JOC Article

Solid-State Photodimerization of Steroid Enones[†]

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Received July 18, 2002

Androst-4-ene-3,17-dione (**1**) and 17α-methyltestosterone (**2**) are dimerized in the solid-state by UV radiation. These substances were selected by a search in the CSD among the steroid enones presenting in the crystalline state an intermolecular short contact between a hydrogen α to a carbonyl group and the oxygen of an enone system. Dimerization occurs by transfer of the hydrogen to the oxygen and connection between the two involved carbons. Androst-4-ene-3,17-dione (**1**) affords dimer **3** and trimer **4**, both formed by connection of the C-16 of a molecule with the C-3 of a near one. Irradiation of 17α-methyltestosterone (**2**) gives the isomeric trienones **5** and **6**. These compounds are reasonably formed by dehydration of unisolated intermediate products **7** and/or **8** obtained by coupling of two molecules through a linkage between the C-2 and the C-3′ carbons. The formation mechanisms of the photoproducts are satisfactory explained on the basis of the molecular arrangement of the monomers in the crystal state. Modeling of the dimeric molecules was done using molecular mechanics calculations. A single-crystal X-ray of the dimer of androst-4-ene-3,17-dione confirms the structural interpretation of spectral data. The conformer found in the solid-state agrees well with the results of molecular mechanics calculations.

Introduction

In recent years, many organic chemists have been involved in solid-state chemistry.[1] In this state, many reactions occur with yields comparable to those in solution with obvious practical advantages. Furthermore, the molecular arrangements in the crystal may allow reactions forbidden in solution. Photodimerizations are the most extensively studied reactions in the solid-state starting from work on the [2 + 2] photocyclizations of cinnamic acid[2] and coumarin.[3] In particular, solid-state photodimerizations have been observed with steroids as, for instance, testosterone propionate,[4] halometasone,[5] and norethisterone.[6]

Recently, we have reported that solid 16-dehydroprogesterone[7] and cholest-4-en-3-one[8] afford dimers by UV irradiation and justified the dimerization processes on the basis of the intermolecular interactions in the relative monomer crystal. In these cases and in halometasone, the driving force of dimerization is always the reactivity of a hydrogen α to a carbonyl group, but the type of dimers obtained depends on the different molecular arrangements of the monomers in the crystal state. In fact the dimer of 16-dehydroprogesterone is determined by the proximity, in the monomer crystal,[7] of the C-17 acetyl group of a molecule to the D ring of another one, whereas the formation of both the dimers of cholest-4-en-3-one is due to the proximity of the A rings in the monomer packing.[9] Likewise, the intermolecular short

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[†] Dedicated to Professor L. Mangoni on the occasion of his 70th birthday.

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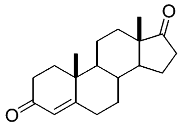
10.1021/jo0204808 CCC: $22.00

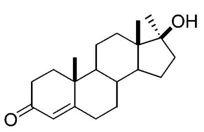
contact between C-21 and C-2′ in the halometasone monohydrate crystal supports the formation of the obtained dimer.[5]

Results and Discussion

In continuing our studies on the behavior of crystalline steroidal enones under UV irradiation, an effort was made to select substances with molecular packing suitable for photodimerization. The search was carried out in the Cambridge Structural Database version 5.22 (October 2001)[10] using ConQuest 1,3 Software. All structures of steroid enones presenting intermolecular short contact between a hydrogen α to a carbonyl group and the oxygen of an enone system were considered. The following selection criteria were used: intermolecular H···O distances within 2.6 Å, C−H···O angles greater than 150° and H···O═C angles in the range 90° ± 45°. Using these parameters, 12 structures (reported in the Table 1S of the Supporting Information) have been found. Among them, only two, androst-4-ene-3,17-dione (**1**) and 17α-methyltestosterone (**2**), are commercially available. Preliminary powder diffraction spectra of these substances, obtained by evaporation of $CHCl_3$ solutions, agreed with the single-crystal data reported in the literature.[11,12]

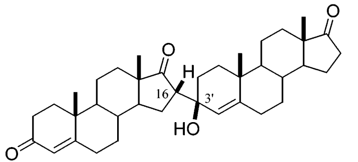


1



2

Androst-4-ene-3,17-dione (**1**) presents in the crystal[11] a short intermolecular contact between the α-oriented hydrogen at C-16 methylene carbon and the carbonyl oxygen at C-3′ of a screw-related molecule. This substance was irradiated using a UV lamp for 4 h to give dimer **3** in 29% yield together with a minor amount of trimer **4**.



