# PHOTOACTIVATION OF DISTAL CARBONYL GROUPS IN STEROIDAL KETONES: INTRAMOLECULAR ENERGY TRANSFER CONTROL OF MULTIPLICITY
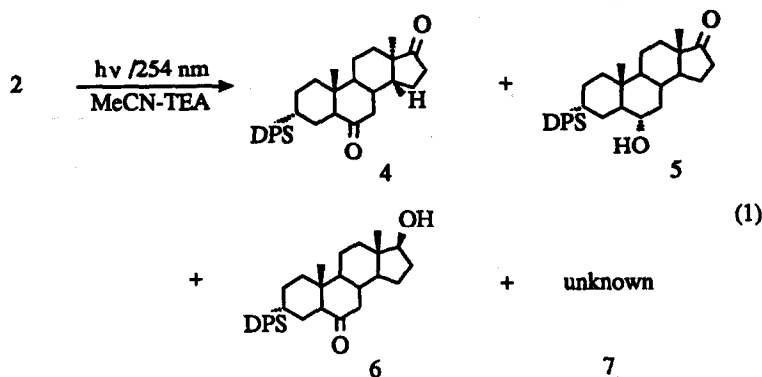
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Abstract : *Photolysis of 3α-dimethylphenylsiloxy-5α-androstane-6,17-dione in acetonitrile in the presence of triethylamine with 254 nm light initiates photoreduction and photoepimerization of the 6-keto and 17-keto functionalities, respectively. A two-step intramolecular singlet-singlet energy transfer mechanism is proposed to explain the photoepimerization.*

We have recently reported that 3α-dimethylphenylsiloxy-5α-androstane-11,17-dione[1] (1) undergoes intramolecular singlet-singlet energy transfer [2-4] (intra-SSET) from the "antenna" dimethylphenylsiloxy (DPS) group to the 11-keto group, which is followed by intramolecular triplet-triplet energy transfer to the 17-keto group. The result is a site-specific photoreduction of the ketone more distal to the antenna, the 11-keto group acting as a "singlet-triplet switch". We now describe the photophysics and 254 nm initiated photochemistry of 3α-dimethylphenylsiloxy-5α-androstane-6,17-dione (2), wherein the distal 17-keto functionality is photoepimerized and the proximal 6-keto group is photoreduced upon excitation of the antenna. Evidence presented below indicates that, in this case, the photochemistry of the 17-keto group is attributable to intra-SSET between the 6- and 17-keto functionalities, with the presence of the 6-keto group dramatically enhancing the efficiency of DPS sensitized photoepimerization by comparison with, e.g. the steroidal monoketone, 3α-dimethylphenylsiloxy-5α-androstan-17-one (3).
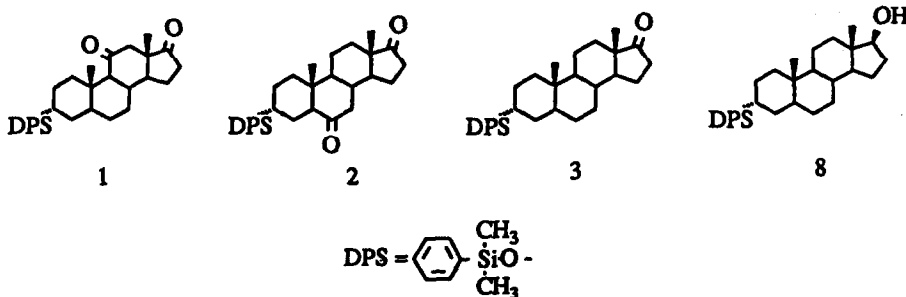
The dione 2 was readily prepared by silylation of the parent steroidal alcohol and has been fully characterized by NMR and IR spectroscopy, mass spectrometry and elemental analysis. Photolysis of 2 (14.3 mM) in acetonitrile with triethylamine (TEA, 64.8 mM) in a Rayonet reactor (New England Ultraviolet Co.) with 4 254-nm lamps for 75 min at r.t. gave the epimer 4, mono-reduced products 5 and 6, and an as yet uncharacterized product, 7, in a ratio of 4:5:6:7 = 11.9:6.0:1.1:1.0 by GC analysis (cf. eq. (1)). The structures of the products were confirmed by IR, NMR and mass spectral data.

$$2 \xrightarrow[\text{MeCN-TEA}]{h\nu \,/254 \text{ nm}} \quad \textbf{4} \quad + \quad \textbf{5} \quad (1)$$

$$+ \quad \textbf{6} \quad + \quad \text{unknown} \quad \textbf{7}$$

The photoreduction at both C-6 and C-17 can be completely quenched by cis-piperylene (40 mM). The quantum efficiencies for photoreduction at the C-6 (ϕ^6_{red}) were measured as a function of [TEA] (32.4-92.9 mM) at [2] = 13.7 mM, using a Nd:YAG laser at 266 nm. As had been observed for reduction of C-17 in the steroidal dione 1, a plot of $1/\phi^6_{red}$ vs $1/[\text{TEA}]$ is linear (slope = 1.11 and intercept = 1.03), indicative of one (e.g. triplet) excited state precursor. This is consistent with the fact that the photoreduction of cyclohexanones is generally triplet-derived.[1,2,5] By contrast, the photoepimerization at C-17 is only partially (38%) quenched by the diene and is much less responsive to the [TEA] (also to be expected, since the α-cleavage of cyclohexanones is known to be appreciably singlet derived).[1,6] However, the most striking difference between 1 and 2 is in the relative *efficiencies* of the **photoepimerization and photoreduction reactions.** For 2, reduction of C-17 is minimal and epimerization at this site is even 3.9-fold more efficient than reduction at C-6 (with [TEA] = 60 mM: ϕ_{epi} = 0.18, ϕ^6_{red} = 0.046; see Table 1). In 1, reduction (at C-17; C-11 is virtually inert) generally exceeds epimerization, with the latter process having all but disappeared at 60 mM [TEA]. **Clearly, the photochemical behavior of the 17-keto group functions as a probe of its multiplicity and one must conclude that compound 2 is reacting at C-17 primarily through its singlet state, whereas the chemistry at this ketone in compound 1 derives from the triplet manifold.**

