.4 mmol) of dienone **2** in 20 mL of *trans,trans*-2,4-hexadiene (Chemical Samples, 99%) and 175 mL of ethyl acetate was irradiated, under argon, with a 450-W medium-pressure mercury arc (Pyrex filter). After 3 h of irradiation, TLC on silica with both 1:1 and 1:4 ethyl acetate–toluene indicated consumption of dienone and formation of two separate groups of products. After removal of solvent, the residue was chromatographed on 1600 g of Woelm silica on a 80 × 700 mm column using low pressure. The fraction size was 30 mL. Fractions 320–420 were eluted using 1:1 ethyl acetate–toluene yielding the trans [2 + 2] adduct **33** (5.56 g, 13.2 mmol, 45%): mp 253–258 °C (ethyl acetate–petroleum ether); IR 1770, 1725 cm^{-1}; NMR δ 5.50–6.08 (q, 2 H, C6,7), 5.17–5.42 (m, 2 H), 1.60 (d, J = 4.5 Hz, 3 H), 1.08 (s, 3 H), 1.09 (d, J = 6 Hz, 3 H), 0.94 (s, 3 H); $[\alpha]^{25}_{589}$ −114° (c 0.109, $CHCl_3$), $[\alpha]^{25}_{365}$ −159°; $[\Phi]_{306}$ +6980°, $[\Phi]_{294}$ 0°, $[\Phi]_{264}$ −27 920°, a = +349; $[\theta]_{288}$ +22 410°.

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.25; H, 9.17.

The trans adduct **33** (2.81 g) was dissolved in 200 mL of methanol and placed under nitrogen, and 5 g of potassium *tert*-butoxide was added. After refluxing for 2 h, the mixture was acidified with hydrochloric acid, diluted with water, and filtered. The precipitate was dissolved in acetone, treated with decolorizing charcoal, and filtered through filter aid to yield a light yellow solution. The acetone solution was slowly diluted with water to yield 1.87 g of crystals of the cis-4β,5β [2 + 2] adduct **34**: mp 190–192.5 °C; IR 1775, 1700 cm^{-1}; NMR δ 5.33–6.00 (m, 4 H), 1.63 (d, J = 4 Hz, 3 H), 0.97 (d, J = 6 Hz, 3 H), 0.98 (s, 3 H), 0.79 (s, 3 H, C19); $[\alpha]^{25}_{589}$ −98° (c 0.100, $CHCl_3$), $[\alpha]^{25}_{365}$ −282°.

Anal. Calcd for $C_{28}H_{38}O_3$: C, 79.58; H, 9.06. Found: C, 79.33; H, 9.15.

The cis-4,5 adducts were eluted as a mixture in fractions 230–279 and amounted to 4.58 g (10.9 mmol, 37%). NMR analysis of every fifth fraction of the initial mixture showed [2 + 2] adducts, and the [4 + 2] adduct(s) appeared in the later fractions. The α configuration was assigned because of the positive optical rotations of the fractions, which ranged between 33 and 51° at 589 nm and 126 and 274° at 365 nm. The majority of this mixture consisted of [2 + 2] adducts: the C19 methyl peak remains constant at δ 0.73 while the new secondary methyl peak at δ 1.17 (J = 6 Hz) diminishes and a new peak at δ 1.22 grows. In the last fractions, new methyl doublets appear at δ 1.23 and 1.01 while a new C19 methyl peak appears at δ 0.91. While these new peaks are appearing, the C3 carbonyl IR frequency at 1700 cm^{-1} diminishes at 1700 cm^{-1} and a new band appears at 1725 cm^{-1}. This latter frequency is characteristic of the cis [4 + 2] adduct. The IR also indicated the presence of a trans double bond as a doublet at 965–970 cm^{-1}, although admixture of a cis double bond cannot be eliminated.