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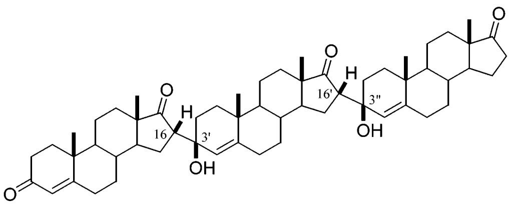

4

Structure **3** was determined on the basis of the physical features of the compound. The elemental analysis is in agreement with the molecular formula $C_{38}H_{52}O_4$; in the EIMS spectrum the ion at *m*/*z* 554, due to the loss of water, and two peaks at *m*/*z* 285 and 287, attributable to the two moieties $C_{19}H_{25}O_2$ and $C_{19}H_{27}O_2$, are present.

In the IR spectrum, besides the carbonyl absorptions at 1690 and 1746 cm^{-1}, a typical band for a hydroxyl group is present at 3550 cm^{-1}.

The ^1H NMR spectrum shows two olefinic protons as two singlets at δ 5.76 and 5.34, a methine proton as a double doublet at δ 2.75 and four methyl singlets at δ 1.19, 1.06, 0.97, and 0.88, respectively; all the other protons are in the δ range 2.5−0.8 ppm.

In the ^{13}C NMR spectrum, only 37 signals are present, being that at δ 35.6 integrated for two carbons in an inverse gate experiment. The DEPT data are consistent with the presence of 4 methyls, 15 methylenes, 9 methines, 7 quaternary carbons, and 3 carbonyl carbons.

The assignment of the carbon signals has been deduced by HMQC and HMBC experiments and comparison with the data of androst-4-ene-3,17-dione.[13] According to the given structure **3**, the proton at δ 5.34, assigned to the C-4′ carbon owing to the heterocorrelations with the C-3′, C-5′, and C-10′ carbons at δ 73.0, 148.6, and 37.4 respectively, is correlated to the C-16 carbon at δ 53.0. Furthermore the proton at δ 2.75, linked to the C-16 carbon, gives cross-peaks with the C-3′ and C-2′ carbons besides the heterocorrelations with the C-14, C-15, and C-17 carbons at δ 49.4, 25.4, and 222.7, respectively.

The *S* configuration at C-16 is attributed on the basis of the NOE interaction of the H-16 proton at δ 2.75 with the H-18 methyl at δ 0.97 whereas the *S* configuration at C-3′ is justified on the basis of the chemical shift of the H-19′ methyl protons at δ 1.06. [14]

Trimer **4** is formed by junctions between the D ring of a molecule and the A ring of a near molecule and between the D ring of this latter and the A ring of a third molecule.

The elemental analysis is consistent with the molecular formula $C_{57}H_{78}O_6$. The ^{13}C NMR spectrum shows only forty-seven signals being many signals integrated for more than one carbon in the inverse gated experiment. The signals have been attributed by HMQC and HMBC experiments and comparison with the data of **3**. In the ^1H NMR spectrum, three olefinic protons at δ 5.74, 5.37, and 5.35, six methyls at δ 1.19, 1.06, 1.05, 0.97, 0.95, and 0.89 are evident, while the remaining signals are overlapped in the δ range 2.5−0.8 ppm. As determined for **3**, also in the trimer **4** the NOE interactions of the H-16 and H-16′ protons at δ 2.78 with the H-18 and H-18′ methyls at δ 0.97 and 0.95 justify the *S* configurations at C-16 and C-16′, as well as the chemical shifts of the H-19′ and H-19″ methyls at δ 1.05 and 1.06 agree with *S* configurations at C-3′ and C-3″.

