Surface Photochemistry: Enone Photocycloaddition by Adsorbed Molecules on Silica Gel and Alumina[1]

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The photocycloaddition of alkenes or allene to steroidal enones has been shown to occur in the adsorbed state. This reaction, normally occurring from the (less hindered) α side, has been found to be directed towards the (more hindered) β side by adsorption of the steroidal enone on a dry silica gel and alumina surface. The adsorption of the enone on silica gel also, apparently, disfavors the conformational inversion in the intermediate biradical required for the formation on trans-fused products. The changes in composition of the products are frequently such as to be synthetically useful, and in some cases, e.g., the addition of allene to **1c** and **1a** on alumina, lead to complete reversal of stereochemistry to that observed in the methanolic solution.

Introduction

The photocycloaddition of cyclic $\alpha\beta$-unsaturated ketones to alkenes and allenes has, for the last two decades, been extensively studied, and it has proved to be powerful synthetic tool in organic synthesis.[4] Much progress has been made in the understanding of the mechanism of the processes involved[4,5] and Corey's initial suggestion[6] of an exciplex intermediate has been amply justified. The further, demonstrated, intermediacy of a 1,4-biradical has, however, rendered the control of stereochemistry in this useful reaction difficult.

When the two faces of the double bond in the alkene are nonequivalent the major photoproduct generally arises from the attack of enone on the less hindered side of the alkene.[7] Similarly, with enones, when the two faces are nonequivalent, the attack by olefin is largely from the less hindered side of the enone.[8–11] Some years ago, wiesner proposed that the stereochemistry of the enone cycloaddition to alkenes or allene could be predicted from a presumed conformational posture of the enone excited state, and an initial, assumed, bond formation at the β carbon: this resultant stereochemistry might or might not derive from the steric ease of approach of the olefin.[12] Exceptions to this empirical rule have now been reported.[13]

The steroidal enone has a nearly flat overall structure, but has different steric features on its two faces, thus rendering approach to the double bond in photocycloaddition susceptible, in principle, to steric control. This group of substances seemed suitable for the study of specific steric effects on the process of photocycloaddition, particularly if the ease of approach were capable of modification. One technique that seemed suitable to achieve this modification was that of prior adsorption of the reactants on a surface. Recently, there has been great activity in several laboratories concerning the photochemistry of adsorbed organic molecules on solid oxide supports.[14] Such adsorption has been shown to modify drastically the behavior of radical pairs.[14b,c,15] However, very few reports have as yet been made of the occurrence of bimolecular photoreactions of adsorbed species.[14d,16]

The surface of silica gel is characterised by the presence of terminal silanol functions (isolated, geminal, vicinal) and of siloxane bridges, usually with accompanying physisorbed water molecules.[17] Physicochemical and infrared studies,[18] and more recently NMR studies,[19] have led to an acceptable, if incomplete, picture. The activity of silica gel depends strongly upon the amount of physisorbed water present on the surface. This decreases with increasing temperature, and for temperatures higher than −230 °C it is reduced to near zero.[20] It is generally accepted that for equilibrated surfaces there are ~6 SiOH/nm^2.[21]

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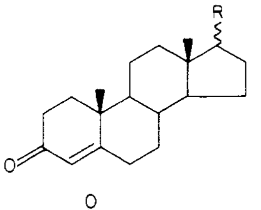
The principle sites responsible for the adsorption of organic molecules on the silica gel surface are the surface silanol groups,[22] and the forces responsible for the adsorption of organic molecules are (1) electrostatic interactions,[22] (2) London-type dispersion forces, arising from induced dipole interactions,[23] and (3) hydrogen bonding.[21] The comparatively strong binding of organic molecules containing π bonds or lone pairs is largely by hydrogen bonding to the silanols or to the physisorbed water:[24] the degree of interaction depends upon the treatment of the silica gel and polarity of the substrate.[17] The strongest simple form of adsorption for organic molecules occurs with thermally dehydrated silica gel having only isolated silanol groups. On the other hand, the fully hydroxylated silica surface is better in providing multiple adsorption sites for polyunsaturated hydrocarbons that can "fit" the adsorbant.[24] The situation with regards to alumina as a substrate is even more complex.[25]

Our guiding principle in these investigations was that steroidal enones should assume a position with its less hindered α face toward the bulk of the gel, leaving the more hindered β side open to attack. The principal binding was presumed to be the hydrogen bonding to the ketone lone pair, the main bulk of the molecule being held down by π bonding to the double bond, with contributions from other polar functions that might be also present elsewhere in the molecule since, for effective hindrance, "single point" binding must surely be inadequate.

