Anal. Calcd for $C_9H_9N_4Cl$: C, 51.80; H, 4.35. Found: C, 51.60; H, 4.24.

Preparation of 7,8,9,10-Tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (9). 6-Chloro-7,8,9,10-tetrahydro-*s*-triazolo[3,4-*a*]phthalazine (**13**, 1.0 g) and 100 mg of 10% palladium on carbon were added to 150 mL of 95% ethanol, and the pH of the solution was adjusted to 9 with ammonium hydroxide. The hydrogenation was carried out in a Paar apparatus with an initial pressure of 45 psi of H_2 and continued for 2 h. The reaction mixture was filtered through Celite and the solvent removed under vacuum. The residue was dissolved in water and extracted with chloroform to yield 0.69 g (83%) of a light brown solid (mp 105–108 °C). The product was then sublimed at 100 °C (1 mm) to yield a white solid (mp 132–134 °C) which exhibited the following spectra: IR 3120, 2940, 2870, 1615, 1540, 1495, 1450, 1420, 1340, 1185, 1170, 980, 935 cm^{-1}; ^1H NMR δ 9.01 (s, 1 H, H_3), 8.08 (s, 1 H, H_6), 3.12 (m, 2 H, H_{10}), 2.76 (m, 2 H, H_7), 1.94 (m, 4 H, $H_{8,9}$); ^{13}C NMR δ 148.1 (C_6), 144.8 (C_{10b}), 138.5 (C_3), 133.6 and 129.3 (C_{6a} and C_{10a}), 25.7, 23.1, 21.6, and 20.7 (C_{7-10}); UV (EtOH) λ_{max}(pH 1) 264 nm (ϵ 5100), λ_{max}(pH 7) 237 (3600), 282 (3100), λ_{max}(pH 11) 282 (3250); mass spectrum (EI), *m/e* (relative intensity) 175 (12.1), 174 (M^+, 100.0), 173 (43.5), 146 (36.9).

Anal. Calcd for $C_9H_{10}N_4$: C, 62.05; H, 5.79; N, 32.16. Found: C, 61.89; H, 5.65; N, 32.36.

Acknowledgment. The authors wish to thank Professors M. Tisler and B. Stanovnik of the University of Ljubljana, Yugoslavia, for their generous supply of compound 1 as well as for their many discussions of our results, Dr. V. Kramer of Josepf Stefan Institute, Ljubljana, Yugoslavia, for the high-resolution mass spectrometric analysis, Dr. E. G. Paul and Mr. S. L. Baxter for their help in obtaining the ^{13}C NMR results, and Dr. G. R. Revankar for this many helpful discussions concerning the experimental procedures. Research grants from the Brigham Young University College of Physical and Mathematical Sciences and the Associated Students of Brigham Young University are gratefully acknowledged.

Registry No. **1**, 274-83-9; **2a**, 73453-17-5; **2b**, 73453-18-6; **2c**, 73453-19-7; **2d**, 73453-20-0; **2e**, 73453-21-1; **3a**, 73453-22-2; **3b**, 73453-23-3; **3c**, 73453-24-4; **3d**, 73453-25-5; **3e**, 73453-26-6; **4**, 50357-95-4; **5**, 73453-27-7; **6**, 73453-28-8; **7**, 73453-29-9; **8**, 73453-30-2; **9**, 73075-03-3; **10**, 935-79-5; **11**, 67279-24-7; **12**, 66597-78-2; **13**, 66978-72-1; 1-butanol, 71-36-3; 1-octanol, 111-87-5; cyclohexanol, 108-93-0; benzyl alcohol, 100-51-6; 1,4-butanediol, 110-63-4; 4-hydroxy-5,6,7,8-tetrahydro-1(2*H*)-phthalazinone, 73453-31-3; hydrazine, 302-01-2; methanol, 67-56-1.

Photochemistry of 11α- and 11β-Hydroxy Steroidal 1,4-Dien-3-ones and 11α- and 11β-Hydroxy Steroidal Bicyclo[3.1.0]hex-3-en-2-ones in Neutral and Acidic Media[1a]

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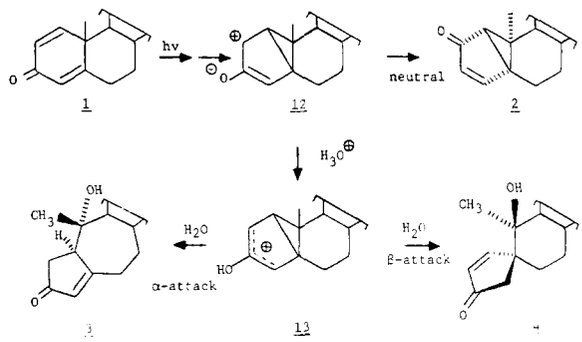
The photolysis of prednisolone, **1b**, its 21-acetate, **1c**, and 11α-hydroxypregna-1,4-dien-3,20-dione, **1d**, in dioxane yielded the lumiproducts **2b**, **2c**, and **2d**, respectively. Further photoisomerization of the 11β-hydroxy lumiproducts **2b** and **2c** in dioxane gave 17α,21-dihydroxy-1β,11β-oxy-10α-pregna-2,20-dione, **9a**, and 21-acetoxy-17α-hydroxy-1β,11β-oxy-10α-pregna-2,20-dione, **9b**, respectively, whereas the 11α-hydroxy lumiproduct **2d** yielded 2,11α-dihydroxy-4-methyl-19-norpregna-1,3,5(10)-trien-20-one, **7a**. Photolysis of **1b** and **1c** in acidic conditions afforded the 1β,11β-oxy steroids **9a** and **9b** as the major photoproducts together with the expected rearranged bicyclo[5.3.0] systems **3b** and **3c** and spiro steroids **4b** and **4c**, respectively. Photolysis of **1d** under acidic conditions only afforded **3d** and **4d**. The mechanism of these photoisomerization reactions is discussed. The influence of the 11α- and 11β-hydroxyl function on the photochemistry of the cross-conjugated cyclohexadienones and the bicyclo[3.1.0]hex-3-en-2-one systems in aqueous acetic acid and in dioxane, respectively, is explained.

The photochemistry of cross-conjugated cyclohexadienones has been intensely studied because of their facile and fascinatingly complex photochemical rearrangement reactions. These rearrangement reactions have been the topic of a number of excellent reviews.[2] Recently, the photochemistry of the medicinally important steroid prednisone acetate (**1a**) was reinvestigated by Williams et al.[1] The structure of lumiprednisone acetate[3] was revised to that of a bicyclo[3.1.0]hex-3-en-2-one ring A system (**2a**)

Scheme I. General Photoisomerization Paths of Cross-Conjugated Dienones



and a new photochemical rearrangement of this intermediate reported.[1] Since the photochemical reactions of cross-conjugated cyclohexadienones and their resulting lumiproducts are extremely sensitive to changes in struc-

(1) (a) For the previous paper in this series see: Williams, J. R.; Moore, R. H.; Li, R.; Blount. J. F. *J. Am. Chem. Soc.* **1979**, *101*, 5019. (b) Temple University. (c) Medical Foundation of Buffalo.

(2) For reviews, see: (a) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183. (b) Chapman, O. L. *Ibid.* **1963**, *1*, 323. (c) Schaffner, K. *Ibid.* **1966**, *4*, 81. (d) Kropp, P. *J. Org. Photochem.* **1973**, *1*, 1. (e) Chapman, O. L.; Weiss, D. S. *Ibid.* **1973**, *3*, 197. (f) Schuster, D. I. *Acc. Chem. Res.* **1978**, *11*, 65.

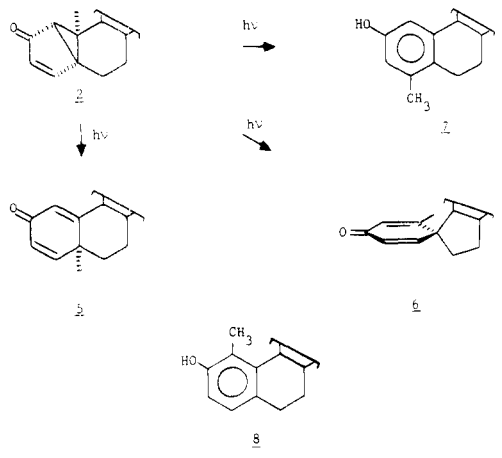
(3) (a) Barton, D. H. R.; Taylor, W. C. *Proc. Chem. Soc.* **1957**, *96*, 147. (b) *J. Am. Chem. Soc.* **1958**, *80*, 244. (c) *J. Chem. Soc.* **1958**, 2500. (d) *Helv. Chim. Acta* **1959**, *42*, 2604.