The formation of the dimer **3** can be rationalized on the basis of the crystal packing of androst-4-ene-3,17-dione.[11] In this structure, chains of molecules arrange around the screw axis parallel to the *c* direction forming head-to-tail infinite sequences (Figure 1). In each chain the shortest intermolecular contact (3.44 Å) occurs between the C-16 methylene carbon and the carbonyl oxygen at C-3′. The α−oriented hydrogen at C-16 points right toward the carbonyl oxygen O-3′ of the near molecule with the distance H···O-3′ = 2.40 Å and the angle C-16−H···O-3′ = 168°. Starting from these obser-

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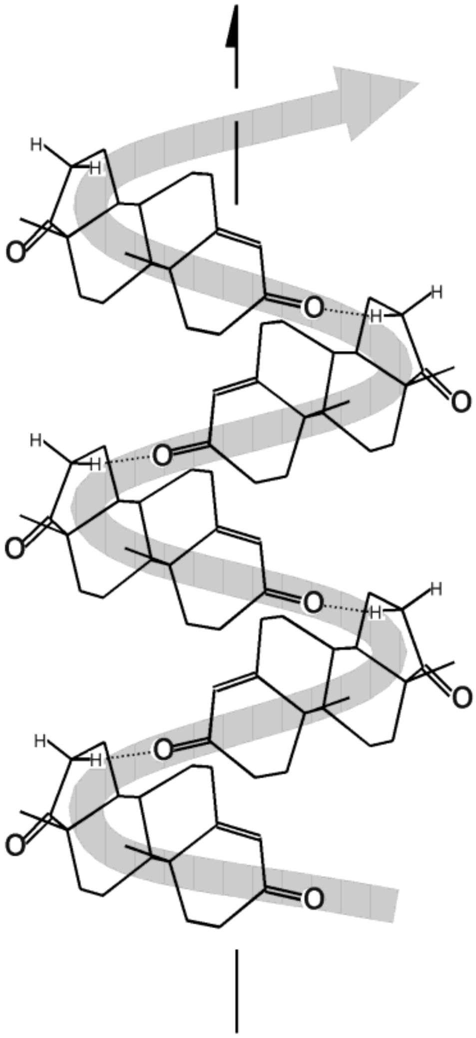

FIGURE 1. View of the crystal packing of androst-4-ene-3,17-dione (**1**). Molecules are arranged around the crystallographic screw axis forming head-to-tail chains. Dotted lines indicate the short interactions between H-16 and O-3′.

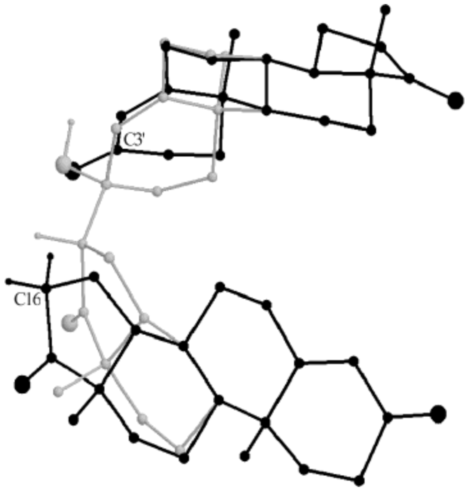

FIGURE 2. Optimized model of the dimer **3** (shaded lines) through HyperChem and MM$^+$ force field with superimposed two screw related conformers of **1** (dark lines) as they are in the crystal.