The Photocycloaddition of 2 to 1-Vinylcyclohexene. A solution of 10.0 g (29.4 mmol) of dienone **2** in 30 mL of 1-vinylcyclohexene[63] and 165 mL of ethyl acetate was irradiated under argon for 4.75 h with a 450-W medium-pressure mercury arc (Pyrex filter), when TLC indicated almost complete reaction. The solvent was removed under reduced pressure on a rotary evaporator. In preparation for column chromatography, the oily residue was dissolved in benzene, whereupon 2.1 g (4.7 mmol) of **38** crystallized: mp 283–285 °C; IR 1780, 1725 cm^{-1}; NMR δ 5.65 (s, 2 H), 5.42 (m, 1 H), 2.92 (apparent t, 1 H, 4β-H), 1.07 (s, 3 H), 0.95 (s, 3 H); NMR (C_6D_6) δ 5.85 (dd, J = 11, 2 Hz, 1 H), 5.52 (d, J = 11 Hz, 1 H), 5.33 (m, 1 H), 0.83 (s, 3 H), 0.82 (s, 3 H); $[\alpha]^{25}_D$ +55.8° [c 0.113, $CHCl_3$]; $[\Phi]_{305}$ +4210°, $[\Phi]_{286}$ 0°, $[\Phi]_{270}$ −2420°, $[\Phi]_{252}$ 0°; a = +66; $[\theta]_{290}$ +5735°.

Anal. Calcd for $C_{30}H_{40}O_3$: C, 80.31; H, 8.99. Found: C, 80.72; H, 9.00.

The residue was chromatographed on 1.7 kg of Mallinckrodt CC-7 silica and elution with ethyl acetate–benzene (1:9) gave 4.10 g (9.15 mmol, 31%) of the cis-4α,5α [2 + 2] adduct **40**: mp 103–105 °C (methanol–water); IR 1780, 1705 cm^{-1}; NMR δ 5.62 (m, 3 H), 3.28 (m, 1 H), 0.96 (s, 3 H), 0.73 (s, 3 H); NMR (C_6D_6) δ 5.42 (m, 3 H), 3.08 (m, 1 H), 0.82 (s, 3 H), 0.60 (s, 3 H); $[\Phi]_{319}$ 1547°, $[\Phi]_{290}$ 0°; a = +15; $[\theta]_{289}$ +340°.

Anal. Calcd for $C_{30}H_{40}O_3$: C, 80.31; H, 8.99. Found: C, 80.60; H, 8.90.

The following fractions gave an additional 4.78 g (10.7 mmol, total 52%) of the trans [4 + 2] adduct **38**.

Another compound, formed in low yield and intermediate in polarity between **38** and **40**, was detected by TLC. A sample of this compound was isolated from contaminating **34** and **32** by thick-layer chromatography on a 2-mm E. Merck Silica Gel-60 plate (1:3 ethyl acetate–benzene). The desired compound was found between 3.5 and 6 cm with considerable overlapping. Extraction with chloroform and crystallization from ether–petroleum ether gave 35 mg of pure cis [4 + 2] adduct **41**: mp 242–252 °C; IR 1775, 1725 cm^{-1}; NMR δ 5.64 (s, 2 H), 5.33 (br d, $J \simeq 6$ Hz, 1 H), 0.95 (s, 3 H), 0.90 (s, 3 H); NMR (C_6D_6) δ 5.81 (dd, J = 10.5, 2 Hz, 1 H), 5.53 (d, J = 10.5 Hz, 1 H), 5.28 (br d, $J \simeq 6$ Hz, 1 H), 0.80 (s, 3 H), 0.66 (s, 3 H); $[\alpha]^{25}_D$ −10.5 ± 3° (c 0.103, $CHCl_3$), $[\alpha]^{25}_{365}$ +58.4 ± 3° (c 0.103, $CHCl_3$); $[\Phi]_{309}$ +4486°, $[\Phi]_{296}$ 0°, $[\Phi]_{272}$ −5832°; a = +103; $[\theta]_{295}$ +8075°.

Anal. Calcd for $C_{30}H_{40}O_3$: C, 80.31; H, 8.99. Found: C, 79.95; H, 8.90.

Compound **35** was recovered unchanged after treatment with sodium methoxide in methanol.

Elution of the chromatography column with ethyl acetate–benzene (1:3) gave 1.52 g (3.4 mmol, 12%) of the 6α,7α [4 + 2] adduct **42**: mp 272–282 °C (ether–petroleum ether); IR 1785, 1680, 1670, 1615 cm^{-1}; UV 242.5 nm (ϵ 13 000); NMR δ 5.70 (d, J = 1 Hz, 1 H), 5.25 (m, 1 H), 1.22 (s, 3 H), 1.00 (s, 3 H); $[\Phi]_{345}$ −2747°, $[\Phi]_{315}$ 0°, $[\Phi]_{290}$ +2258°; a = −50; $[\theta]_{318}$ −4163°.