0022-3263/80/1945-2324$01.00/0

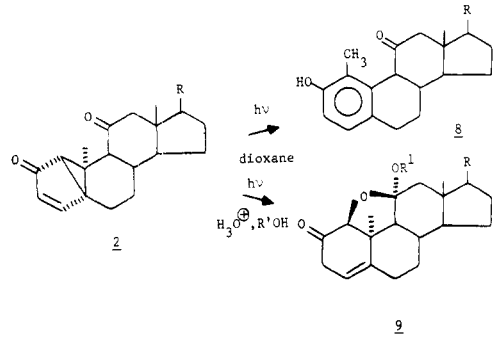
Table I. Circular Dichroism Spectra of Lumiproducts

compd	λ_{max}, nm ($\Delta\epsilon$)	λ_{max}, nm ($\Delta\epsilon$)	crossover λ, nm	λ_{max}, nm ($\Delta\epsilon$)	crossover λ, nm	λ_{max}, nm ($\Delta\epsilon$)
2a		343 (-5.21)	313	277 (+12.22)	253	225 (-11.71)
2b		340 (-6.51)	313	284 (+10.38)	256	235 (-9.02)
2c		340 (-4.28)	314	284 (+11.45)	256	235 (-11.66)
2d		342 (-3.28)	313	283 (+8.63)	256	236 (-5.81)
2e[5b,6]	357 (-3.71)	344.5 (-3.77)	309	272 (+10.3)	250	short-wavelength negative CD

Scheme II. Photoisomerization Paths of Bicyclo[3.1.0]hex-3-en-2-ones



Scheme III. Photoisomerization of 11-Keto Steroidal Bicyclo[3.1.0]hex-3-en-2-ones



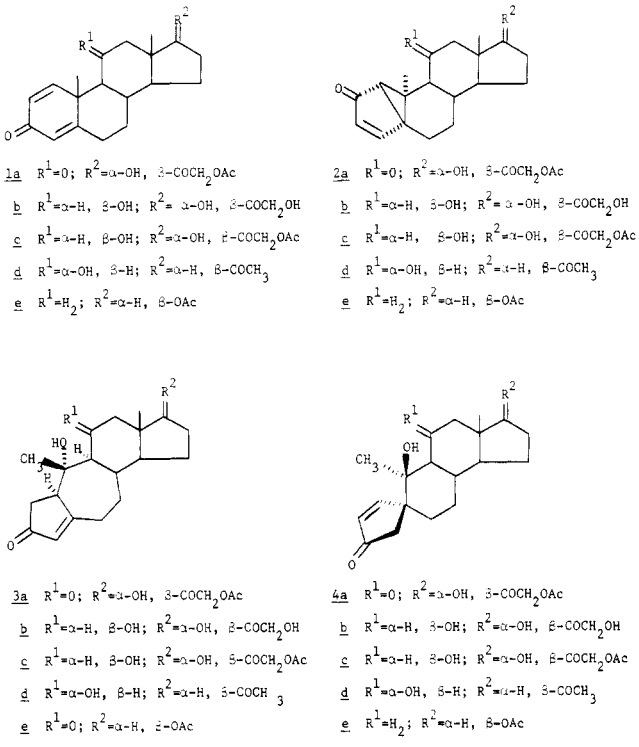
ture[2] and solvent medium,[2] we chose to study the effect of changing ring C substituents on these photochemical reactions.

It is now generally accepted that photoisomerizations of cross-conjugated cyclohexadienones take place via an $n \rightarrow \pi^*$ excited triplet state and show a strong solvent dependence as outlined in Scheme I.[2] The resulting lumiketone **2** is similar in electronic structure to a cross-conjugated cyclohexadienone in which one of the olefins is now a cyclopropyl group, thus it was not too surprising that this chromophore, bicyclo[3.1.0]hex-3-en-2-one, is extremely photolabile and can undergo the solvent-dependent photoreactions shown in Schemes II[2c,d] and III.[1] As can be seen in Scheme III, the 11-keto function completely changes the photoisomerization paths for steroidal bicyclo[3.1.0]hex-3-en-2-ones.

The aim of this study was to investigate the effect of 11α- and 11β-hydroxyl functions on the solvent-dependent photochemical reactions of steroids with A rings containing either a cross-conjugated cyclohexadienone or a bicyclo[3.1.0]hex-3-en-2-one chromophore. Furthermore, the steroids selected for this study were the medicinally important[4] 11β-hydroxy steroids prednisolone (**1b**) and prednisolone 21-acetate (**1c**).

Results

A. Irradiations in Neutral Media. Irradiation of **1b** or **1c** in dry dioxane with 254-nm light afforded lumi-



prednisolone **2b** and **2c** in 42 and 78% yields, respectively. The assignment of the structure and stereochemistry of **2b** and **2c** was by comparison of their spectral data with those of the lumiproduct **2a** and other steroidal lumiproducts.[1,5] The NMR spectra of **2b** (**2c**) showed two doublets centered at δ 7.24 (7.24) and 5.77 (5.79) with J = 5.5 (6.0) Hz, indicating the presence of an α,β-unsaturated ketone in the A ring. Double-irradiation experiments indicated that H-1 of **2b** (**2c**) is coupled to both H-3 and H-4 through the carbonyl group. This phenomenon was also observed for **2a**[1] and other lumiproducts.[5] Proof of the stereochemistry of the lumiproducts **2b** (**2c**) comes from a comparison of their circular dichroism (CD) spectra with those of other lumiketones (see Table I). In all cases, **2b** and **2c** show negative Cotton effects of similar magnitude and position to those reported in the literature.[1,6] Final proof for the structure **2c** comes from Jones oxidation of the 11-hydroxyl group to afford the known 11-keto

(4) Windholz, M., Ed., "The Merck Index", 9th ed.; Merck and Co.: Rahway, NJ, 1976; p 7510.

(5) (a) Duter, H.; Ganter, C.; Ryf, H.; Utzinger, E. C.; Weinberg, K.; Schaffner, K.; Arigoni, D.; Jeger, O. *Helv. Chim. Acta* **1962**, *45*, 2346. (b) Frei, J.; Ganter, C.; Kagi, D.; Kocsis, K.; Miljkovic, M.; Siewinski, A.; Wenger, R.; Schaffner, K.; Jeger, O. *Ibid.* **1966**, *49*, 1049.

(6) Schaffner, K.; Snatzke, G. *Helv. Chim. Acta* **1965**, *48*, 347.

(7) (a) Ganter, C.; Utzinger, E. C.; Schaffner, K.; Arigoni, D.; Jeger, O. *Helv. Chim. Acta* **1962**, *45*, 2403. (b) Kropp, P. J.; Erman, W. F. *J. Am. Chem. Soc.* **1963**, *85*, 2456.