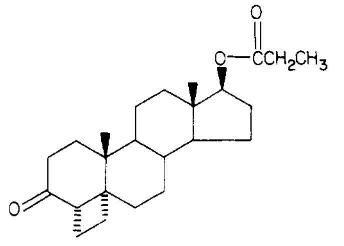
We report here that photocycloaddition of enones can, indeed, be induced on dry silica gel and on alumina, and that under these conditions the stereochemistry of the reaction is different from that found in solution. Methanol was chosen for comparison as polar solvent, since it has been shown by Leermakers that silica gel approximates methanol on the Kosower Z scale.[26] More recently it has been shown to be closer to 30:70 CH_3OH/H_2O.[27,28]

Results and Discussion

The cycloaddition of testosterone propionate **1a** to ethylene in methanol was carried out by the procedure of Rubin[8] to give the 4α5α (**2a**) and 4α5β (**2c**) isomers as major photocycloadducts: in addition the 4β5β isomer, **2b**, was detected as a minor adduct by HPLC analysis. Analysis by GLC of the mixture was complicated by the fact that the 4α5β isomer, **2c**, isomerized to 4β5β, **2b**, at the required column temperature of 230 °C. The photocycloaddition of **1a** to ethylene in ethyl acetate again gave **2a** and **2c** as major cycloadducts, together with **2b** (4β5β), previously unreported,[8] in minor amount. In contrast, irradiation of **1a** on silica gel resulted in preferential attack on the β face. In addition, the yield of **2c** (trans isomer) was reduced to trace amounts.



1a, R = $-O\overset{O}{\overset{\|}{C}}CH_2CH_3$
1b, R = β-OH
1c, R = α-OH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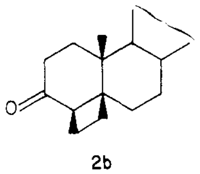
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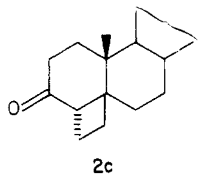
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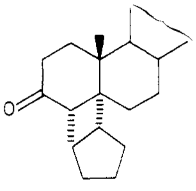
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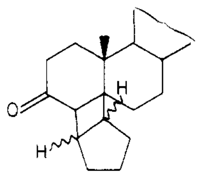
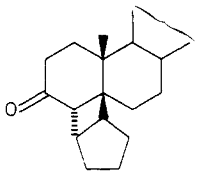


3b 3d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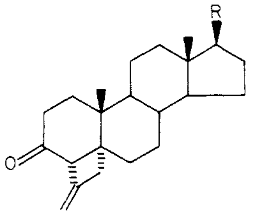
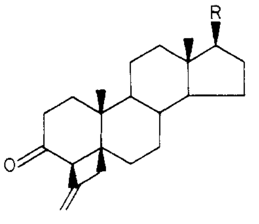
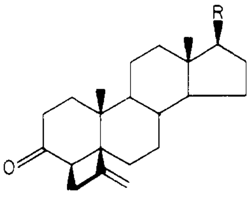


4a, R = $-O\overset{O}{\overset{\|}{C}}CH_2CH_3$, H
5a, R = (=O)



4b, R = $-O\overset{O}{\overset{\|}{C}}CH_2CH_3$, H
5b, R = (=O)



4c, R = $-O\overset{O}{\overset{\|}{C}}CH_2CH_3$, H
5c, R = (=O)

Since the formation of trans-fused systems require conformational inversion in the intermediate biradical,[4d] the effect of lowering the temperature was investigated. At low temperature in methanol α addition was favored by ~7:1, whereas on silica gel at the same temperature β addition was favored (Table I). Both low temperature and adsorption on silica gel apparently disfavor the inversion required for the formation of trans-fused products. Phytocycloaddition of **1a** to cyclopentene both on silica gel and in solution gave the known[8] 4α5α and 4α5β isomers (**3a** and **3c**) together with the previously unreported 4β5β isomer (**3b**). As previously reported,[8] the trans isomer was isomerized on heating to **3d**, a further cis isomer. From R_f on TLC, retention time on GLC, and melting point the two cis β isomers, **3b** and **3d**, were clearly different. They were both assigned the cis 4β5β stereochemistry based on the sign and magnitude of the Cotton effect in the circular dichroism spectra, **3b** $[\Theta]_{294} = -6511$, **3d** $[\Theta]_{299} = -7772$ (lit.[8] $[\Theta]_{299}$ -6639)8 and analogy with **6** ($[\Theta]_{291} = -4300$[9]). Presumably the two isomers are cis–syn–cis and cis–anti–cis, but none of the spectral techniques available to us enabled a decision to be made as to allocation of stereochemistry. These results contrast with those of Lenz in the addition

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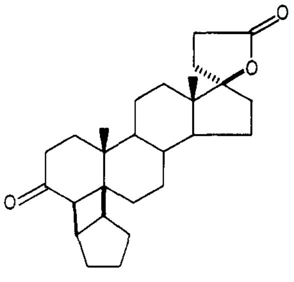
of cyclopentene to **7**,[9] in which case the reaction yielded the 4α5α and 4α5β isomers, together with ~10% of the 4β5β product; however, on heating, the trans isomer yielded the photochemically obtained 4β5β adduct, which contrast with our results wherein the photochemically obtained *cis*-β-**3b** and thermally isomerized *cis*-β-**3d** are different compounds.