Anal. Calcd for $C_{30}H_{40}O_3$: C, 80.31; H, 8.99. Found: C, 80.26; H, 8.85.

Epimerization of the Trans [4 + 2] Adduct 38. A solution of 1.00 g of **38** in 200 mL of methanol was refluxed, under nitrogen, with 2.0 g of sodium methoxide. After 18 h, the solution was cooled, concentrated to a small volume, and diluted with diluted hydrochloric acid. Filtration and drying gave 835 mg of the 4β,5β [4 + 2] adduct **39**: mp 168–175 °C; IR 1785, 1725 cm^{-1}; NMR δ 5.50 (m, 3 H), 1.04 (s, 3 H), 1.02 (s, 3 H); $[\alpha]^{25}_D$ −11.8 ± 3°, $[\alpha]^{25}_{365}$ −165.7 ± 3° (c 0.102, $CHCl_3$); $[\Phi]_{308}$ −7739°, $[\Phi]_{294}$ 0°, $[\Phi]_{268}$ +9085°; a = −168; $[\theta]_{294}$ −12 337°.

Anal. Calcd for $C_{30}H_{40}O_3$: C, 80.31; H, 8.99. Found: C, 79.96; H, 9.28.

The Photocycloaddition of the Dienone 2 to 1,1′-Bicyclohexenyl. 1,1′-Bicyclohexenyl was prepared from 1,1′-dihydroxy-1,1′-bicyclohexyl[64] by treatment with dilute sulfuric acid.[65] Crystallization from methanol gave material which was 94% pure by VPC on a 6 ft 3% OV-1 column. A solution of 10.0 g (29.4 mmol) of dienone **2** and 12.22 g of 1,1′-bicyclohexenyl (75.4 mmol) in 280 mL of ethyl acetate was irradiated, under nitrogen, with a 450-W mercury arc (Pyrex filter). After 10.5 h of irradiation a precipitate had formed which was filtered. An additional 5.0 g (31 mmol) of diene was then added and the irradiation was continued for an additional 5 h. The resulting precipitate was filtered (total weight 1.5 g) and found to be a mixture of very polar degradation products of the dienone, which did not move from the origin on TLC on silica with ethyl acetate. The resulting solution was evaporated and the residue was chromatographed on 1 kg of E. Merck silica. Elution with benzene gave 4.23 g of diene fractions which consisted of 21% of starting diene and varying amounts of 16 other compounds. Elution with 2% ethyl acetate–benzene gave 2.99 g (5.95 mmol, 20%) of the cis [4 + 2] adduct **43**: mp 296–299 °C (ether–petroleum ether); IR 3030, 1780, 1725 cm^{-1}; NMR δ 5.58 (m, 2 H), 1.03 (s, 3 H), 0.94 (s, 3 H); $[\Phi]_{308}$ +3700°, $[\Phi]_{295}$ 0°, $[\phi]_{276}$ −5100°, $[\Phi]_{252}$ 0°; a = +97; $[\theta]_{289}$ +7900°.

Anal. Calcd for $C_{34}H_{46}O_3$: C, 81.23; H, 9.22. Found: C, 80.86; H, 9.40.

Further elution with 10% ethyl acetate–benzene returned 0.55 g of starting dienone **2**. The remainder of the steroid was located in the column wash fractions and was found to be equivalent to the precipitate formed in the irradiation and discarded.

The adduct **43** could be recovered unchanged after refluxing for 18 h with sodium methoxide in methanol.

