

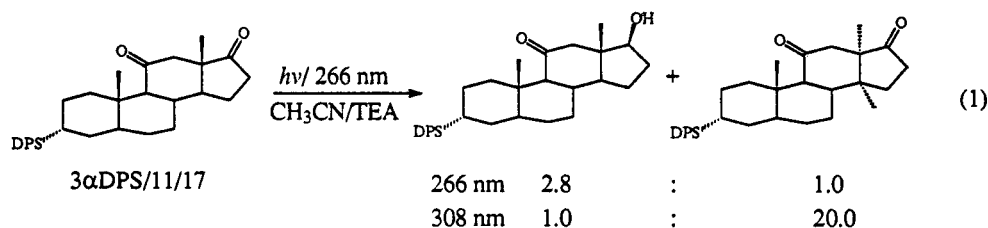
Photochemical activation of distal chromophores by antenna substituents in polyfunctional molecules

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Abstract. Steroids have been prepared which bear a dimethylphenylsiloxy (DPS) group and additional ketone or olefin functionalities. The DPS group has been used to harvest photons in order to direct the excitation energy to the remote target acceptor groups. Examples of intramolecular singlet-singlet and triplet-triplet energy transfer are described, with the DPS group placed at C3, C6 or C17. An earlier example of the role of an 11-keto group in acting as a "singlet/triplet switch" has been extended to activation of an ethylidene group at C17.

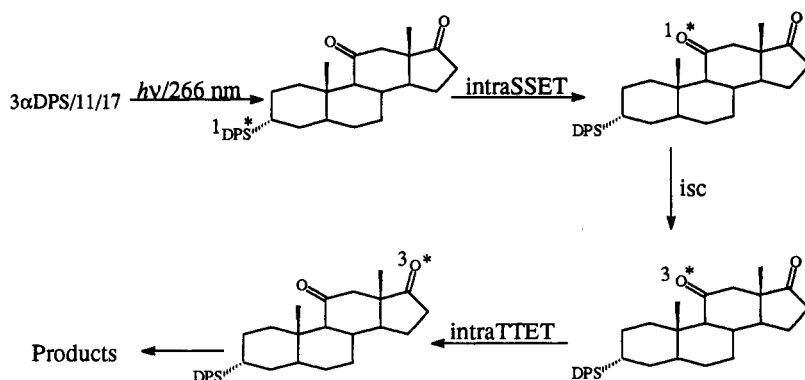
A long term objective of our program has been to explore the use of "antenna" chromophores to harvest photons and thence efficiently and selectively activate a distal functionality in complex organic substrates. The prototype systems we have employed have utilized steroids as frameworks, upon which have been "mounted" the antenna and target (ketone) groups. The dimethylphenylsiloxy (DPS) chromophore has served as the "antenna" because it provides the requisite properties we have outlined (1) for such antennas, i.e. it is readily attached and detached from (alcohol) substrates; is highly absorbent at a wavelength of light (266 nm) not appreciably absorbed by the (ketone) target; is capable of efficient, exothermic intramolecular singlet and triplet energy transfer to the target by the exchange mechanism (the latter feature facilitating selectivity of energy transfer to one of several targets) and has a short (ca. 1 nsec) singlet lifetime (thus inhibiting secondary and intermolecular singlet sensitization processes).(2) We have found it useful to code the steroids used in these studies in order to easily represent the relative distances between the antenna "donor" and the nearest acceptor, and between the two acceptors. For example, 3 α -dimethylphenylsiloxy-5 α -androstandione is abbreviated as 3DPS/11/17 (see below) and coded as D---A₁--A₂.

Our recently published studies have involved the activation of a C17 ketone by initial excitation of a C3 DPS group, employing a second carbonyl functionality at two intermediate sites, C11 (3) and C6.(4) The C-17 ketone functionality turns out to be an excellent "reporter" of excited state multiplicity because its singlet state efficiently undergoes Norrish Type I cleavage, with minimal competitive intersystem crossing, and its triplet is readily reduced. The basic chemistry for the 11/17 system is given in equation 1, where one observes that excitation of the DPS group in 3 α DPS/11/17, using the 266 nm line of a Nd/YAG laser, affords C17 chemistry with a product mix markedly different from that observed when the ketones are directly excited with the 308 nm line of a XeCl excimer laser.