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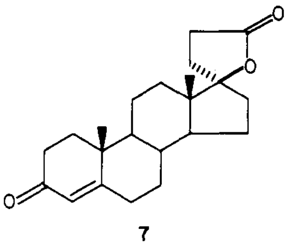

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Comparison of the relative amounts of α vs. β attacks in methanol and on silica gel is rendered difficult by the presence of a major amount of the ambiguous trans isomer formed in methanolic solution at room temperature. Methanol and silica gel may be better compared at −78 °C, where similar (and smaller) amounts of trans isomer are present: again, the product ratio shifts in favor of β approach by a factor of 2.

One method of avoiding the stereochemical ambiguity in mode of approach introduced by the formation of trans-fused products—it has not yet been decisively shown whether the α or β bond from the enone is formed first in the products, or, indeed, whether there is any consistent rule[29]—is to use an addend where strain precludes their formation. Such is the case with allenes. Photocycloaddition of **1a** to allene in methanol solution resulted in preferential reaction from the α side in a ratio of 5:1 at room temperature increasing to 9:1 at −78 °C. In contrast, on silica gel β products were slightly favored and the ratios were essentially temperature independent: from methanol to silica gel the ratio changed by about one order of magnitude.

These adducts were characterized as follows. The separation of the silica gel reaction gave **4c** in 6% yield, based on the initial starting material. The cycloadducts were well separated on TLC, but adducts **4b** and **4c** were not well resolved by GLC. The cis α and β adducts, **4a** and **4b**, showed low field proton signals in the ^{1}H NMR at δ 3.06 and 3.13, respectively, attributed to the methine proton at C-4: an indication of head to head regiochemistry. This was also substantiated by the medium intensity untraviolet maximum at ~293 nm, characteristic of β,γ unsaturated ketones.[30] In contrast, **4c** showed a very weak UV absorption maximum, characteristic of an unperturbed carbonyl group, and no low-field signal was detected at ~3.0 ppm, both features indicating a head-to-tail regiochemistry. The stereochemistry at the ring junction was assigned from the sign of the Cotton effect in the CD spectra of the isomeric adducts: an examination of Drieding models for isomeric octant diagrams suggested that the sign should be negative for **4b** and **4c** and positive for the α cis adduct **4a**. The stereochemistry assignment, i.e., 4α5α and 4β5β, draws analogy with that reported in literature for β,γ unsaturated ketones and for ethylene adducts.[8-10]

In this study alumina was also used as the adsorbent. The preference for β products was even stronger than on silica gel, as observed during the irradiation of **1a** and allene on alumina which resulted in the complete reversal of stereochemistry from that observed in methanolic solution.

Since allene addition always results in the formation of a cis-fused adduct, one cannot, from the stereochemistry discuss whether α or β bond formation occurred first.[4a,5a] Evidence is available, that, in fact, the initial bond formation can be at C_α or C_β,[29] depending upon the structures of alkene and enone involved. According to Wiesner's rule,[12] an overlap of the enone β orbital with a terminal orbital of allene would be required. To the extent that analogy with carbon centered radicals is any guide and that the mechanistic photochemistry is not perturbed by adsorption on the gel, enone addition to a terminal position of the allene should occur.[31] Since this attack at the terminal position is probably unaffected by the adsorption on silica gel the formation of a γ,δ regioisomeric adduct is an indication of, under these conditions and in these products, at least, first bond formation at the α (no the β) position of the steroidal enone.

The most effective binding site in the enone chromophore is the carbonyl oxygen. Only secondary forces require the molecule to lie "flat" on the gel surface, and it is on these forces that the effective protection of one face of the molecule depends since, otherwise the steroid might take up a position orthogonal to the "plane" of the gel. Secondary binding sites must, therefore, be important. The photocycloaddition of **1b** and **1c** to allene was investigated in order to compare the extent of interaction of steroidal enones having equatorial (β) and axial (α) alcoholic functions at C_{17}, respectively, with the surface silanols. With **1b** the extent of attack on the β face in solution and on silica at room temperature was comparable to that found with the corresponding propionylated steroid **1a**. **1a** exhibited a similar behavior at −70 °C as that at room temperature. **1b** which behaves as **1a** does at room temperature was consequently not studied at −70 °C. These observations were not surprising since the oxygen function is on the face away from the gel. However, the epimeric alcohol, 17-epitestosterone, also did not produce, on silica gel, any very striking change as compared with the 17β-propionate, though the results on alumina showed signs of the expected stronger binding. The testosterone and epitestosterone allene adducts were oxidized, to eliminate the stereochemistry at C-17, to obtain the corresponding testosterone–dione adducts, the stereochemistry of which have been already established by us. These results indicate that, irrespective of the 17 substituent, the molecule is lying, at least partly, flat, and that cumulative secondary forces are already important in a large molecule such as a steroid.