The Photocycloaddition of 2 to 2,4-Dimethyl-1,3-pentadiene. A solution of 10.0 g (29.4 mmol) of dienone **2** in 25 g of 2,4-dimethyl-1,3-pentadiene (Aldrich, 98%) and 160 mL of ethyl acetate was irradiated under argon for 7.5 h with a 450-W medium-pressure arc (Pyrex filter). The solvent was removed on a rotary evaporator under reduced pressure and chromatographed on 1.5 kg of Mallinckrodt CC-7 silica. Elution with ethyl acetate–benzene (2:98) gave 1.16 g (2.66 mmol, 9%) of the dienone **44**: mp 136–140 °C (methanol–water); IR 1785, 1670, 1625, 1580 cm^{-1}; UV 291 nm (ϵ 18 500); NMR δ 6.50 (dd, J = 11, 3 Hz, 1 H), 6.05 (dd, J = 11, 1.5 Hz, 1 H), 4.95 (m, 2 H, isopropylene), 3.23 (br s, 2 H, allylic CH_2), 1.42 (br s, 3 H, vinyl CH_3), 1.10 (s, 3 H), 1.02 (s, 6 H), 0.92 (s, 3 H); NMR (C_6D_6) δ 6.52 (dd, 1 H), 5.75 (dd, 1 H), 5.17 (m, 1 H), 5.02 (m, 1 H), 3.50 (br s, 2 H), 1.67 (d, J = 1 Hz, 3 H, vinyl CH_3), 1.13 (s, 3 H), 1.03 (s, 3 H), 0.80 (s, 3 H); $[\alpha]^{25}_D$ ±57 ± 3° (c 0.100, $CHCl_3$).

Anal. Calcd for $C_{29}H_{40}O_3$: C, 79.77; H, 9.23. Found: C, 79.52; H, 9.40.

Elution with ethyl acetate–benzene (1:19) gave 1.70 g (3.90 mmol, 13%) of the ladder compound **45**: mp 247–253 °C (ether–petroleum ether); IR 1785, 1710 cm^{-1}; NMR δ 2.48 (s, only partially resolved, 1 H), 1.23 (s, 3 H), 1.12 (s, 3 H), 1.03 (s, 3 H), 0.97 (s, 6 H); NMR (C_6D_6) δ 2.38 (s, 1 H), 2.27 (s, only partially resolved, 1 H), 1.25 (s, 3 H), 1.00 (s, 3 H), 0.87 (s, 3 H), 0.85 (s, 6 H); $[\alpha]^{25}_D$ +79 ± 3° (c 0.108, $CHCl_3$), $[\alpha]^{25}_{365}$ +232 ± 3°.

Anal. Calcd for $C_{29}H_{40}O_3$: C, 79.77; H, 9.23. Found: C, 79.37; H, 9.17.

Continued elution gave a mixed fraction of 686 mg, followed by 3.02 g (7 mmol, 24%) of the trans [4 + 2] adduct **46**: mp 275–277 °C (ethyl acetate–petroleum ether); IR 1785, 1725 cm^{-1}; NMR δ 5.72 (d, J = 10.5 Hz, 1 H), 5.47 (dd, J = 10.5, 1.5 Hz, 1 H), 4.78 (br s, 1 H), 3.12 (dd, J = 10.5 Hz, 1 H, C4β H), 1.67 (s, 3 H, vinyl CH_3), 1.47 (s, 3 H), 1.20 (s, 3 H), 1.08 (s, 3 H), 0.95 (s, 3 H); $[\alpha]^{25}_D$ +80 ± 3° (c 0.100, $CHCl_3$), $[\alpha]^{25}_{365}$ +380 ± 3°; $[\Phi]_{305}$

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+6545°, $[\Phi]_{287}$ 0°, $[\Phi]_{268}$ −4974°; a = +115; $[\theta]_{289}$ +9512°.

Anal. Calcd for $C_{29}H_{40}O_3$: C, 79.77; H, 9.23. Found: C, 79.38; H, 9.03.

Elution with ethyl acetate–benzene (7:93) gave 2.85 g (6.5 mmol, 22%) of a mixture of 6,7 [4 + 2] adducts. From this mixture, the 6β,7β isomer **48** was isolated by fractional crystallization from ethyl acetate–ether: mp 286–289 °C; IR 3060, 1785, 1670, 1615 cm^{-1}; UV 248 nm (ε 13 500); NMR δ 5.83 (s, 1 H, C4 H), 5.05 (br s, 1 H), 1.58 (br s, vinyl CH_3), 1.18 (s, 3 H), 1.07 (s, 6 H), 1.00 (s, 3 H); $[\alpha]^{25}_D$ −56 ± 3° [c 0.102, $CHCl_3$], $[\alpha]^{25}_{365}$ −448 ± 3°.