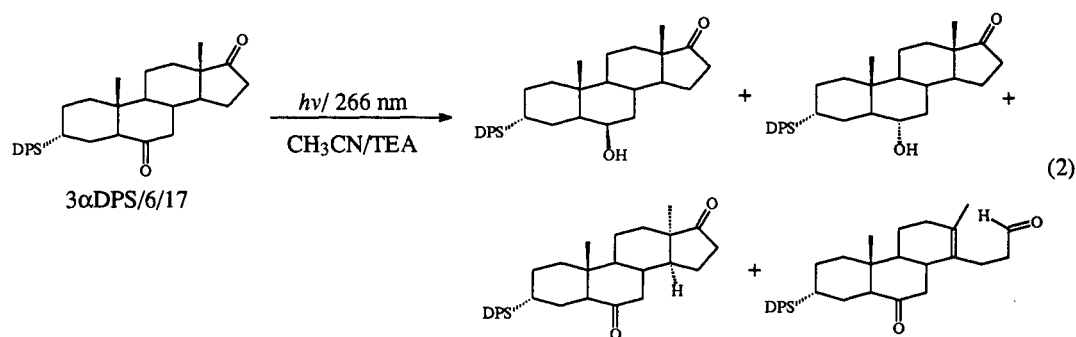
Quenching studies confirm that the reduction by triethylamine (TEA) is triplet derived, while the 308 nm initiated epimerization is singlet derived. Fluorescence spectroscopy indicates rapid ($k_{\text{intraSSET}}$ ca. 3×10^9

sec^{-1}) and efficient ($\phi_{\text{intraSSET}}$ ca. 70-80%) intramolecular singlet-singlet energy transfer (intraSSET) from C3 to C11. Slower ($k_{\text{intraSSET}}$ ca. $2 \times 10^8 \text{ sec}^{-1}$) and less efficient (ca. 20%) singlet energy transfer occurs from C3 to C17. The principal consequence of intraSSET from C3 to C11 is the formation of C17 triplets, via intersystem crossing at C11 and triplet energy hopping from C11 to C17 (the ketone at C11 thus operating as a "singlet \rightarrow triplet switch"; see Scheme 1). Evidence has been presented for intraSSET via a through-bond mediated process (TBI). In addition, there is intraTTET from C3 to C17, also proposed to occur by a TBI, exchange mechanism.