An irradiation was carried out in acidified methanolic solution (HCl, pH 3) to ensure that our observed results were not merely a function of the silanol acidity. No difference from the behavior in methanolic solution was observed.

Although not a steroid, the addition of allene to **8**[32] (12-methoxy-18,19-bisnorpodocarpa-4,8,11,13-tetren-3-one) was briefly studied, to see the effect of a single steric

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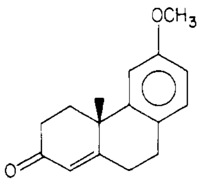
Table I. Conditions[a,b] and the Results of the Cycloaddition of Enones to Alkenes or Allene

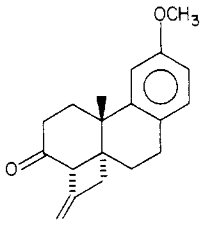
enone	alkenes	temp, °C	time	system	conversn, %	yield,[c] %	product[d]	isomer, % 4α5α	isomer, % 4β5β	isomer, % 4α5β
1a	ethylene	11	1 h	CH_3OH	57		**2a, 2b, 2c**[e]	57	10	32
		11	4 h	EtOAc	90		**2a, 2b, 2c**	67	33	*f*
		−70	1 h 10 min	CH_3OH	24		**2a, 2b, 2c**[e]	82	12	6
		−70	4 h	EtOAc	100		**2a, 2b, 2c**	87	13	*f*
		11	4 h	SiO_2	100		**2a, 2b, 2c**[e]	49	51	trace
		−70	6 h	SiO_2	96		**2a, 2b, 2c**[e]	42	58	trace
	cyclopentene	8	1 h 40 min	CH_3OH	61		**3a, 3b, 3c**	46	22	31[f]
		8	3 h	cyclopentene	100	53.6 (32.6)	**3a, 3b, 3c**	35.5 (28)[g]	15.5 (0)[g]	48.8[f] (72)[g]
		−70	1 h 50 min	CH_3OH	67		**3a, 3b, 3c**	53	41	6[f]
		11	3 h 11 min	SiO_2	46	52	**3a, 3b, 3c**	33	56	10[f]
		−70	7 h 30 min	SiO_2	66		**3a, 3b, 3c**	32	57	10[f]
	allene	11	30 min	CH_3OH	58		**4a, 4b**	83	17	
		11	4 h 15 min	EtOAc	100		**4a, 4b**	84.4	15.6	
		−78	1 h	CH_3OH	75		**4a, 4b**	90	10	
		−78	1 h	EtOAc	100		**4a, 4b**	89	11	
		11	2 h, 4 h 15 min	SiO_2	80, 100	85	**4a, 4b, 4c**	46, 47[g]	54, 53[g,h]	
		−78	3 h	SiO_2	97		**4a, 4b, 4c**	47	53	
		11	3 h	Al_2O_3	80		**4a, 4b, 4c**	20	80	
1b	allene	20	1 h 30 min	CH_3OH	73		**4a, 4b**[i]	82	18	
		20	6 h	SiO_2	85		**4a, 4b, 4c**[i]	59	41	
		20	6 h	Al_2O_3	80		**4a, 4b, 4c**[i]	61	39	
1c	allene	−70	45 min	CH_3OH	100		**5a, 5b**[j]	91.5	8.5	
		20	1 h 30 min	SiO_2	100		**5a, 5b, 5c**[j]	34	66	
		20	45 min	Al_2O_3	100		**5a, 5b, 5c**[j]	6	94	
8	allene	−70	1 h 15 min	CH_3OH	95	52.6	**9a, 9b**	78, 86[g]	22, 14[g]	
		20	5 h	SiO_2	100		**9a, 9b**	58.5	41.5	
10	cyclopentene	20	–	C_6H_6	90	(82.2)[k]	**11a**			(100)[k]
		20	18 h	SiO_2	55	57	**11a, 11b**			66.5[l] 28[m]

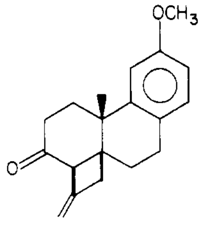
enone	alkenes	temp, °C	time	system	conversn, %	yield,[c] %	product[d]	isomer, % 16α17α	isomer, % 16β17β
12a	ethylene	11	2 h	CH_3OH	55		**13a, 13b**	95	5
		−70	2 h	CH_3OH	20		**13a, 13b**	96.5	3.5
		11	4 h, 18 h	SiO_2	70	50	**13a, 13b**	56, 60[g]	44, 40[g]
		−70	3 h 30 min	SiO_2	86		**13a, 13b**	54.5	44.5
12b	ethylene	20	3 h	CH_3OH	60		**13a, 13b**[n]	96	4
		20	4 h, 10 min	SiO_2	66.5		**13a, 13b**[n]	55	45