Anal. Calcd for $C_{29}H_{40}O_3$: C, 79.77; H, 9.23. Found: C, 79.53; H, 9.08.

The 6α,7α [4 + 2] isomer, which was present in approximately an equimolar amount, was not able to be isolated cleanly either by fractional crystallization or by chromatography. However, the NMR spectrum showed clearly that this isomer was present: NMR ($CDCl_3$) δ 6.15 (d, J = 1.5 Hz, C4 H coupled to the axial 6β-H), 5.25 (br s, vinyl H), 1.18 (s), 1.15 (s), 1.12 (s), 1.00 (s), the vinyl methyl at δ 1.60 was not resolved between the two isomers. Analogous results were obtained in C_6D_6: NMR δ 6.33 (d, J = 1.5 Hz, C4 H), 5.10 (br s), 1.13 (s), 1.12 (s), 0.82 (s), 0.78 (s).

Attempted Epimerization of the 6,7 [4 + 2] Adducts. A solution of 104 mg of pure 6β,7β [4 + 2] isomer **48** in 10 mL of methanol containing 234 mg of sodium methoxide was stirred magnetically, under nitrogen, for 18 h. Acidification with 1 mL of concentrated hydrochloric acid, followed by the addition of 40 mL of water, returned 95 mg of starting material.

A 45:55 mixture (290 mg) of 6β,7β and 6α,7α [4 + 2] adducts **48** and **49** was refluxed under argon in 30 mL of methanol containing 1.0 g of sodium methoxide. After 18 h, the mixture was acidified and diluted with water to return 278 mg of the same ratio of adducts.

Epimerization of 40. A solution of 279 mg of **46** in 50 mL of methanol, containing 1.0 g of sodium methoxide, was stirred magnetically for 3.5 h. The solution was diluted with distilled water and acidified to yield 279 mg of the 4β,5β adduct **47** after drying: mp 247–255 °C; IR 1785, 1725 cm^{-1}; NMR δ 5.55 (br s, 2 H), 4.70 (br s, 1 H), 3.03 (apparent d, $J \simeq 7$ Hz, 1 H), 1.70 (br s, 3 H, vinyl CH_3), 1.15 (s, 3 H), 1.08 (s, 6 H), 1.00 (s, 3 H); $[\alpha]^{25}_D$ +12.4 ± 3° (c 0.105, $CHCl_3$), $[\alpha]^{25}_{365}$ −127 ± 3°; $[\Phi]_{308}$ −6200°, $[\Phi]_{295}$ 0°, $[\Phi]_{264}$ +10 240°; a = −164; $[\theta]_{292}$ −12 203°.

Anal. Calcd for $C_{29}H_{40}O_3 \cdot {}^1/_2H_2O$: C, 78.15; H, 9.27. Found: C, 78.28; H, 9.01.

The Photocycloaddition of 1 to 1,3-Cyclohexadiene. A solution of 10.0 g of 6-dehydrotestosterone acetate (30.5 mmol) in 150 mL of ethyl acetate and 13 mL of 1,3-cyclohexadiene (Aldrich 99%) was irradiated under nitrogen with a 450-W mercury lamp (Pyrex filter) for 5.5 h. The solution was concentrated under reduced pressure and diluted with ether, whereupon 3.78 g (9.3 mmol, 31%) of **53** crystallized: mp 189–190 °C; IR 1740, 1695 cm^{-1}; NMR δ 5.25–6.17 (m, 4 H), 4.67 (t, 1 H, C17α H), 3.20 (m, 1 H, allylic cyclobutane H), 2.04 (s, 3 H, C17β acetate), 0.83 (s, 3 H, C18), 0.77 (s, 3 H, C19); NMR (C_6D_6) δ 5.85 (m, 1 H, cyclohexene H), 5.55 (m, 1 H, cyclohexene H), 5.56 (dd, J = 10, 2.5 Hz, C7 H), 5.34 (dd, J = 10, 2 Hz, C6 H), 4.72 (dd, 1 H, C17α H), 2.92 (m, 1 H, allylic cyclobutane H), 1.74 (s, 3 H, C17β acetate), 0.73 (s, 3 H, C18), 0.66 (s, 3 H, C19); ORD/CD $[\Phi]_{304}$ +4243°, $[\Phi]_{280}$ +2774°; a = +15; $[\theta]_{290}$ +5679°; MS m/e (rel int) 329 (50), 286 (26), 268 (27), 253 (18), 79 (100).

Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.55; H, 8.76.

The mother liquors were stripped and chromatographed on 1.2 kg of Mallinckrodt CC-7 silica, but there was no appreciable separation between **47** and an accompanying cycloadduct. However 1.53 g (4.7 mmol, 15%) of starting dienone **1** was recovered. Since there was no separation, the cycloadduct mixture (4.38 g) was saponified with 5 g of sodium methoxide in 250 mL of ethanol. After 2 h, the solvent was removed and dilute hydrochloric acid was added. The aqueous suspension was extracted with 250 mL of methylene chloride in three portions. The organic phase was dried with sodium sulfate and the solvent was removed. TLC showed a clear separation of the two cycloadducts. The residue was chromatographed on 0.5 kg of silica. Elution with ethyl acetate–benzene (1:9) gave 1.47 g (4.0 mmol, 13%) of the alcohol **54**: mp 199–200 °C (methylene chloride, ethyl acetate); IR 3480, 1680 cm^{-1}; NMR δ 5.3–6.1 (m, 4 H), 3.70 (m, 1 H, C17α H), 3.20 (m, 1 H, allylic cyclobutane H), 0.77 (s, 6 H, C18,19); ORD/CD $[\Phi]_{300}$ +9090°, $[\Phi]_{276}$ +7184°; a = +19; $[\theta]_{288}$ +5498°.

Anal. Calcd for $C_{25}H_{34}O_2$: C, 81.92; H, 9.35. Found: C, 81.97; H, 9.49.

A sample of **54** acetylated with acetic anhydride and pyridine regenerated **53**, identical by IR, NMR, and mixture melting point.

Continued elution gave 1.53 g (4.2 mmol, 14%) of the other cycloadduct, alcohol **56**, which could not be crystallized. Acetylation with acetic anhydride and pyridine at 65 °C gave the acetate **57**, which could be crystallized from acetone–water: mp 126–130 °C; IR 1745, 1705 cm^{-1}; NMR δ 5.3–6.3 (m, 4 H), 4.61 (m, 1 H, C17α H), 3.11 (m, 1 H), 2.01 (s, 3 H, 17β-acetate), 0.88 (s, 3 H, C19), 0.82 (s, 3 H, C18); NMR (C_6D_6) δ 1.75 (s, 3 H, 17β-acetate), 0.75 (s, 3 H), 0.68 (s, 3 H); ORD/CD $[\Phi]_{321}$ +143°, $[\Phi]_{316}$ 0°, $[\Phi]_{282}$ −2819°; a = +30; $[\theta]_{303}$ +1961°; a_{calcd} = +24; MS m/e (rel int) 408 (parent, 0.2), 329 (71), 286 (13), 79 (100).

Anal. Calcd for $C_{27}H_{36}O_3$ C, 79.37; H, 8.88. Found: C, 79.40; H, 8.95.

One-Equivalent Hydrogenation of 53. A solution of 1.13 g (2.7 mmol) of **47** was hydrogenated at room temperature and 2 psi in the presence of 150 mg of 5% Pd/C for 72 h. The catalyst was filtered and the solvent was evaporated. The residue was crystallized from ether–petroleum ether to give 0.872 g (89%) of **55** in two crops: mp 172–173 °C; IR 1745, 1710 cm^{-1}; NMR δ 5.83 (dd, J = 10.5, 2 Hz, 1 H, C7), 5.50 (dd, J = 10.5, 1.5 Hz, 1 H, C6), 2.02 (s, 3 H, 17β-OAc), 0.82 (s, 3 H, C18), 0.73 (s, 3 H, C19); ORD/CD $[\Phi]_{310}$ +4704°, $[\Phi]_{288}$ 0°, $[\Phi]_{270}$ +2599°; a = +73; $[\theta]_{290}$ +6313°, a_{calcd} = +77; m/e (rel int) 410 (parent, 23%), 395 (15, P − CH_3), 329 (63, P − C_6H_{10} + H), 286 (41, 329 − CH_3CO), 133 (100).