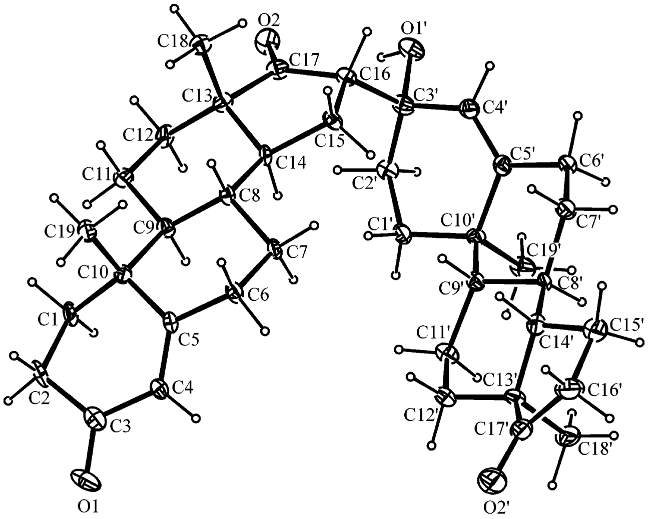

FIGURE 3. Perspective view of the dimer **3** from the single-crystal X-ray study with the labeling for non-H atoms. Displacement ellipsoids are shown at the 20% probability level.

vations, the following hypothesis is proposed. The dimerization process occurs through the transfer of the α-oriented hydrogen from C-16 of a molecule to O-3′ of the neighboring one followed by formation of a covalent bond between C-16 and C-3′. This process can propagate along the chain of molecules and thereby produce trimer **4**.

Modeling of the dimer **3** was performed by means of molecular mechanics calculations using the Allinger force field[15] and the HyperChem 4.5 program.[16] Figure 2 shows the optimized dimer with superimposed two screw related conformers of the monomer **1** as found in the crystal. Only moderate conformational changes on the monomer are required to form **3**. This explains the high yield in the dimeric product. Moreover, the involvement of the α-oriented C-16 hydrogen in this dimerization process is consistent with the S configurations both at C-16 and C-3′, as assigned on the basis of NMR experiments. The latter observation can be extended to the trimer **4**.

To achieve a definitive proof of the dimer structure and of the proposed dimerization scheme, the single-crystal X-ray analysis of the photodimerized product **3** was carried out. The final X-ray model of **3** is shown in Figure 3. The crystal study establishes that the dimerization occurs through the junction between C-16 and C-3′ carbons and confirms the overall structure given by NMR interpretation, including the relative stereochemistry at C-16 and C-3′. Moreover, it is to be noted that the conformation adopted in the crystal is very like the one resulting from the molecular mechanical optimization.

17α-Methyltestosterone (**2**) presents in the hemihydrate crystal[12] a proximity between the A rings of two neighboring molecules and the shortest contact is C-2·····O-3′ = 3.39 Å. UV irradiation of this substance gives two products identified as the trienones **5** and **6**.

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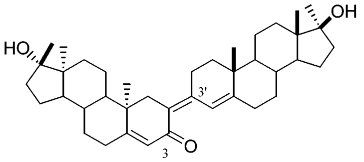
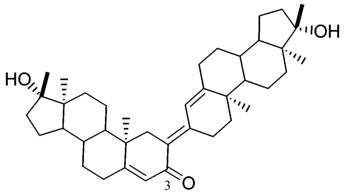


5



6

The most abundant dimer **5** has elemental analysis and ^{13}C NMR spectrum in agreement with the molecular formula $C_{40}H_{58}O_3$. The IR spectrum shows the carbonyl absorption at 1654 cm^{-1} and in the UV spectrum two bands at 342 and 244 nm are present. The ^{1}H NMR spectrum shows two olefinic protons as two singlets at δ 5.85 and 5.73, two methylene protons as doublets at δ 2.71 and 1.56, six methyls as four singlets at δ 1.23, 1.21 1.06 and 0.88, the last two integrated for six protons; all the other protons are in the 2.5−0.8 ppm range. On the basis of the ^{13}C NMR spectrum and a DEPT experiment, in the molecule are present a carbonyl carbon, six olefinic carbons, two of them protonated, in addition to six methyls, 15 methylenes, six methines and six quaternary carbons. The carbon and the proton signals have been attributed by HMQC and HMBC experiments and by comparison with the data of 17α-methyltestosterone. According to the proposed structure the H-4 at δ 5.73 as well as the H-1 protons at δ 2.71 and 1.56 are related to the C-3 carbonyl carbon at δ 199.6 and the C-2 olefinic carbon at δ 134.6. To this latter carbon is also related the H-4′ proton at δ 5.85 which, together with the H-2′ protons at δ 2.38 and 2.50, gives cross-peaks with the C-3′ carbon at δ 129.2. The stereochemistry *Z* at the double bond C-2 − C-3′ has been assigned on the basis of the NOE interaction between the H-1 proton at δ 2.71 and the H-2′ proton at δ 2.50.