[a] 450-W medium-pressure Hg lamp. [b] 0.1 mmol of enone and 1 mmol of alkene or allene on 3 g of silica gel or alumina. [c] Isolated yield (based on the recovered starting material) of cycloadducts after chromatography, literature values in parentheses, the cycloadducts from the irradiation of **1c** and **12b** with allene were not isolated due to limited availability of the expensive steroid, the quantitative separation of **2b** and **2c** from the irradiated mixture of **1a** and ethylene was rendered difficult due to their identical R_f values on TLC. [d] Analyses of GLC. [e] Analyses by GLC and HPLC. [f] Analyzed as the thermally isomerized cis isomer. [g] Relative ratio of isolated adducts, literature values in parentheses from ref 8. [h] 43.8% of **4b** and 9.16% of **4c**, (relative yield wrt total isolated adducts) isolated after chromatography. [i] Analyzed after propionylation. [j] Analyzed after oxidation. [k] From ref 8, only one adduct formed and 10% of unidentified products. [l] 5.5% unidentified cycloadduct. [m] **11b**. [n] Analyzed after acetylation.

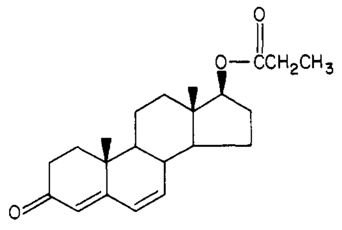
center. In methanolic solution and on silica gel two adducts **9a** and **9b** were obtained. There stereochemistry was tentatively arrived at by analogy with **1a**: the difference in product composition found between methanol at −70 °C and silica gel was small, but indicated a shift toward β face addition.

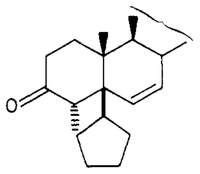

8

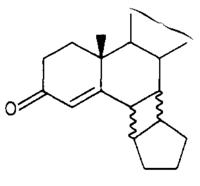

9a


9b

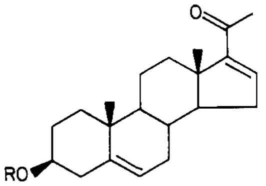
The photocycloaddition of cyclopentene to 17β-hydroxy-$\Delta^{4,6}$-androstadien-3-one 17β-propionate (**10**) has been reported[8] to give **11a** in 82.3% yield. On silica gel this remained the major product, but 28% attack, to give **11b**, was also found. The structure of the 6,7 cycloadduct **11b** followed from the UV spectra (λ_{max} (MeOH) 255 nm, ε 12000), ^{1}H NMR (δ 5.7 brs, 1 H), IR (ν 1655, 1720 cm^{-1}), and mass spectrum: no attempt was made to determine the stereochemistry at the ring junction. The increased addition at the γ,δ position is consonant with the view that the primary binding is at the carbonyl funciton, and hence that end of the chromophore is closest to the gel surface, thus leaving the 6,7 bond relatively exposed.


10

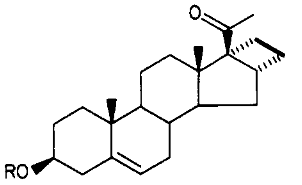

11a


11b

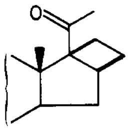
The final study was an endeavor to determine whether rigidity of the enone function was necessary for the effect of silica gel to be manifested. For this purpose the 20-ketones **12a** and **12b** were employed.



12a, R = $-\overset{\overset{O}{\|}}{C}CH_3$
12b, R = H



13a



13b

The photocycloaddition of **12a** to ethylene in benzene solution was carried out by the procedure of Sunder-Plassman et al.[10] to give the 16α17α (**13a**) and 16β17β (**13b**) isomers. In methanolic solution the α addition was favored by 19:1, whereas on silica gel a shift toward β face addition was observed. In **12b** the extent of attack on the β face in solution and on silica was comparable to that obtained with the corresponding acetylated steroid **12a**. This was not unexpected since the alcoholic function is on the face away from the gel.

Conclusion

The studies described above demonstrate that mixed photocycloaddition reactions are possible on dry silica and alumina surfaces. The steric course of steroidal enone photocycloaddition can be modified by prior adsorption of the steroid on the silica gel or alumina. Results are consistent with the view that this adsorption takes place on the gel from the less hindered face (α) leaving the β face more available for reaction. It appears likely that adsorption on the surface disfavors conformational inversion in the intermediate 1,4 biradical which is required for trans addition to occur. In the case of allene photocycloaddition to steroidal enones, the formation of γ,δ regioisomeric adducts on silica suggests that the first bond is formed at the steroid C_α position.