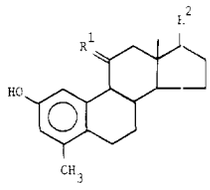
Table II. ^{13}C NMR Chemical Shifts (δ) of 2-Hydroxy-4-methyl Steroids

carbon	1	2	3	4	5	6	7	8	9	10	11
7a	113.8	153.4	119.1	135.9	120.8	24.3	27.8	36.9	51.2	141.3	70.5
7b	109.9	153.6	114.6	137.7	126.8	26.5*	27.5*	37.8	44.6	141.5	26.4*

carbon	12	13	14	15	16	17	18	19	20	21
7a	49.2	44.8	55.4	23.4	21.8	63.5	14.0	21.5	209.9	31.3
7b	37.1	42.9	50.0	23.3	27.5*	83.0	12.0	19.9	171.8	21.2

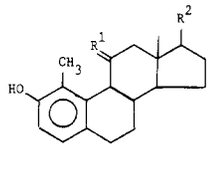
steroid, lumiprednisone acetate (**2a**).[1]

Further irradiation of **2b** for 21 h in dioxane with 366-nm light resulted in photoisomerization to the new steroid **9a**

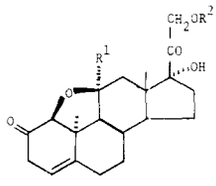


7a R^1=α-OH, β-H; R^2=α-H, β-$COCH_3$

b R^1=H_2; R^2=α-H, β-OAc



8a R^1=O; R^2=α-OH, β-$COCH_2OAc$



9a R^1=H; R^2=H

b R^1=H; R^2=Ac

c R^1=OH; R^2=Ac

d R^1=OCH_3; R^2=Ac

in 86% yield. If a uranium glass filter is not used, then the rate of this photoisomerization reaction could be greatly increased. Irradiation of **2b** in ethanol with 313- and 366-nm light afforded **9a** in 90% yield after only 45 min. The structure of the 1,11-oxy steroid **9a** was proven by its method of synthesis and by comparison of its spectral properties with those of the 1,11-oxy steroid **9c**.[1] **9c**, which has added a molecule of water, was prepared by irradiation of prednisone 21-acetate (**1a**) in aqueous acetic acid. It structure was proven by an X-ray analysis of the methoxy derivative **9d** prepared by recrystallization of **9c** from methanol.[1] The infrared spectrum of **9a** showed two nonconjugated carbonyl absorptions at 1724 and 1710 cm^{-1} and an ultraviolet spectrum (λ_{max} 286 nm (ϵ 384)) very similar to those reported for **9c**.[1] The NMR spectrum of **9a** shows a one-proton broad doublet (J = 8 Hz) at δ 5.38 due to H-4, very similar in shape and position to that for H-4 in **9c** (δ 5.37, J = 7 Hz).[1]

Irradiation of the 11α-hydroxypregna-1,4-diene-3,20-dione **1d** in dioxane yielded the expected lumiproduct **2d** in 47% yield. The NMR spectrum of **2d** showed two doublets centered at δ 7.28 and 5.91 with J = 6 Hz, characteristic of the α,β-unsaturated ketone system in ring A. The stereochemistry of **2d** was proven by comparison of its CD curve with those of other lumiketones (see Table I).

Further irradiation of the 11α-hydroxy lumiketone **2d** yielded the phenol **7a** whose structure was deduced in the following manner. The infrared spectrum showed a single band at 842 cm^{-1}. The NMR spectrum showed broadened singlets at δ 7.47 and 6.58 (J < 2 Hz), indicating that the protons are 1,3 or 1,4. Oxidation of the 11α-hydroxyl group to the carbonyl produced no upfield shift of the aromatic methyl group at δ 2.23, thus the methyl group cannot be at C-1, thereby eliminating one of the four possible meta substitution arrangements.[1]

The ^{13}C NMR spectrum of **7a** is given in Table II together with that of **7b** prepared by photolysis of the analogous lumisteroid **2e**.[5a] As can be seen from the table, there is good agreement between the ^{13}C NMR spectrum of **7a** and the known structure **7b**. Furthermore, the method of synthesis of **7a** is identical with that for **7b**.[5a]

B. Irradiations in Aqueous Acetic Acid. Irradiation of **1b** (**1c**) in 50% aqueous acetic acid gave three photoproducts. The first of these was identified as the rearranged bicyclo[5.3.0]system **3b** (**3c**) in 20% (20%) yield by comparison of its method of formation and spectral properties with those of **3a**. The structure of **3a** is based on chemical studies and an X-ray analysis of isophotosantonic lactone, the analogous photoproduct derived from irradiation of α-santonin in acidic media.[8] Jones oxidation of **3c** afforded the known ketone **3a**.[1]

The second photoproduct isolated was the 1,11-oxy steroid **9a** (**9b**) obtained in 64% (50%) yield.

The third photoproduct was the spiro steroid **4b** (**4c**) obtained in 16% (19%) yield. The structure of **4b** (**4c**) was assigned on the basis of spectral data and analogy with the spiro steroid **4e** obtained by irradiation of 17-acetoxy-1-dehydrotestosterone (**1e**) in acidic media.[7a] For example, the NMR spectrum of **4c** showed a doublet of doublets centered at δ 7.75 and 6.13 with J = 6 Hz, similar to those of **4e** at δ 7.80 and 6.13, J = 6 Hz.[7a] Since the structure of **4e** was based on chemical correlations which were not completely unambiguous, an X-ray analysis of **4c** was obtained to prove the absolute configurations at C-5 and C-10. The single crystal used was found to contain a molecule of ethyl acetate. The formula of the photoproduct as well as the intramolecular geometry including bond distance, valency angles, and endocyclic torsion angles is depicted in Figure 1. Estimated standard deviations for the bond distances and angles are in the ranges 0.005–0.01 Å and 0.3–0.6°, respectively. Two independent hydrogen bonds [O(11β)→O(10β) 2.96 Å and O(17α)→O-(26) 2.79 Å] are observed in the crystal structure. Figure 2 is a stereoscopic drawing of the photoproduct which illustrates the overall conformation of the molecule as well as the configurations at all asymmetric centers. The atomic positional and thermal parameters have been deposited.

Irradiation of 11α-hydroxypregna-1,4-diene-3,20-dione (**1d**) afforded only the two expected rearrangement products: the bicyclo[5.3.0] system, **3d**, and the spiro steroid **4d** in 40 and 10% yields, respectively. The structure for **3d** was assigned on the basis of its spectral data and method of synthesis. The NMR showed a characteristic

(8) Asher, J. D.; Sim, G. A. *Proc. Chem. Soc.* **1962**, 111.

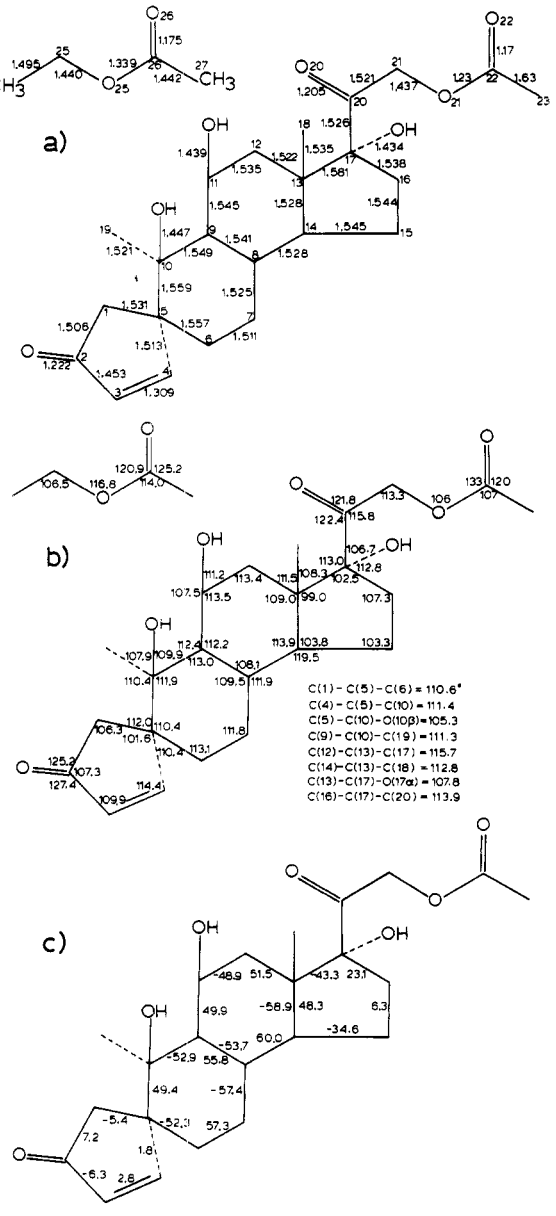


Figure 1. Intramolecular geometry of the prednisolone acetate photoproduct ethyl acetate complex **4c** including (a) bond angles, (b) valency angles, and (c) endocyclic torsion angles. A torsion angle α–β–γ–δ is positive if, when viewed down the β–γ bond, the α–β bond will eclipse the γ–δ bond when rotated less than 180° in a clockwise direction.