The less abundant dimer **6** has physical properties similar to those of **5**. The elemental analysis and the ^{13}C NMR data agree with the same molecular formula $C_{40}H_{58}O_3$. The IR spectrum shows an absorption at 1653 cm^{-1} and the UV spectrum exhibits bands at 337 and 242 nm. In the ^{1}H NMR spectrum the H-4 and H-4′ protons were shifted at δ 5.65 and 6.08, respectively. In the HMBC spectrum the H-4 proton and the H-1 proton at δ 2.88 give cross-peaks with the C-3 carbonyl carbon at δ 199.5 and the C-2 olefinic carbon at δ 133.8; the H-4′ proton gives cross-peaks with the C-2 carbon and the C-3′ carbon at δ 129.2.

The stereochemistry E at the double bond C-2 − C-3′ has been assigned on the basis of the NOE interaction of the H-1 proton at δ 2.88 and the H-4′ proton at δ 6.08.

Trienones **5** and **6** cannot be considered the direct products of photodimerization of **2**, but their formation may be explained by a mechanism similar to that described for **1** and subsequent dehydration of the products. In the hemihydrate crystal of **2**, the α-oriented hydrogen at C-2 points toward the carbonyl oxygen O-3′ with distance 2.55 Å and angle C-2-H···O-3′ = 150° so that, after the hydrogen transfer, the connection between the C-2 and C-3′ carbons produces dimers with the S stereochemistry at C-2. Furthermore, the C-2 carbon is nearly coplanar with the neighboring enone system so that both the dimer **7**, with the S configuration at C-3′, and the dimer **8**, with the R configuration, are possible. Modeling[16] of **7** and **8** (Figure 4), starting from the crystal pattern of **2**, indicates that the formation of dimer **7** requires more moderate conformational changes in comparison with those for **8**. Therefore, the formation of **7** appears favored in the solid state because it does not significantly disturb the crystal-environment. The dehydration of **7** and/or **8** gives **5** and **6**. It is hard to establish if the dehydration occurs during the irradiation or the subsequent workup of the reaction mixture, even if an ^{1}H NMR spectrum of the crude photoirradiated product already shows the signals of the trienone **5**.

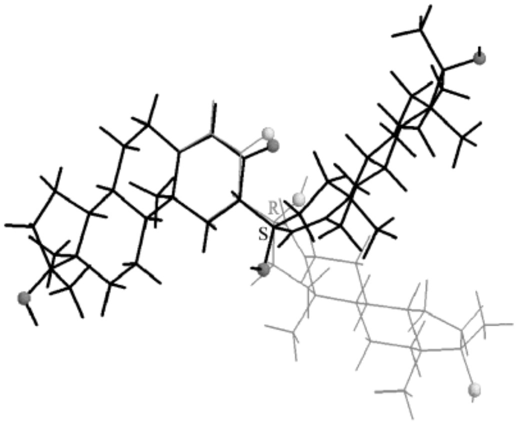
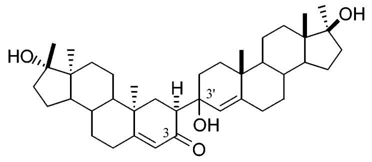


FIGURE 4. Optimized modeling by HyperChem of the two dimers **7** (dark lines) and **8** (light lines).



7 3′ (*S*)
8 3′ (*R*)

In conclusion, photodimerization processes continue to be an intriguing and open field of research and the analysis of the crystal features of the monomers is a useful approach to predict the course of dimerization.

Experimental Section

General Methods. Irradiation was performed with a 500 W high-pressure mercury lamp. The NMR spectra were recorded at 500 MHz for ^{1}H and 125 MHz in $CDCl_3$ solutions. Proton-detected heteronuclear correlations were measured using HMQC (optimized for $^{1}J_{HC}$ = 140 Hz) and HMBC (optimized for $^{1}J_{HC}$ = 7 Hz). IR spectra were determined in $CHCl_3$ solns on a FT-IR spectrometer. Analytical TLC was performed on Merck Kieselgel 60 F_{254} plates with 0.2 mm film thickness. Spots were visualized by UV light or by spraying with H_2SO_4−AcOH−H_2O (1:20:4) followed by heating for 5 min at 110 °C.