Anal. Calcd for $C_{27}H_{38}O_3$: C, 78.98; H, 9.33. Found: C, 78.88; H, 9.34.

Two-Equivalent Hydrogenation of 53. A solution of 514 mg of **53** in 20 mL of isopropyl alcohol was hydrogenated in the presence of 500 mg of 10% palladium on carbon at 60 °C and 60 psi for 24 h. After cooling, the catalyst was filtered and the solvent was removed in vacuo. Crystallization from ether gave 252 mg (50%) of **51**: mp 215–222 °C; IR 1735, 1700 cm^{-1}; NMR δ 4.64 (t, 1 H, 17α-H), 2.02 (s, 3 H, 17β-OAc), 0.80 (s, 6 H, C18,19); NMR (C_6D_6) δ 4.73 (t, 1 H, 17α-H), 1.78 (s, 3 H, 17β-OAc), 0.75 (s, 3 H, C18), 0.63 (s, 3 H, C19); ORD/CD $[\Phi]_{309}$ +5529°, $[\Phi]_{291}$ 0°, $[\Phi]_{268}$ −4538°; a = +101; $[\theta]_{291}$ +8169°; a_{calcd} = 100; MS m/e (rel int) 412 (parent, 0.2), 331 (100, P − cyclohexene + H), 289 (8, 331 − CH_2CO), 271 (14, 331 − CH_3CO_2H), 253 (8, 271 − CH_3).

Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.62; H, 9.76.

Hydrogenation of 57. A solution of 127 mg of **57** in 30 mL of dioxane was hydrogenated at 25 °C and atmospheric pressure in the presence of 40 mg of 5% palladium on carbon for 69.5 h. The catalyst was filtered and the solvent was removed in vacuo. The residue was crystallized from ether–petroleum ether to yield 59 mg (47%) of **58**: mp 110–112 °C; IR 1745, 1695 cm^{-1}; NMR δ 4.59 (t, 1 H, 17α-H), 2.02 (s, 3 H, 17β-OAc), 0.80 (s, 3 H, C18), 0.77 (s, 3 H, C19); MS m/e (rel int) 412 (parent, 0.1), 352 (0.2, P − CH_2CO_2H), 331 (100, P − cyclohexene + H), 271 (19, 331 − CH_3CO_2H).

Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.39; H, 9.91.

The Photocycloaddition of Testosterone Acetate (3) to Cyclohexene. A solution of 5.0 g (15 mmol) of testosterone acetate (**3**) in 35 mL of cyclohexene and 155 mL of ethyl acetate was irradiated, under nitrogen, for 2.5 h with a 450-W medium-pressure mercury arc (Pyrex filter). After removal of the solvent in vacuo, the residue was chromatographed on 0.65 kg of Mallinckrodt CC-7 silica. Elution with ethyl acetate–petroleum ether (1:19) gave 1.85 g (4.5 mmol, 30%) of **52**: mp 217–221 °C (ether–petroleum ether); IR 1740, 1705 cm^{-1}; NMR δ 4.67 (t, 1 H, 17α-H), 2.03 (s, 3 H, 17β-OAc), 0.79 (s, 6 H C18,19); NMR (C_6D_6) δ 4.78 (t, 1 H, 17α-H), 1.77 (s, 3 H, 17β-OAc), 0.75 (s, 3 H, C18), 0.62 (s, 3 H, C19); $[\alpha]^{25}_D$ 6.0 ± 1.5° (c 1.007, $CHCl_3$), $[\alpha]^{25}_{365}$ 91.9 ± 1.5°; ORD/CD $[\Phi]_{308}$ +2084°, $[\Phi]_{293}$ 0°, $[\Phi]_{268}$ −3074°; a = +52; $[\theta]_{290}$ 4085°, a_{calcd} = +50.

Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.35; H, 9.61.

Continued elution gave 0.57 g of a mixture, followed by 1.164 g of **51** (3.5 mmol, 24%) identical with a sample of the same

compound prepared by hydrogenation of **53**.