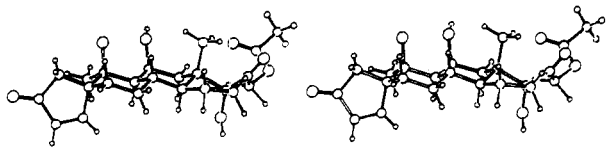


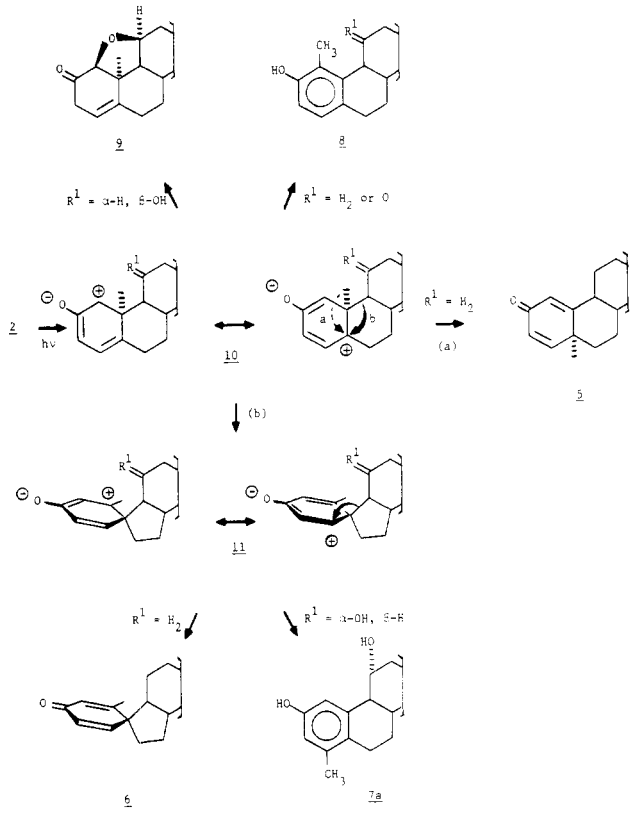
Figure 2. Stereoscopic drawing of the prednisolone acetate photoproduct (**4c**).

singlet at δ 5.95 due to H-3 and a broad multiplet at δ 4.15 due to H-11. The NMR of the second product (**4d**) showed the characteristic olefinic absorption of an enone with doublets centered at δ 7.73 and 6.11, due to H-1 and H-2 (J = 6 Hz). H-11 occurred as a broad multiplet at δ 4.11.

Discussion

Photolysis of prednisolone (**1b**), its 21-acetate (**1c**), and 11α-hydroxypregna-1,4-diene-3,20-dione (**1d**) in neutral conditions, such as in dioxane, afforded the expected lumiproducts **2b**, **2c**, and **2d**, respectively. Therefore the presence of an α- or β-hydroxyl group at the C-11 position in ring C of a steroid does not change the general photoisomerization path of an A ring cross-conjugated cyclohexadienone when irradiated in neutral media.

Scheme IV. Photoisomerization of Steroidal Bicyclo[3.1.0]hex-3-en-2-ones



However the lumiproducts, **2b–d**, which can themselves be regarded as cross-conjugated systems in which one of the double bonds has been replaced with a cyclopropane ring (bicyclo[3.1.0]hex-3-en-2-one system) are themselves photolabile as seen in Schemes II[2c,d] and III.[1] The mechanism of these photoisomerizations can be explained in terms of the known photochemistry of the bicyclo[3.1.0]-hex-3-en-2-one skeleton as shown in Scheme IV.[2c,d] Cleavage of the cyclopropyl bond which forms part of the cyclopentenone ring almost always occurs, giving rise to the possible intermediate zwitterion **10**.[2d] This explanation has received support by the observation of a blue-colored glass when **2a** was irradiated at 77 K.[1] Blue-colored intermediates[9] and cyclopropanones[10] have previously been observed when lumiproducts are irradiated at low temperatures.

The intermediate **10** can now potentially rearrange in a number of ways: (a) 1,2 migration of the angular methyl group at C-10 leading to the cross-conjugated dienone **5** or to the phenol **8**[1] or (b) rearrangement through spiro structure **11** which can collapse to the spiro cross-conjugated dienone **6** or undergo further 1,2-bond migration to yield the 4-methylphenol **7**. When a C-11 ketone is present, this latter mode of rearrangement involving the spiro structure **11** appears not to occur as judged by the photoisomerization products of 11-keto steroidal bicyclo-[3.1.0]hex-3-en-2-ones summarized in Scheme III.[1] The reason for the absence of this pathway could be that

(9) (a) Fisch, M. H. *J. Chem. Soc. D* **1969**, 1472. (b) Fisch, M. H.; Richards, J. H. *J. Am. Chem. Soc.* **1968**, *90*, 1547.
(10) Barber, L. L.; Chapman, O. L.; Lassila, J. D. *J. Am. Chem. Soc.* **1969**, *91*, 3664.

cleavage of the 9–10 bond and migration of C-9 to the electron deficient C-5 would involve the formation of partial positive charge on C-9. Since C-9 is adjacent to the already electron-deficient C-11 carbonyl carbon, the formation of two neighboring electron-deficient carbon atoms is avoided.

Application of these mechanisms to the photoisomerization reactions of 11α- and 11β-hydroxy steroidal bicyclo[3.1.0]hex-3-en-2-ones satisfactorily explains the results observed. Photolysis of the 11β-hydroxy steroidal bicyclo[3.1.0]hex-3-en-2-one **2b** (**2c**) in dioxane yields the new 1,11-oxy steroid **9a** (**9b**). Dreiding models show that the 11β-hydroxyl group is set up to trap the C-1 carbonium ion and yield **9**, whereas the 11α-hydroxyl group is too far away. A similar 1,11-oxy steroid (**9c**) was obtained when the 11-keto lumiprednisone **2a** was irradiated in acidic media.[1] Nucleophilic attack of the carbonyl oxygen on the C-1 carbocation resulted in a new carbonium ion at C-11 which was attacked by the solvent.[1] In the absence of the blocking effect of the C-11 ketone, the C-11α-hydroxy compound **2d** rearranges via the spiro compound **11** to yield the 2-hydroxy-4-methylphenyl (A ring) steroid **7a**. This reaction has precedence in that the lumisteroid **2e** is photoisomerized to **7b** under identical conditions.[5a] Further recent support for this hypothesis is found in the rearrangement of carbonium ions similar to **10**, via **11**, to afford 2-alkoxy-4-methylphenyl (A ring) steroids.[11]

Photolysis of cross-conjugated cyclohexadienones under acidic conditions is well-known to afford different products from those obtained in neutral conditions.[2] The dominant reaction is solvent attack on a protonated intermediate, leading to the formation of two products which have incorporated a molecule of solvent.[2]

Photolysis of prednisolone (**1b**) and its 21-acetate (**1c**) in aqueous acetic acid yielded a new product in addition to the expected bicyclo[5.3.0] systems **3b** (**3c**) and spiro steroids **4b** (**4c**). This new product is the 1,11-oxy steroid **9a** (**9b**) and was obtained as the major product (50% yield). Apparently the 11β-hydroxy steroids **1b** and **1c** photoisomerize faster to the lumiproducts **2b** and **2c**, which upon further photolysis are trapped intramolecularly by the 11β-hydroxyl to form the 1,11-oxy steroids **9a** and **9b**. This was confirmed by the ready conversion of the lumiproduct **2b** (**2c**) to the 1,11-oxy steroid **9a** (**9b**) by irradiation in aqueous acetic acid.