Irradiation of Androst-4-ene-3,17-dione (1). Androst-4-ene-3,17-dione (**1**) (200 mg) solidified onto the surface of a Pyrex flask from a $CHCl_3$ solution was irradiated for 4 h to give a mixture of unreacted **1** (96 mg), **3** (58 mg), and **4** (35 mg), separated by flash chromatography on silica gel ($CHCl_3$−acetone 4:1), beside not identified more polar material (10 mg). Compound **3** (purified by TLC, yield 29%) has: EIMS *m/z* 554 [M − H_2O]$^+$, 287 [$C_{19}H_{27}O_2$]$^+$, 285 [$C_{19}H_{25}O_2$]$^+$; IR ν_{max} ($CHCl_3$) 3550, 1746, 1690 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.76 (s, 1H, H-4), 5.34 (s, 1H, H-4′), 2.75 (dd, 1H, H-16), 1.19 (s, 3H, H-19), 1.06 (s, 3H, H-19′), 0.97 (s, 3H, H-18), 0.88 (s, 3H, H-18′); ^{13}C NMR ($CDCl_3$) δ 35.6 (C-1), 33.9 (C-2), 199.1 (C-3), 124.3 (C-4), 169.8 (C-5), 32.0 (C-6), 30.9 (C-7), 35.2 (C-8), 53.5 (C-9), 38.6 (C-10), 20.8 (C-11), 30.3 (C-12), 48.9 (C-13), 49.4 (C-14), 25.4 (C-15), 53.0 (C-16), 222.7 (C-17), 14.8 (C-18), 17.3 (C-19) 32.4 (C-1′), 32.8 (C-2′), 73.0 (C-3′), 124.0 (C-4′), 148.6 (C-5′), 32.2 (C-6′), 31.5 (C-7′), 35.6 (C-8′), 52.6 (C-9′), 37.4 (C-10′), 20.1 (C-11′), 30.1 (C-12′), 47.8 (C-13′), 51.3 (C-14′), 21.7 (C-15′), 35.7 (C-16′), 220.8 (C-17′), 13.8 (C-18′), 20.2 (C-19′). Anal. Calcd for $C_{38}H_{52}O_4$: C, 79.67; H, 9.16. Found: C, 79.56; H, 9.14. **4** (purified by TLC, yield 15%) has: EIMS *m/z* 571 [$C_{38}H_{51}O_4$]$^+$, 287 [$C_{19}H_{27}O_2$]$^+$, 285 [$C_{19}H_{25}O_2$]$^+$; IR ν_{max} ($CHCl_3$) 3555, 1748, 1693 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.74 (s, 1H, H-4), 5.37 (s, 1H, H-4′), 5.35 (s, 1H, H-4”), 2.78 (dd, 2H, H-16 and H-16′), 1.19 (s, 3H, H-19), 1.06 (s, 3H, H-19”), 1.05 (s, 3H, H-19′), 0.97 (s, 3H, H-18), 0.95 (s, 3H, H-18′), 0.88 (s, 3H, H-18); ^{13}C NMR ($CDCl_3$) δ 35.9 (C-1), 34.0 (C-2), 199.2 (C-3), 124.5 (C-4), 169.9 (C-5), 32.3 (C-6), 30.6 (C-7), 35.4 (C-8), 53.8 (C-9), 38.6 (C-10), 21.0 (C-11), 30.3 (C-12), 49.4 (C-13), 49.7 (C-14), 25.6 (C-15), 53.2 (C-16), 223.0 (C-17), 15.0 (C-18), 17.3 (C-19), 32.7 (C-1′), 32.3 (C-2′), 73.1 (C-3′), 124.5 (C-4′), 148.5 (C-5′), 31.7 (C-6′), 31.1 (C-7′), 35.8 (C-8′), 52.6 (C-9′), 37.6 (C-10′), 20.7 (C-11′), 30.6 (C-12′), 49.0 (C-13′), 50.1 (C-14′), 25.6 (C-15′), 53.2 (C-16′), 221.0 (C-17′), 15.2 (C-18′), 20.2 (C-19′), 32.7 (C-1″), 32.9 (C-2″), 73.1 (C-3″), 124.5 (C-4″), 148.5 (C-5″), 32.3 (C-6″), 31.4 (C-7″), 35.9 (C-8″), 52.5 (C-9″), 37.6 (C-10″), 20.3 (C-11″), 30.1 (C-12″), 48.0 (C-13″), 51.5 (C-14″), 21.9 (C-15″), 35.8 (C-16″), 221.0 (C-17″), 13.8 (C-18″), 20.3 (C-19″). Anal. Calcd for $C_{57}H_{78}O_6$: C, 79.67; H, 9.16. Found: C, 79.55; H, 9.09.