Significantly, at a [TEA] = 60 mM ϕ_{epi} (0.18) for 2 is 5.3-fold greater than that (0.034) for the monoketone 3. This indicates that sensitization by the antenna is occuring via a two step intra-SSET, in which the 6-keto chromophore effectively relays singlet energy from the DPS antenna to the 17-keto group. The 17-keto singlet state in 2 is therefore more efficiently populated than is the case in 3, which must rely on a more long-range direct intra-SSET. Alternative modes of excitation at C-17 in 2 and 3 can be readily excluded. The lack of quenching by cyclohexanone of the photoreduction of 3 eliminates intermolecular singlet-singlet energy transfer.[1] Co-excitation of the 17-keto chromophore at 266 nm would not be expected in the presence of the antenna since ϵ_{266} for cyclopentanone is 13.5-fold lower than that for the DPS group. The overall mechanism is presented in Scheme 1.

Table 1. Emission and Photochemical Quantum Efficiencies and Singlet Lifetimes in Acetonitrile

Steroid	ϕ_f^a	τ_f^b (ns)	$\phi_{intraSSET}^c$	ϕ_{epi}^d (17-C=O)	ϕ_{red}^d (17-C=O)	ϕ_{red}^d (6-C=O)
1	0.0017	0.27	0.78	0	0.023	–
2	0.00063	<0.25	0.88	0.18	–	0.046
3	0.0047	0.95	0.21	0.034	0.010	–
8	0.0053	1.20	–	–	–	–

a. Excitation at 254 nm with using toluene in cyclohexane as a reference.

b. Using a PTI LS-1 lifetime fluorimeter with excitation at 266 nm and emission at 288 nm. c. This can be derived from either τ_f or ϕ_f data. For compounds 1 and 3, $\phi_{intra-SSET} = (\tau_f^8 - \tau_f^n)/\tau_f^8$, where n represents one of the DPS steroidal ketones, and 8 (3α-dimethylphenylsiloxy-5α-androstan-17β-ol) functions as a reference; because of the short lifetime of 2, $\phi_{intra-SSET}$ was calculated from $\phi_{intra-SSET} = (\phi_f^8 - \phi_f^n)/\phi_f^8$. The lifetime indicated by such a value would be about 0.15 ns. d. The quantum efficiencies were measured using 266-nm laser light at [steroid] = 15 mM and [TEA] = 60 mM.

Scheme 1
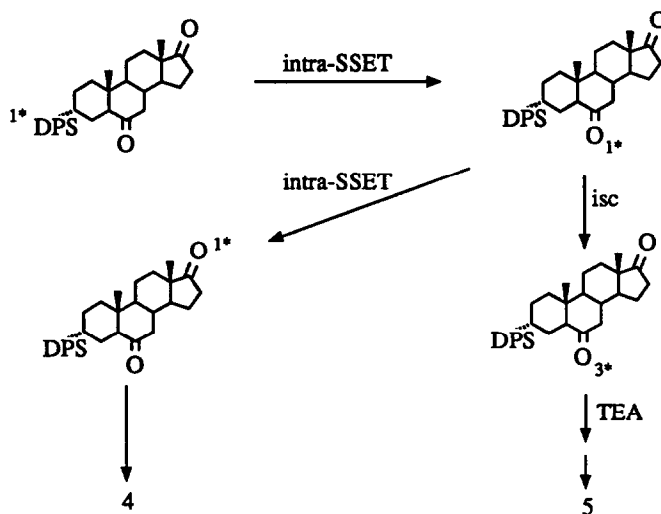
The proposal of a two-step intra-SSET in 2 is supported by a comparison of this compound's fluorescence efficiency (ϕ_f) and singlet lifetime (τ_f) with respect to the monoketone, 3, and the steroidal alcohol, 8 (Table 1). One notes that both ϕ_f and τ_f for 2 are greatly reduced relative to 8, the consequence of intra-SSET in the dione. The efficiencies of intra-SSET ($\phi_{intra-SSET}$) can be calculated from the τ_f and/or ϕ_f values (see Table 1) wherein one observes that energy transfer for 2 (88%)[7] is appreciably more efficient than in the mono-ketone, 3 (21%).

A comparison of the photophysics and photochemistry of compounds 1 and 2 reveals a striking example of intra-SSET control of excited state multiplicity in the distal functionality. In 1, intra-SSET is inefficient so that energy is transferred to the 17-keto group through triplet energy transfer (the 11-keto group acts as a S_1-T_1 switch; photoreduction dominates). In 2, intra-SSET between the 6 and 17 positions is efficient and leads to photoepimerization. The different properties of these substrates are not explicable through a consideration of interchromophore distances, since the two keto groups are clearly closer in 1 than in 2 (3.9 Å and 6.2 Å for 1 and 2, respectively, by x-ray crystallographic analysis of 3β-dimethylphenylsiloxy-androstane-17-one). It seems likely that intra-SSET involves "through-bond" interactions within the rigid steroidal skeleton[8] and further studies to test this possibility are in progress.

References and Notes

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7. Calculated with the assumption that direct intra-SSET from the DPS to the 17-keto group is minimal.
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