The isolation of photoproducts derived from lumi-intermediates when cross-conjugated dienones are irradiated in acidic media is not without precedent. For example, the isolation of 4-methylphenol **7b** as well as **3** and **4** when 1-dehydrotestosterone 17-acetate (**1e**) is irradiated in aqueous acetic acid may be explained as proceeding via the lumi-intermediate **2**, followed by 1,2-bond migration to the spiro intermediate **11** and a second 1,2 migration to the phenol **7**.[7a]

The general photoisomerization paths of cross-conjugated dienones are found in Scheme I.[2] In acidic media, it is proposed that the zwitterion **12** is protonated to yield **13**, C-10 of which is then attacked either from the α side to yield the bicyclo[5.3.0] system **3** or from the β face to afford the spiro steroid **4**. The results of varying C-11 substitution on the photolysis of steroidal 1,4-dien-3-ones in acidic media are summarized in Table III. Irradiation of the C-11 unsubstituted 1,4-dienone **1e** results in an approximately 50:50 ratio of **3** and **4**, with the former being slightly favored. This same ratio occurs when a C-11β-hydroxyl group is present in **1b** and **1c**. The lower yield of **3** and **4** in these cases is probably due to the ready formation of the 1,11-oxy steroid **9** in this system. When the 11α-hydroxyl group is present (**1d**), then the yield of **3d** is four times that of **4a**, indicating that α attack is favored. A C-11 ketone (**1a**) exclusively favors α attack and yields only **3a**. The reason for the increased α attack is hydrogen bonding between the C-11 oxygen in **1a** and **1d** and the attacking nucleophile. Dreiding models indicate that the α face of the steroid is free for this reaction to occur, whereas the C-18 methyl group blocks the formation of hydrogen bonds on the β face.

Table III. Photolysis of Steroidal 1,4-Dien-3-ones in Acidic Media

1,4-dien-3-one	bicyclo-[5.3.0] system	% yield	spiro steroid	% yield	1,11-oxy-steroid	% yield
1a[1]	3a	80	4a	-	-	-
1b	3b	16	4b	16	9a	50
1c	3c	20	4c	19	9b	16
1d	3d	40	4d	10	-	-
1e[7b]	3e	29	4e	27	-	-

In conclusion, summarizing the photolyses in dioxane solution, it can be said that the C-11 hydroxyl group does not affect the photochemical rearrangement of cross-conjugated cyclohexadienones **1** to the bicyclo[3.1.0]hex-3-en-2-one system **2**, but it does effect the photolysis of **2**. Further irradiation of **2** has afforded three types of products: a 4-methylphenol (**7**), a new cross-conjugated dienone (**5**), and a spiro cross-conjugated dienone (**6**). These are summarized in Scheme II. However, in the case of the 11β-hydroxy steroidal bicyclo[3.1.0]hex-3-en-2-one **2b** (**2c**) the 11β-hydroxyl group attacks C-1 to yield a 1,11-oxy compound **9a** (**9b**), whereas in the case of its epimer **2d**, the 11α-hydroxyl is too far away to be involved and yields the normal 4-methylphenol **7a**.

Photolysis of steroidal cross-conjugated cyclohexadienones **1** in acidic media usually affords the rearranged bicyclo[5.3.0] system **3** and the spiro steroid **4**. In the case of the 11β-hydroxy cyclohexadienone **1b** (**1c**) these two products are found together with a third, the 1,11-oxy product **9a** (**9b**), which is also the major product. Apparently in acidic conditions **1b** (**1c**) yields the bicyclo-[3.1.0]hex-3-en-2-one system **2b** (**2c**) which undergoes very rapid photoisomerization to the 1,11-oxy product **9a** (**9b**). The 11α-hydroxypregna-1,4-diene-3,20-dione **1d**, which does not have the capability of forming a 1,11-oxy compound, yielded the expected bicyclo[5.3.0] system **3e** in increased yields and the spiro steroid **4d**. Thus the C-11 functionality does affect the photochemistry of **1** in acidic media, but only in the cases where hydrogen bonding is possible (**1a** and **1d**).

Experimental Section

Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. IR spectra were taken in KBr with a Perkin-Elmer 225 spectrophotometer. UV absorption spectra were measured in methanol on a Cary 14 spectrophotometer. NMR spectra were recorded at 100 MHz on a Varian XL-100 spectrometer fitted with a Nicolet NTCFT 1180 pulse system and at 90 MHz on a Perkin-Elmer R32 spectrometer. Chemical shifts are reported in δ (ppm) from the internal standard Me_4Si in chloroform-*d* with a minimum of Me_2SO-d_6 added for solubility, unless otherwise stated. Optical rotations were measured on an O. C. Rudolph & Sons Model 63 Polarimeter equipped with a photoelectric indicator, using a 1-dm cell with methanol as the solvent. Circular dichroism spectra were measured on a Jasco J-41A spectropolarimeter. TLC was carried out on silica gel GF plates with 10% methanol in chloroform as the eluant. Analytical high-performance LC was carried out on a Waters Associates 0.25

(11) Davis, B. R.; Rewcastle, G. W.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. 1* 1978, 736.

in. × 25 cm μC_{18} column, eluting with 50% aqueous methanol. Preparative LC was carried out with a 0.5 in. × 50 cm column packed with Waters Associates 37–75 μPorasil A, eluting with from 1–10% methanol in chloroform. Prednisolone (Upjohn Co.) had mp 231–233 °C dec (lit.[4] mp 240–241 °C dec). Prednisolone 21-acetate (Upjohn Co.) had mp 231–233 °C dec (lit.[4] mp 237–239 °C dec). 11α-Hydroxypregna-1,4-diene-3,20-dione, **1d** (Upjohn Company), had mp 226–227 °C (lit.[12] mp 225–227 °C). 1,4-Dioxane was purified by refluxing over sodium for 24 h followed by distillation under argon.

Lumiprednisolone (2b). Prednisolone (**1b**) (0.500 g, 1.387 mmol) in 60 mL of purified 1,4-dioxane was irradiated through quartz with a 2.5-W low-pressure mercury lamp for 2 h under argon. The dioxane was filtered and evaporated in vacuo. Preparative LC followed by recrystallization from ethyl acetate gave lumiprednisolone (**2b**): 0.208 g (0.583 mmol, 42%); mp 233–234 °C; $[\alpha]_D$ −73.2° (*c* 1.26); UV (methanol) λ_{max} 262 (shoulder, ε 2300), 234 nm (4120); IR 1700 (C=O), 1670 (C=O), 1435, 1008 cm^{-1} (cyclopropyl); NMR δ 7.24 (d, 1, *J* = 5.5 Hz, H-4), 5.77 (d, 1, *J* = 5.5 Hz, H-3), 4.82 (s, 1, exchanges with D_2O, OH), 4.36 (s, 1, H-11), 4.8–4.0 (complex, 2, upon D_2O exchange forms AB q at 4.41, *J* = 19 Hz, Δν = 43 Hz, H-21), 3.79 (t, 1, *J* = 5 Hz, exchanges with D_2O, 21-OH), 3.49 (d, 1, *J* = 4 Hz, exchanges with D_2O, 11-OH), 1.24 (s, 3, H-19), 0.83 (s, 3, H-18), 2.7–1.9 (complex).

Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83. Found: C, 69.73; H, 7.72.

Lumiprednisolone Acetate (2c). Prednisolone acetate (**1c**, 1.00 g, 2.49 mmol) in 220 mL of dry dioxane was irradiated through quartz with a 2.5-W low-pressure mercury lamp for 3.5 h under a nitrogen atmosphere. Dioxane was removed in vacuo. Crystallization from ethyl acetate gave 780 mg (1.94 mmol, 78%) of lumiprednisolone acetate (**2c**): mp 212–215 °C; $[\alpha]_D$ −36.7° (*c* 2.77); UV (ethanol) λ_{max} 265 (shoulder, ε 2500), 233 nm (4730); IR 1750, 1703, 1678, 1658, 1570, 1006 cm^{-1} (cyclopropyl); NMR δ 7.24 (d, 1, *J* = 6 Hz, H-4), 5.79 (d, 1, *J* = 6 Hz, H-3), 4.97 (AB q, 2, *J* = 18 Hz, Δν = 39 Hz, H-21), 4.88 (s, 1, exchanges with D_2O, OH), 4.36 (s, 1, H-11), 3.19 (d, 1, *J* = 4 Hz, exchanges with D_2O, 11-OH), 2.14 (s, 3, acetate), 1.26 (s, 3, H-19), 0.86 (s, 3, H-18), 2.7–1.3 (complex).

Anal. Calcd for $C_{23}H_{30}O_6$: C, 68.63; H, 7.51. Found: C, 68.21; H, 7.19.