A fraction containing 0.25 g of a mixture was followed by 0.82 g (2.0 mmol, 13%) of the 4β,5β isomer **50**: mp 210–220 °C (methanol–water); IR 1745, 1695 cm^{-1}; NMR δ 4.56 (t, 1 H, 17α-H), 2.04 (s, 3 H, 17β-OAc), 0.82 (s, 3 H, C18), 0.78 (s, 3 H, C19); NMR (C_6D_6) δ 4.60 (t, 1 H, 17α-H), 1.77 (s, 3 H, 17β-OAc), 0.75 (s, 3 H, C18), 0.58 (s, 3 H, C19); $[\alpha]^{25}_D$ −21.2 ± 3° (*c* 0.099, $CHCl_3$), $[\alpha]^{25}_{365}$ −218.2 ± 3°; ORD/CD $[\Phi]_{312}$ −392°, $[\Phi]_{294}$ 0°, $[\Phi]_{272}$ +4002°; a = −79; $[\theta]_{294}$ −6395°, a_{calcd} = −78.

Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.68; H, 9.74.

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Experiments Directed toward the Total Synthesis of Terpenes. 23. Synthesis of 4a-Methyl-4,4a,7,8-tetrahydro-9*H*-benzocycloheptene-2(3*H*),5(6*H*)-dione (B-Homo Wieland–Miescher Ketone): A Versatile Intermediate for Terpene Synthesis[1]

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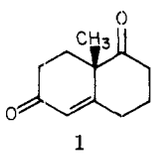
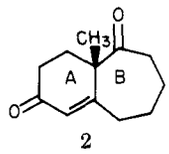
An efficient four-step synthesis of a B-homo Wieland–Miescher ketone (**2**) from 2-methoxybenzosuberone (**3**) in 36% overall yield is described. Entry into the hydrobenzosuberan series is also available through Diels–Alder reaction between the methoxy(silyloxy)butadiene **10** and 2-methylcycloheptenone (**11**). These syntheses make this useful intermediate readily available.

The Wieland–Miescher ketone **1** has served in numerous steroid and terpene syntheses[3a] and has been used as the substrate for several other synthetic transformations.[3b] The utility of this diketone stems from both its obvious structural relationship to the steroid–terpenoid series and also the versatility of the differentiable functional groups present. The value of this system has led to the development of efficient, large-scale synthetic procedures for its ready preparation.[4]

In connection with programs directed toward the total synthesis of several diverse natural products it became apparent that a similar, but potentially even more versatile, dicyclic starting material was the B-homo derivative **2**.[5]



1



2

Derivatives of this B-homo Wieland–Miescher ketone **2** possess the same basic structural characteristics as the diketone **1** but have the added feature that after an intramolecularly engineered contraction of the seven-membered B-ring, a standard six-membered ring results that has a functionally substituted one-carbon appendage at a predetermined site. Thus, further elaboration of ring systems and/or side chains on the basic decalin structure in a regiospecific manner becomes possible.

As attractive as this concept is for synthetic design, before the versatility of the homo diketone **2** can be realized, a convenient and efficient synthesis for the material must be available.

The diketone **2** has in fact been prepared in a two-step Robinson annelation of 2-methyl-1,3-cycloheptanedione with methyl vinyl ketone in 20–30% yield.[6] However, the synthesis of 2-methyl-1,3-cycloheptanedione involves a three-step ring expansion from the monoketal of dihydro-

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(2) Predoctoral Fellow of the National Science Foundation, 1973–1976.

(3) For instance, see: Stork, G. *Pure Appl. Chem.* **1964**, *9*, 131. (b) Venkataramaru, P. S.; Reusch, W. *Tetrahedron Lett.* **1968**, 5283. Grieco, P. A.; Ferrino, S; Oguri, T. *J. Org. Chem.* **1979**, *44*, 2593–94.

(4) Ramachandran, S.; Newman, M. S. *Org. Synth.* **1961**, *41*, 38.

(5) The term "Wieland–Miescher ketone" is used to refer to 4a-methyl-4,4a,7,8-tetrahydro-2(3*H*),5(6*H*)-naphthalenedione (Wieland, P.; Miescher, K. *Helv. Chim. Acta* **1950**, *33*, 2215). While there are in principle several "homo-Wieland–Miescher ketones", the term as used here refers to the benzosuberone derivative **2** in which the B ring of the octalindione has been enlarged by the addition of a methylene group.

(6) Selvorajon, R; John, J. P.; Narayanan, K. V.; Swaminathan, S. *Tetrahedron* **1966**, 22, 949.

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