Irradiation of 17α-Methyltestosterone (2). Compound **2** (300 mg) solidified onto the surface of a Pyrex flask from a $CHCl_3$ solution was irradiated for 4 h to give a mixture of unreacted **2** (250 mg), and a mixture of **5** and **6** (25 mg), separated by flash chromatography on silica gel (hexane−acetone 4:1). TLC chromatography (benzene−acetone−hexane 7.5:1.5:1) gave pure **5** (15 mg, 5%) and **6** (5 mg, 1%). **5** has: MALDI−TOF *m/z* 586 [M]$^+$, 568 [M − H_2O]$^+$; IR ν_{max} ($CHCl_3$) 1654 cm^{-1}; UV (λ_{max}, ϵ) 342, 12 000; 244, 43 300; ^{1}H NMR ($CDCl_3$) δ 5.85 (s, 1H, H-4′), 5.73 (s, 1H, H-4), 2.71 (d, 1H, J = 9.2 Hz, H-1), 1.23 (s, 3H, H-20), 1.21 (s, 3H, H-20′), 1.06 (s, 3H, H-19), 1.06 (s, 3H, H-19′), 0.88 (s, 3H, H-18), 0.88 (s, 3H, H-18′); ^{13}C NMR ($CDCl_3$) δ 37.2 (C-1), 134.6 (C-2), 199.6 (C-3), 126.6 (C-4), 167.2 (C-5), 35.10 (C-6), 32.6 (C-7), 37.5 (C-8), 54.4 (C-9), 37.2 (C-10), 20.9 (C-11), 31.5 (C-12), 45.6 (C-13), 50.5 (C-14), 23.2 (C-15), 38.9 (C-16), 81.7 (C-17), 13.9 (C-18), 16.4 (C-19), 25.7 (C-20), 35.0 (C-1′), 25.6 (C-2′), 129.3 (C-3′), 118.6 (C-4′), 151.3 (C-5′), 33.9 (C-6′), 32.6 (C-7′), 37.5 (C-8′), 54.1 (C-9′), 40.1 (C-10′), 20.7 (C-11′), 31.3 (C-12′), 45.4 (C-13′), 50.4 (C-14′), 23.2 (C-15′), 38.9 (C-16′), 81.5 (C-17′), 13.9 (C-18′), 18.2 (C-19′), 25.8 (C-20′). Anal. Calcd for $C_{40}H_{58}O_3$: C, 81.86; H, 8.18. Found: C, 81.76; H, 8.14. **6** has: MALDI− TOF *m/z* 586 [M]$^+$, 568 [M − H_2O]$^+$; IR ν_{max} ($CHCl_3$) 1652 cm^{-1}; UV (λ_{max}, ϵ) 337, 14 000; 242, 43 600; ^{1}H NMR ($CDCl_3$) δ 6.08 (s, 1H, H-4′), 5.65 (s, 1H, H-4), 2.88 (d, 1H, J = 12.5 Hz, H-1), 1.24 (s, 3H, H-20′), 1.19 (s, 3H, H-20), 1.06 (s, 3H, H-19), 1.06 (s, 3H, H-19′), 0.90 (s, 3H, H-18), 0.89 (s, 3H, H-18′); ^{13}C NMR ($CDCl_3$) δ 37.9 (C-1), 133.8 (C-2), 199.5 (C-3), 125.4 (C-4), 167.5 (C-5), 34.3 (C-6), 33.0 (C-7), 37.9 (C-8), 54.2 (C-9), 40.0(C-10), 20.9 (C-11), 31.5 (C-12), 45.6 (C-13), 50.5 (C-14), 23.3 (C-15), 38.9 (C-16), 81.7 (C-17), 13.9 (C-18), 16.4 (C-19), 25.7 (C-20), 35.0 (C-1′), 25.6 (C-2′), 129.3 (C-3′), 118.6 (C-4′), 151.3 (C-5′), 33.7 (C-6′), 32.6 (C-7′), 37.0 (C-8′), 54.2 (C-9′), 36.6 (C-10′), 20.9 (C-11′), 31.5 (C-12′), 45.4 (C-13′), 50.5 (C-14′), 23.3 (C-15′), 38.9 (C-16′), 81.7 (C-17′), 14.0 (C-18′), 18.1 (C-19′), 25.7 (C-20′). Anal. Calcd for $C_{40}H_{58}O_3$: C, 81.86; H, 8.18. Found: C, 81.92; H, 8.34.