Lumiprednisone Acetate (2a). Jones reagent was added dropwise with stirring to a solution of 200 mg (0.498 mmol) of **2c** in 5 mL of acetone until a reddish brown coloration persists. The resulting mixture was poured into 25 mL of ice water and extracted with 150 mL of ether. The ether extract was dried and concentrated in vacuo to give 170 mg of crude product. Crystallization from ethyl acetate gave 123 mg (61.9%) of lumiprednisone acetate (**2a**) as colorless crystals, mp 227–229 °C; IR and NMR spectra of this product are identical with those of lumiprednisone acetate obtained by irradiation of prednisone acetate (**1a**) in dioxane at 2537 Å.[1] The mixture melting point also showed no depression, mp 228–230 °C.

11α-Hydroxylumipregna-1,4-diene-3,20-dione (2d). 11α-Hydroxypregna-1,4-diene-3,20-dione (**1d**, 300 mg, 0.913 mmol) was dissolved in 60 mL of dry dioxane. The solution was irradiated for 1 h under nitrogen with a 2.5-W low-pressure mercury lamp. The solution was filtered to obtain 46 mg of unreacted starting material (**1d**). Preparative LC with 1% ethanol in chloroform as eluant gave 143 mg (0.435 mmol, 47% yield) of 11α-hydroxylumipregna-1,4-diene-3,20-dione (**2d**): mp 76–79 °C; $[\alpha]_D$ = −326° (*c* 0.11); UV (ethanol) λ_{max} 272 (shoulder, ε 1690), 223 nm (4110); IR 3410, 1688 (C=O), 1567 (C=C), 1350, 1164, 1020 cm^{-1} (cyclopropyl); NMR ($CDCl_3$) δ 7.28 (d, 1, *J* = 6 Hz, H-4), 5.91 (d, 1, *J* = 6 Hz, H-3), 3.83 (d of d, 1, J_1 = 11, J_2 = 5 Hz, H-11), 3.10 (br, 1, OH), 2.14 (t, 2, *J* = 11 Hz, H-9, H-12), 2.10 (s, 3, H-21), 1.48 (s, 3, H-19), 0.63 (s, 3, H-18), 2.8–0.8 (complex).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 77.02; H, 8.44.

2,11α-Dihydroxy-4-methyl-19-norpregna-1,3,5(10)-trien-20-one (7a). 11α-Hydroxypregna-1,4-diene-3,20-dione (**1d**, 2.287 g, 6.963 mmol) was dissolved in 110 mL of dioxane and irradiated for 1 h under nitrogen with a 450-W high-pressure Hanovia lamp through a Pyrex filter. The residue obtained by evaporation of the solvent in vacuo was separated by preparative liquid chromatography on a Waters Associates Preparative LC/System 500 on a silica gel column, eluting with a mixture of 9% hexane, 18% 2-butanone, and 73% dichloromethane, giving starting material (1.692 g, 74%) and phenol **7a** (0.367 g, 16% actual, 62% corrected for starting material). Recrystallization from chloroform gave **7a**: mp 111–113 °C dec; $[\alpha]_D$ +12.2° (*c* 2.55); UV (methanol) λ_{max} 282 (ε 2000) and 277 nm (2000), becoming 294 (shoulder, 1900) and 285 (2400) upon addition of base; IR 3400, 2935, 2878, 1690 (carbonyl), 1661, 1615, 1583, 1418, 1358, 1307, 1220, 1057, 1025, 841 cm^{-1}; NMR δ 7.47 (br s, 1, H-3), 6.58 (br s, 1, H-1), 4.04 (complex, 1, H-11), 2.22 (s, 3, H-19), 2.14 (s, 3, H-21), 0.58 (s, 3, H-18), 2.8–1.2 (complex).

Anal. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.55; H, 8.30.

Photolysis of 600 mg of the lumisteroid **2d** in 120 mL of dioxane for 3 h with a 450-W high-pressure lamp with a Pyrex filter followed by evaporation of the solvent in vacuo and column chromatography afforded 143 mg of **2d** and 107 mg of **7a** (23% yield).

17β-Acetoxy-2-hydroxy-4-methyl-19-norpregna-1,3,5-(10)-triene (7b). Phenol **7b** was prepared according to the method of Jeger et al.[5a] Dienone **1e** (1.0 g) in 150 mL of dioxane was irradiated for 1 h with a 450-W high-pressure mercury lamp in a quartz well. Column chromatography gave a total of 275 mg of phenol **7b**: mp 202–204 °C; IR 3325, 2910, 1729, 1699, 1629, 1599, 1268, 854, 837 cm^{-1}; NMR δ 0.81 (s, 3, H-18), 2.05 (s, 3, OAc), 2.14 (s, 3, C-4 Me), 4.76 (t, *J* = 7 Hz, 1, H-17), 6.59 (br s, 1, H-1 or H-3), 6.71 (br s, 1, H-1 or H-3) [lit.[5a] mp 203–204 °C; IR 3625, 1723, 1624, 1600, 1260, 853, 835 cm^{-1}; NMR δ 0.81 (s, 3), 2.07 (s, 3), 2.15 (s, 3), 4.75 (br, 1), 6.56 (d, *J* = 2.5 Hz, 1), 6.68 (d, *J* = 2.5 Hz, 1)].

17α,21-Dihydroxy-1β,11β-oxy-10α-pregna-4-ene-2,20-dione (9a). Photolysis of 99 mg of **2b** in dioxane for 21 h with a 450-W Hanovia lamp fitted with a canary glass filter afforded, after evaporation of the solvent and recrystallization from ethyl acetate–chloroform, 85 mg (86%) of **9a**: mp 120–121 °C; $[\alpha]_D$ −161° (*c* 1.79); UV (methanol) λ_{max} 285.7 nm (ε 384); IR 3430 (OH), 1724 (C=O), 1710 (C=O), 1118, 1051, 1006 cm^{-1}; NMR δ 5.38 (br d, 1, *J* = 8 Hz, H-4), 4.87 (s, 1, exchanges with D_2O, OH), 3.8 (br s, 1, exchanges with D_2O, OH), 4.8–3.9 (complex, 2, upon exchange with D_2O gives an AB q at 4.40, 2, *J* = 20 Hz, Δν = 46 Hz, H-21), 1.41 (s, 3, H-19), 0.73 (s, 3, H-18), 3.3–1.0 (complex).

Anal. Calcd for $C_{21}H_{28}O_5$: C, 69.98; H, 7.83. Found: C, 69.91; H, 7.69.

A much faster photoisomerization of **2b** to **9a** was observed when the reaction was done in ethanol with a Pyrex filter, resulting in a 90% yield of **9a** after only 45 min.

Photolysis of Prednisolone (1b) in 45% Aqueous Acetic Acid. Prednisolone (**1b**, 10.00 g, 27.74 mmol) in 1200 mL of 45% aqueous acetic acid (v/v) was irradiated for 3 h under nitrogen by a 450-W high-pressure Hanovia lamp through a Pyrex filter. The residue obtained by evaporation of the solvent in vacuo was separated by preparative liquid chromatography on a Waters Associates Preparative LC/System 500 on a silica gel column. Elution with 7% methanol in chloroform afforded 5.013 g of **9a** (13.91 mmol, 50%), 1.246 g of starting material (**1b**, 3.45 mmol, 12%), 1.654 g of spiro compound **4b** (4.37 mmol, 16%), and 1.648 g of bicyclo[5.3.0]decane product **3b** (4.35 mmol, 16%).

Upon recrystallization from methanol, the spiro product gave pure **4b**: mp 229–231 °C dec; $[\alpha]_D$ +52° (*c* 2.23); UV (methanol) λ_{max} 296 nm (ε 173), 229 (9200); IR 3430, 2935, 1713 (carbonyl), 1677 (unsaturated carbonyl), 1583 (olefin), 1410, 1375, 1261, 1181, 1138, 1100 941 cm^{-1}; NMR δ 7.97 (d, 1, *J* = 5 Hz, H-2), 6.18 (d, 1, *J* = 5 Hz, H-1), 5.4–4.1 (complex, exchanges with D_2O giving an AB q at 4.46, 2, *J* = 19.8 Hz, Δν = 36.4 Hz, H-21, and a br s at 4.5, 1, OH), 3.0–1.2 (complex), 1.06 (s, 3, H-19), 0.86 (s, 3, H-18).

Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.98. Found: C, 66.25; H, 8.08.

Recrystallization from methanol afforded colorless bicyclo-[5.3.0]decane product **3b**: mp 228–229 °C; $[\alpha]_D$ +113° (*c* 1.87); UV (methanol) λ_{max} 236 nm (ε 13 500); IR 3400, 1703 (C=O), 1671 (C=O), 1599 (C=C), 1111 cm^{-1}; NMR δ 5.86 (s, 1, H-3), 4.81 (s, 1, exchanges with D_2O, OH), 4.7–3.6 (complex, 4, exchanges with D_2O giving an AB q at 4.46, 2, *J* = 20 Hz, Δν = 40.3 Hz, H-21

(12) Kubota, T.; Hayashi, F. *Tetrahedron* **1967**, *23*, 995.

and 2 OH), 2.2–1.3 (complex), 1.18 (s, 3, H-19), 0.90 (s, 3, H-18).

Anal. Calcd for $C_{21}H_{30}O_6$: C, 66.65; H, 7.98. Found: C, 66.78; H, 8.30.

Photolysis of Prednisolone Acetate (1c) in 45% Aqueous Acetic Acid. Prednisolone acetate (**1c**, 2.00 g, 4.969 mmol) in 475 mL of 45% aqueous acetic acid (v/v) was irradiated for 2.5 h under nitrogen through Pyrex with a 450-W high-pressure Hanovia lamp. The solvent was evaporated in vacuo and the residue chromatographed on silica gel. Elution with 10% acetone in chloroform (v/v) gave 773 mg (1.913 mmol, 38.5%) of **9b**, 320 mg (0.795 mmol, 16.0%) of starting material (**1c**), and 402 mg (0.956 mmol, 19.2%) of **4c**. Elution with 40% acetone in chloroform (v/v) gave 421 mg (1.001 mmol, 20.1%) of **3c**. Recrystallization of **3c** from methanol–water gave colorless crystals: mp 211–213 °C dec; $[\alpha]_D$ +150° (*c* 1.58); UV (ethanol) λ_{max} 235 nm (ϵ 14 100); IR 1715, 1680 (carbonyl), 1600 (olefin), 1232 cm^{-1} (olefin); NMR δ 5.91 (br, 1, H-3), 5.05 (AB q, 2, J = 17 Hz, $\Delta\nu$ = 33 Hz, H-21), 4.70 (s, 1, H-11), 4.66 (s, 1, exchanges with D_2O, OH), 3.84 (s, 1, exchanges with D_2O, OH), 3.19 (s, 1, exchanges with D_2O, OH), 2.20 (s, 3, H-21), 1.25 (s, 3, H-19), 0.87 (s, 3, H-18), 2.4–1.2 (complex).

Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.70; H, 7.67. Found: C, 65.61; H, 7.48.

Recrystallization of **4c** from ethyl acetate gave the spiro steroid as colorless needles: mp 226–228 °C dec; $[\alpha]_D$ +66° (*c* 2.00); UV (ethanol) λ_{max} 228 nm (ϵ 10 000); IR 1750, 1715, 1678 (carbonyl), 1578 (olefin), 1370, 1260, 1230 cm^{-1}; NMR δ 7.75 (d, 1, J = 6 Hz, H-1), 6.13 (d, 1, J = 6 Hz, H-2), 4.95 (AB q, 2, J = 18 Hz, $\Delta\nu$ = 16 Hz, H-21), 3.5 (s, 1, exchanges with D_2O, OH), 3.3 (s, 1, exchanges with D_2O, OH), 2.20 (s, 3, H-23), 1.09 (s, 3, H-19), 0.94 (s, 3, H-18), 3.0–1.1 (complex).

Anal. Calcd for $C_{23}H_{32}O_7$: C, 65.70; H, 7.67. Found: C, 65.83; H, 7.71.

A single crystal grown from ethyl acetate solution was used for the X-ray measurements of the lattice parameters and intensities. The systematic absences in the diffraction pattern indicated the space group to be $P2_12_12_1$. The unit cell constants were determined from least-squares analysis of the θ values for 37 reflections to be a = 17.378 (1), b = 21.291 (1), c = 7.353 (4) Å, resulting in a unit cell volume of 2720.7 $Å^3$. Integrated intensities for 3179 independent reflections having $\theta > 75°$ were measured on an Enraf-Nonius CAD-4 diffractometer with Cu Kα radiation. After the Lorentz and polarization corrections $[(1 + \cos^2 2\theta)/(2 \sin 2\theta)]$ had been applied to the intensity data, normalized structure factor amplitudes were computed, and the structure was solved by a straightforward application of direct-method techniques and found to be the ethyl acetate complex of spiro steroid **4c** ($C_{23}H_{32}O_7$, mol wt 420.5). The density was calculated to be 1.24 g cm^{-3} on the basis of the presence of four molecules of steroid and ethyl acetate (Z = 4) in the cell.

The positional and anisotropic thermal parameters of all nonhydrogen atoms were refined by full-matrix least-squares analysis with the 2547 reflections for which the observed intensity was greater than twice the corresponding standard deviation. These reflections were regarded as having intensities significantly greater than the background, and the weights used during refinement were the quantities $(1/\sigma_F^2)$. After several refinement cycles, it was apparent that the geometry of the acetate side chain (as measured by deviations of bond distance and angles from their expected values) was becoming progressively worse. Consequently, the two carbon atoms and the carbonyl oxygen of the acetate moiety were removed, and a Fourier map was computed. The atoms which had been removed reappeared in locations near their original positions, and it was not possible to discern a second set of peaks which would be consistent with the hypothesis that the acetate group might be disordered. Nevertheless, the attempted refinement of these positions gave the same results as had been experienced previously, and a second attempt to locate alternative positions for these atoms by removing C(21) and O(21), as well as the acetate atoms themselves, did not yield any new atomic positions. Therefore, the three nonhydrogen atoms in the acetate group were included in subsequent structure factor calculations at the positions observed on the last Fourier map, but neither the positional nor isotropic thermal parameters of these atoms were refined. The hydrogen atoms in the steroid moiety, other than those in the acetate group and on O(10β), were located on a Fourier difference map, and the positional and isotropic thermal parameters for these atoms were refined in the final least-squares cycles. The final reliability index, R (defined as $\sum||F_o| - |F_c||/\sum|F_o|$), was 8.2% for the 2547 reflections used in the refinement and 9.6% for all data.

Table IV. Photochemistry of Lumisteroids 2 To Yield 1,11-Oxy Steroids 9[b]

lumisteroid → 1,11-oxy steroid	solvent: dioxane	solvent: ethanol	solvent: 45% aqueous acetic acid
2b → 9a	45%	39%	27%
2c → 9b	41%[a]	27%	29%

[a] 72% yield if corrected for 2c recovered. [b] Percent yields of 9a and 9b.

Oxidation of Bicyclo[5.3.0] System 3c with Jones Reagent. Jones reagent was added dropwise with stirring under a nitrogen atmosphere to a solution of 60 mg (0.148 mmol) of **3c** in 5 mL of acetone until reddish brown coloration persists. The reaction mixture was poured into 25 mL of ice water and extracted with 150 mL of ether. The ethereal solution was dried and concentrated under vacuo to give 52 mg of crude product (0.125 mmol, 86.0%). Crystallization from ethyl acetate gave 45 mg (0.108 mmol, 73.0%) of 11-keto bicyclo[5.3.0] system **3a** as colorless crystals, mp 246–248 °C. Mixture melting point with authentic **3a** showed no depression, mp 246–247 °C. The IR spectra of this compound and authentic **3a** were identical.