Experimental Section

CD Spectra were measured after calibration with *d*-Camphorsulfonic acid. GC, analyses were performed on an instrument equipped with FID detectors and a 6 ft × 2 mm glass column with 3% OV 101 on Chromosorb W. HPLC analyses were performed on an instrument using a μ Porasil column. Melting points were measured on a Reicheret hot stage apparatus and are uncorrected.

Materials. Methylene chloride was dried over CaH_2. Spectral grade methanol was used. Testosterone propionate (BDH), testosterone (Aldrich), and 3β-acetoxypregna-5,16-dien-20-one (Steraloids) were recrystallized before use. 17β-Hydroxy-$\Delta^{4,6}$-androstadiene-3-one 17β-propionate was prepared by the literature procedure.[33] Cyclopentene was distilled before use. Allene (Matheson) and ethylene (Canadian Liquid Air) were used directly from the cylinder. Merck silica gel 60 (E. M. Merck, 35–70 mesh) and alumina (neutral, ICN Pharmaceutical) were used in all irradiation experiments.

Procedure for Sample Preparation and Irradiation on Dry Silica and Alumina. A preweighed sample of silica gel (~3g) was introduced into a Pyrex tube equipped with a side arm in apparatus described previously,[34] and to it was added a sample of enone (0.1 mmol). The silica gel was dried at 200 °C (3 h, 0.3 torr). The silica gel was then allowed to cool to room temperature under vacuum, the enone was dropped on the gel, and dry methylene chloride (25 mL) was condensed on to the gel by cooling the Pyrex cylinder containing the silica gel at −78 °C. The slurry was shaken well in order to dissolve the enone and the methylene chloride was removed by distillation back to the original container. The silica gel was further dired in vacuum for 6 h. In the case of cyclopentene a preweighed sample (~1 mmol) was condensed into the Pyrex cylinder cooled to −78 °C. In the case of gases (ethylene, allene), the Pyrex cylinder, containing gel and enone, of total capacity ~43 mL was cooled to 0 °C and the gas was introduced at 1 atm pressure. In the case of alumina as an adsorbent, a preweighed sample of alumina (~3g) was dried overnight in an oven at 200 °C. The alumina sample was then allowed to cool to room temperature and transfered to a Pyrex cylinder: the remainder of the procedure was as outlined above. In the case of preparative scale irradiations 8–9 g of silica, enone (1–2 mmol) and methylene chloride (30 mL) were introduced into a Pyrex cylinder of total capacity 88 mL. After evaporating the solvent, olefin was introduced as described above. The Pyrex cylinder was then sealed and rotated on its long axis in front of 450-W medium-pressure Hg lamp. The low-temperature irradiation was performed by rotating the Pyrex cylinder immersed in a methanol/dry ice bath. Irradiation times varied considerably depending upon the substrate and conversion required.

Product Analysis. After extracting the silica gel with ether and with methanol the irradiation products were analyzed by GC or HPLC. In GC, analyses, a known amount of internal standard (17β-hydroxyandrosta-1,4-dien-3-one) was added to the concentrated irradiation mixture. The sample was analyzed taking an average of at least two injections for each determination. A calibration response curve was constructed for each compound analyzed. In the case of preparative scale irradiation the products were separated by flash chromatography or preparative TLC. For all the compounds isolated appropriate spectra and precise massess were recorded.

Solution Irradiations. A solution of enone (~0.05 M) in ethyl acetate or methanol was irradiated while a continuous stream of ethylene or allene was bubbled through the solution. In the case of cyclopentene, a preweighed amount was added to the enone solution in the required solvent. The low temperature irradiation was performed by immersing the Pyrex tube in a dry ice–methanol bath.

Photocycloaddition of Testosterone Propionate 1a to Ethylene. Authentic samples of **2a** mp 184–185 °C (lit.[8] mp 187–188 °C), **2b** mp 71–72 °C (lit.[8] mp 73–75 °C), and **2c** mp 148–151 °C (lit.[8] mp 152–153 °C) were prepared by the literature procedure.[8,35] GC analyses (column temperature 230 °C) of the irradiation products were complicated by the thermal isomerization of **2c** to **2b**. The isomeric adducts were separable by analytical HPLC with benzene–ethyl acetate 9.5/0.5 (v/v). The retention times for the individual peaks were correlated with authentic samples.