Crystal Data and Structure Refinement of 3. Small single crystals were obtained by slow evaporation from an ethanol-ethyl ether solution (5:1) of the photodimerized product **3**. A sample of size 0.14 × 0.10 × 0.04 mm was used for the crystallographic study. Accurate cell parameters were obtained by least-squares refinement of the setting angles of 25 reflections in the θ range 22° < θ < 26° using the Cu Kα graphite-monochromated radiation and an Enraf-Nonius CAD-4F diffractometer.[17] All the diffraction measurements were performed at room temperature (293 K). Crystal data: $C_{38}H_{52}O_4$, M_w = 572.84, monoclinic system, space group $P2_1$, Z = 2, cell constants: a = 7.968(2) Å, b = 12.110(2) Å, c = 16.546(2) Å, β = 94.50(7)°, V = 1591.7(8) Å^3, D_c = 1.195 g cm^{-3}.

3321 Independent reflections (θ_{max} = 73°) were collected in the $\omega - 2\theta$ scan mode, as suggested by peak-shape analysis. The crystal and equipment stability was checked by the intensities of four standard reflections monitored every 3 h. No significant intensity decay was observed.

The structure was solved by direct methods using SIR92 package.[18] The refinement (on F) was carried out by full-matrix least-squares method on the positional and anisotropic temperature parameters of non-hydrogen atoms. At convergence, hydrogens were positioned (distances Csp^3−H = 1.02 Å, Csp^2−H = 0.98 Å, O−H = 0.95 Å) on the basis of geometrical considerations taking in account, for methyls and hydroxyl groups, the indications of difference Fourier map. All the hydrogens were included in the last refinement, as fixed atoms with B_{iso} values set equal to B_{eq} of the respective parent atom. The final discrepancy R factor was 0.063 for the 1900 observed reflections with $I > 1\sigma(I)$ and 378 variables. R_w = 0.064, $w = 1/[\sigma^2(F_o) + (0.02F_o) + 0.1]$.[19] S = 1.09, residual electron densities within the range −0.26 and 0.18 e Å^{-3}. All calculations were performed on a MicroVAX 3100 computer using Enraf-Nonius SDP software.[20]

The final parameters for non-hydrogen atoms are given in Table 2S that, together with anisotropic displacement parameters, calculated hydrogen parameters and molecular geometry, has been deposited as Supporting Information.

Acknowledgment. NMR experiments were performed on a 500 MHz spectrometer of Consortium INCA (L488/92, Cluster 11A). X-ray experiments were performed by the equipments of the “Centro Interdipartimentale di Metodologie Chimico-fisiche” of the University Federico II (Naples).

Supporting Information Available: Structures of the steroid enones from the search in the Cambridge Structural Database. Crystallographic data of compound **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0204808

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