Photolysis of 11α-Hydroxypregna-1,4-diene-3,20-dione (1d) in Acidic Media. 11α-Hydroxypregna-1,4-diene-3,20-dione (**1d**, 0.913 mmol) was dissolved in 150 mL of 50% aqueous acetic acid (v/v). The solution was flushed with nitrogen and irradiated for 2 h with a 450-W Hanovia lamp. The solvent was evaporated in vacuo and separated by preparative LC on a 0.5 in. × 0.5 m porasil A column, eluting with 2% methanol in chloroform (v/v) to give after recrystallization from ethanol 125 mg of **3d** (0.330 mmol, 39.7%): mp 201–202 °C dec; $[\alpha]_D$ +144° (*c* 1.27); UV λ_{max} 280 (ϵ 517), 236 nm (21 100); IR 3340 (OH), 1684 (C=O), 1602 cm^{-1} (C=C); NMR δ 5.95 (s, 1, H-3), 5.05 (br s, 1, OH), 4.15 (m, 1, H-11), 2.14 (s, 3, H-21), 1.06 (s, 3, H-19), 0.69 (s, 3, H-18), 3.5–1.1 (complex).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.56; H, 8.56.

Also eluted was 32 mg of **4d** (0.0924 mmol, 10.1%): mp 184–187 °C; $[\alpha]_D$ +59° (*c* 1.80); UV λ_{max} 229.5 (ϵ 6330); IR 1718, 1705 (carbonyl), 1583 (olefin), 1358, 1182, 1156, 1095, 1048, 792 cm^{-1}; NMR δ 7.73 (d, J = 6 Hz, 1, H-1), 6.11 (d, J = 6 Hz, 1, H-2), 4.11 (m, 1, H-11), 2.14 (s, 3, H-21), 1.24 (s, 3, H-19), 0.69 (s, 3, H-18), 2.9–1.1 (m).

The mass spectrum showed a parent ion at m/e 346 (9), 328 (100, P – H_2O), 310 (69, P – $2H_2O$), 194 (64), 135 (32), 109 (53), 96 (63).

Oxidation of 4c. Spirohydroxyprednisolone acetate (**4c**, 60 mg, 0.148 mmol) was dissolved in 2 mL of acetone and placed under a nitrogen atmosphere. Jones reagent was added dropwise until the reddish brown color persisted. The mixture was poured into 20 mL of ice water and extracted with chloroform. The chloroform solution was dried and evaporated in vacuo. Crystallization from methanol gave 45 mg (0.108 mmol, 73%) of **4a** as white crystals: mp 253–255 °C; $[\alpha]_D$ +86° (*c* 0.76); UV (ethanol) λ_{max} 217.5 nm (ϵ 6600); IR 1740, 1718, 1682 (carbonyl), 1580 (olefin), 1370, 1260, 1232, 1000 cm^{-1}; NMR δ 8.00 (d, 1, J = 6.0 Hz, H-4), 6.09 (d, 1, J = 6.0 Hz, H-3), 5.75 (s, 1, exchanges with D_2O, OH), 4.88 (AB q, 2, J = 17.6 Hz, $\Delta\nu$ = 16.1 Hz, H-21), 3.95 (s, 1, OH), 2.09 (s, 3, H-23), 1.08 (s, 3, H-19), 0.51 (s, 3, H-18), 3.2-0.6 (complex).

Anal. Calcd for $C_{23}H_{50}O_7$: C, 66.01; H, 7.23. Found: C, 65.82; H, 6.99.

Photolysis of Lumisteroids 2b and 2c. General Procedure. Lumisteroid **2b** or **2c** (300 mg) in 110 mL of solvent was irradiated under nitrogen for 2 h with a 450-W medium-pressure mercury arc with a quartz filter. Chromatography on silica gel (40 g) with 20% ethyl acetate in chloroform (v/v) as eluant gave upon evaporation of the solvent in vacuo the isolated yields of the

1,11-oxy steroids listed in Table IV.

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Registry No. 1a, 125-10-0; **1b**, 50-24-8; **1c**, 52-21-1; **1d**, 2417-44-9; **1e**, 2363-59-9; **2a**, 73397-96-3; **2b**, 73397-97-4; **2c**, 73454-02-1; **2d**, 73397-98-5; **2e**, 2363-60-2; **3a**, 72779-19-2; **3b**, 73397-99-6; **3c**, 73398-00-2; **3d**, 73398-01-3; **3e**, 73398-02-4; **4a**, 73398-03-5; **4b**, 73398-04-6; **4c**, 73398-05-7; **4d**, 73398-06-8; **4e**, 73398-07-9; **7a**, 73398-08-0; **7b**, 1855-85-2; **9a**, 73398-09-1; **9b**, 73398-10-4.

Supplementary Material Available: Atomic coordinates and isotropic thermal parameters for the prednisolone acetate photoproduct ethyl acetate complex **4c** (2 pages). Ordering information is given on any current masthead page.

Photochemistry of Nitrodibenzo[*b*,*e*][1,4]dioxins in the Presence of Primary Amines

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While 1-nitrodibenzo[*b*,*e*][1,4]dioxin is stable toward irradiation in the presence of amines, the 2-nitro isomer (NDD) reacts to yield two isomeric (alkylamino)hydroxynitrodiphenyl ethers and *N*-(alkylamino)-2-nitrophenoxazine when irradiated in polar solvents containing a primary amine. In apolar solvents, however, only the nitrophenoxazine is obtained. The reaction is established to occur through the triplet state of NDD, which reacts with the amine to form an exciplex. If the medium is sufficiently polar, the exciplex dissociates to the solvatated radical ions, from which the diphenyl ethers arise.

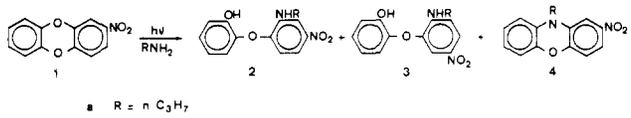
In the frame of our studies on the photochemistry of nitro-substituted heterocyclic compounds in the presence of bases,[1] we turned our attention to the nitrodibenzo-[*b*,*e*][1,4]dioxins. Since the latter appear to be rather similar to the nitrodiphenyl ethers, a photochemical reaction with nucleophiles is expected, on the basis of the photochemical behavior of nitroanisoles and nitroveratroles.[2]

In the present work, it is shown that 1-nitrodibenzo-[*b*,*e*][1,4]dioxin is stable even on prolonged irradiation in the presence of amines, whereas 2-nitrodibenzo[*b*,*e*][1,4]-dioxin (NDD, **1**) is consumed on irradiation in the presence of primary amines, although stable in inert solvents. This reaction takes place with various primary amines, although it is not observed when bulky groups are present, as in the case of *tert*-butylamine.

Irradiation of **1** in the presence of *n*-propylamine, followed by chromatographic separation, gave three products in significant yield when the reaction was carried out in polar solvents, while a single product, corresponding to the minor one in the previous case, was obtained on irradiation in cyclohexane (see Scheme I, and Table I).

To the two main products obtained in polar solvents could be attributed the gross structure of (alkylamino)-hydroxynitrodiphenyl ethers, arising from the cleavage of one of the two ethereal bridges, on the basis of analytical and spectroscopic data. However, the choice among the four possible formulas required a closer examination.

Scheme I



Scheme II

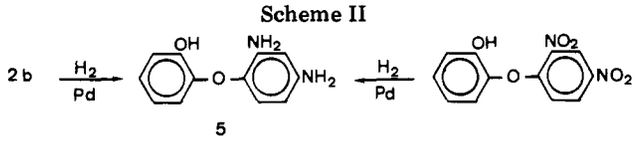


Table I. Percent Yield of the Photoproducts from 2-Nitrodibenzo[*b*,*e*][1,4]dioxin (1)

		product yield, %		
solvent	amine (1 M)	2	3	4
t-BuOH/H_2O (95/5)	*n*-$PrNH_2$	56	24	7
	$PhCH_2NH_2$	53	24	
MeCN	*n*-$PrNH_2$	30	25	11
C_6H_{12}	*n*-$PrNH_2$			28

Compound **2** was identified by direct comparison. The benzylamino derivative (**2a**) was prepared and transformed by catalytic hydrogenation into the diamino derivative (**5**) (Scheme II). This was shown to be identical with authentic 2,4-diamino-2′-hydroxydiphenyl ether, unambiguously prepared by reduction of the corresponding dinitro derivative.

As for compound **3a**, the choice was possible on the basis of its ^1H NMR spectrum, which showed that the hydrogen atom in the meta position with respect to the nitro group is vicinal to an amino group and not to a hydroxy group: the corresponding signal, easily identified from its chemical

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