Photocycloaddition of Testosterone Propionate 1a to Cyclopentene. Irradiation of **1a** (350 mg, 1.0 mmol) and 4 mL (45 mmol) of cyclopentene was performed by the literature procedure.[8] The residue after the distillation of cyclopentene was crystallized from ethyl acetate to give 40 mg of **3a**[35] mp 217–218 °C lit.[8] mp 215–217 °C). Chromatography of the mother liquor by flash column with 7:3 (v/v) petroleum ether–ether gave an additional 40 mg of **3a** and 35 mg of **3b** previously unreported:[8] mp 151–155 °C; ^{1}H NMR ($CDCl_3$) δ 4.50 (m, 1H), 0.90 (s, 3 H), 0.83 (s, 3 H): IR ($CHCl_3$) ν 1680 1720 cm^{-1}; CD (CH_3OH) $[\Theta]_{294}$ −6511; exact mass calcd for $C_{27}H_{40}O_3$ 412.2977, obsd 412.2970. In addition 110 mg of **3c**[35] was isolated: mp 166.5–167.5 °C (lit.[8] mp 168–169,5 °C).

Irradiation of Testosterone Propionate 1a and Cyclopentene on Silica Gel. Irradiation of 700 mg (2 mmol) of **1a** and 358 mg (5 mmol) of cyclopentene on 10.5 g of silica gave 714 mg of oil. Flash chromatography, as outlined above, gave 51 mg

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[33] Angello, E. J.; Laubach, G. O. *J. Am. Chem. Soc.* **1960**, *82*, 4293.

[34] Abdel-Malik, M.; de Mayo, P. *Can. J. Chem.*, in press.

[35] Spectra data was found identical with the reported in literature.

of **3a**, 109 mg of mixed isomers, and 48 mg of **3b**.

Thermal Isomerization of 3c to 3d. Isomerization of **3c** to **3d** was accomplished by the literature procedure.[8] Crystallization from methanol gave an analytically pure sample of **3d**:[35] mp 139–140 °C (lit.[8] mp 140–141 °C). The cycloadduct **3b** isolated from photocycloaddition in solution and on silica showed different R_f value on TLC, different retention time on GC, and different melting point than **3d** isolated from the thermal isomerization of trans cycloadduct **3c**.

Irradiation of Testosterone Propionate 1a and Allene on Silica Gel. Irradiation of (157 mg, 0.45 mmol) **1a** and allene on 7.8 g of silica gave 190 mg of oil. Flash chromatography on silica with 8:2 (v/v) petroleum ether–ether gave 61 mg of **4a** as a white crystalline solid, mp 148.5–150 °C [^{1}H NMR ($CDCl_3$) δ 4.96 (br s, 2 H), 4.43 (t, $J = 8$ Hz, 1 H), 3.06 (m, 1 H), 0.90 (s, 3 H), 0.83 (s, 3 H); IR ($CHCl_3$) ν 1725, 1690, 900 cm^{-1}; UV (CH_3OH) 293 nm (ϵ 187); CD (CH_3OH) $[\Theta]_{292}$ +2128; exact mass calcd for $C_{25}H_{26}O_3$ 384.2664 obsd 374.2660], together with 19 mg of mixed isomers, 58 mg of **4b** [mp 103.5–105 °C; ^{1}H NMR ($CDCl_3$) δ 4.90 (brs, 2 H), 4.53 (t, $J = 8$ Hz, 1 H), 3.13 (m, 1 H), 0.93 (s, 3 H), 0.83 (s, 3 H); IR ($CHCl_3$) ν 1730, 1690, 900 cm^{-1}; UV (CH_3OH) 295 nm (ϵ 180); CD(CH_3OH) $[\Theta]_{292}$ −2523; exact mass calcd for $C_{25}H_{36}O_3$ 384.2664, obsd 384.2657], and 12 mg of **4c**: mp 79–81 °C; ^{1}H NMR ($CDCl_3$) δ 4.93 (brs, 2 H), 4.47 (t, $J = 8$ Hz, 1 H), 1.0 (s, 3 H), 0.76 (s, 3 H); IR ($CHCl_3$) ν 1720, 1680, 900 cm^{-1}; UV (CH_3OH) 284 nm (ϵ 30.7); CD (CH_3OH) $[\Theta]_{284}$ −1256; exact mass calcd for $C_{25}H_{36}O_3$ 384, 2664, obsd 384, 2659. GC analyses of the crude irradiation product showed two peaks with ratio ~1:1.

Photocycloaddition of Testosterone 1b to Allene. The photocycloaddition of **1b** and allene in methanol, on silica and alumina, was performed as previously described. The irradiation products were treated with propionic anhydride and pyridine (overnight at room temperature) and the products analyzed (GC).

The photocycloaddition of **1b** and allene in acidic methanolic solution (HCl, pH 3) was performed and no difference in behavior than in methanol was observed.

Photocycloaddition of 17-Epitestosterone 1c to Allene. Irradiation of 6 mg of **1c** and allene in methanol, on silica and alumina, was performed as outlined above. The resulting yellow residue was oxidized with sodium dichromate solution, by the procedure of Brown,[36] to the corresponding dione cycloadducts **5a–c**.

Irradiation products from the phytocycloaddition of **1b** and allene were also similarly oxidized to the cycloadducts **5a–c** as shown by retention times on GC and R_f values on TLC.

Photocycloaddition of 12-Methoxy-18,19-bisnorpodocarpa-4,8,11,13-tetraen-3-one 8 to Allene. Irradiation of (150 mg, 0.6 mmol) **8** and allene at −78 °C in methylene chloride gave a yellow oil which was crystallized from methanol to give 40 mg of **9a**: mp 70–72 °C; ^{1}H NMR ($CDCl_3$) δ 7.12–6.64 (m, 3 H), 5.06–4.88 (m, 2 H), 3.78 (s, 3 H), 1.12 (s, 3 H); IR ($CHCl_3$) ν 1685, 900 cm^{-1}; exact mass calcd for $C_{19}H_{22}O_2$ 282.1620, obsd 282.1616. Chromatography of the mother liquid by PTLC 9/1 (v/v) ether–hexane, 11 developments) gave an additional 38 mg of **9a** and 12 mg of **9b** as an oil: ^{1}H NMR ($CDCl_3$) 7.12–6.64 (m, 3 H), 5.06–4.88 (t, 2 H), 3.78 (s, 3 H), 1.12 (s, 3 H); IR ($CHCl_3$) 1690, 900 cm^{-1}; exact mass calcd for $C_{19}H_{22}O_2$ 282.1620, obsd 282.1619; 2,4-dinitrophenylhydrazone mp 102–104 °C; exact mass calcd for $C_{25}H_{26}N_4O_5$ 462.1903, obsd 462.1903; temperature for G.C. analyses 195 °C.

Irradiation of 17β-Hydroxy-$\Delta^{4,6}$-androstadien-3-one 17β-Propionate 10 and Cyclopentene on Silica Gel. Irradiation of **10** (260 mg, 0.76 mmol) and cyclopentene (250 mg, 3.6 mmol) on 10 g of silica gave 312 mg of yellow oil. Purification by PTLC (6/4 v/v hexane–ether, 3 developments) gave 29 mg of **11b** [mp 160–163 °C; ^{1}H NMR ($CDCl_3$) δ 5.7 (brs, 1 H), 4.7 (m, 1 H); IR ($CHCl_3$) ν 1655, 1720 cm^{-1}; UV (CH_3OH) 255 nm (ϵ 12 000); exact mass calcd for $C_{27}H_{38}O_3$ 410.2820, obsd 410.2820], 61 mg of **11a**[35] [mp 161–163 °C (lit.[8] mp 164.5–165.5 °C)], 118 mg of **10**, and 6 mg of unidentified cycloadduct as an oil: exact mass calcd for $C_{27}H_{38}O_3$ 410.2820, and obsd 410.2820.

Photocycloaddition of 3β-Acetoxypregna-5,16-dien-20-one 12a to Ethylene. The authentic samples[35] **13a**, mp 187–190 °C (lit.[10] mp 186–187 °C), and **13b**, mp 193–194.5 °C (lit.[10] mp 195–196 °C), were prepared by the literature procedure. Preparatively, **12a** (100 mg, 0.28 mmol) and ethylene on 8 gm of silica were irradiated. The resulting oil was purified by PTLC (9/1 (v/v) benzene–ethyl acetate, 3 developments) to give **13a** (21 mg), **13b** (14 mg), and **12a** (35 mg). Column temperature for analysis: 210 °C. The photocycloaddition of 3β-hydroxypregna-5,16-dien-20-one (**12b**) to ethylene was carried out in the usual way and the products analyzed after acetylation.

Acknowledgment. We thank the Natural Science and Engineering Research Council of Canada for financial support.

Registry No. **1a**, 57-85-2; **1b**, 58-22-0; **1c**, 481-30-1; **2a**, 30786-69-7; **2b**, 30598-78-8; **2c**, 30598-77-7; **3a**, 94131-80-3; **3b/3d** cis-anti-cis deriv, 94131-81-4; **3c**, 94131-82-5; **3d/3b** cis-syn-cis deriv., 94131-83-6; **4a**, 88147-14-2; **4b**, 88147-15-3; **4c**, 88147-17-5; **5a**, 94042-38-3; **5b**, 94131-84-7; **5c**, 94042-39-4; **8**, 23963-73-7; **9a**, 94042-40-7; **9b**, 94131-85-8; **9b** 2,4-DNP deriv, 94042-41-8; **10**, 25862-97-9; **11a**, 94198-67-1; **11b**, 94042-42-9; **12a**, 94042-43-0; **12b**, 1162-53-4; **13a**, 10030-06-5; **13b**, 7769-14-4; SiO_2, 7631-86-9; Al_2O_3, 1344-28-1; ethylene, 74-85-1; cyclopentene, 142-29-0; allene, 463-49-0.

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(36) Brown, H. C.; Garg, C. P.; Liu, K. I. *J. Org. Chem.* **1971**, *36*, 387.