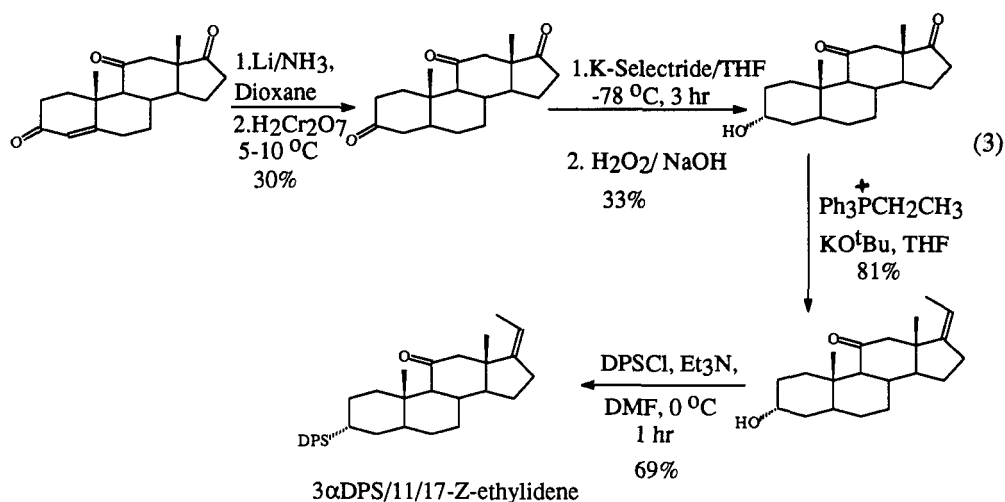
Scheme 1

The photochemistry of $3\alpha\text{DPS}/6/17$ (a D--A₁---A₂ system) is markedly different (equation 2). Here we observe that intraSSET from the DPS group to C6 is also rapid ($k_{\text{intraSSET}}$ = ca. $3 \times 10^9 \text{ sec}^{-1}$) and efficient ($\phi_{\text{intraSSET}}$ ca. 76%), but this energy transfer is followed by a ca. 85% efficient intraSSET from C6 to C17. The result is that the chemistry observed at C17 is now exclusively singlet derived epimerization. IntraSSET from DPS to C6 is more than 2 fold less efficient for the 3β isomer. There is also a modest amount of triplet derived reduction at C6 (ϕ_{red} = 0.046 at 60 Mm TEA)) with a 3α DPS antenna, but no such reduction is observed when the DPS group is β . TBI exchange energy transfer is proposed for both the DPS \rightarrow C6 and the C6 \rightarrow C17 intraSSET.

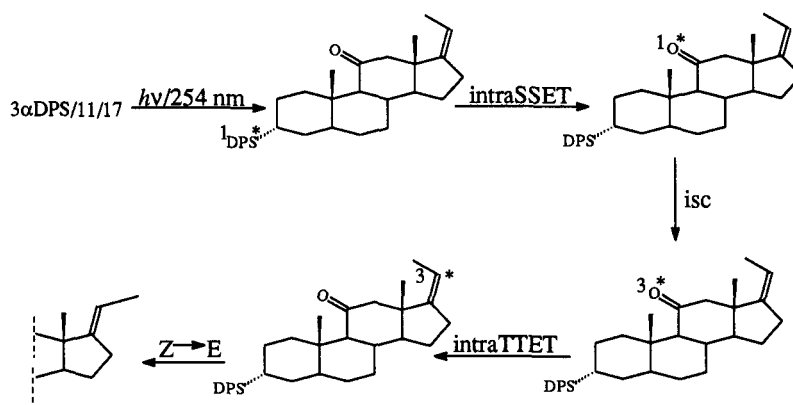


These observations are particularly interesting because of the general search for *chemical* consequences of through-space (TS) and through-bond (TB) M.O. interactions.(5) Examples from ground-state chemistry are limited,(6) and are even more sparse in the area of excited state chemistry,(7) though both phenomena are well documented by photophysical studies in the excited state.(8)

The singlet \rightarrow triplet conversion proposed in Scheme 1 has been tested using 3α -(dimethylphenylsiloxy)-5 α -androstane-17-(Z)-ethylidene ($3\alpha\text{DPS}/11/17$ -Z-ethylidene)(see equation 3). In this molecule, the ultimate olefin acceptor can only be activated by intraTTET. A comparison of the effectiveness of activation relative to a molecule lacking the C11 ketone (i.e. $3\alpha\text{DPS}/17$ -Z-ethylidene) has confirmed the role of the C11 functionality as a singlet \rightarrow triplet switch.



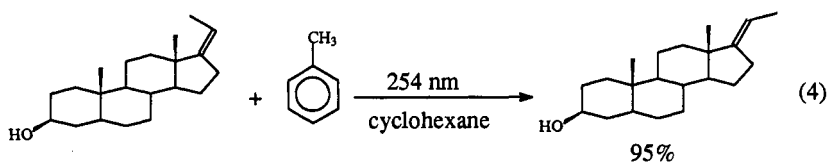
As expected, 3 α DPS/17-Z-ethylidene shows strong DPS fluorescence with a ϕ_f of 0.013, comparable to the value of 0.0053 previously observed for the corresponding 17-alcohol.(3) The presence of the carbonyl group in 3 α DPS/11/17-Z-ethylidene reduces ϕ_f to 0.0024. The singlet lifetimes for the two compounds are 2.63 nsec and 549 psec respectively. Thus, there is ca. 80% efficient intraSSET from the DPS group to the ketone (values of 68-78% were estimated for this efficiency in the 3 α DPS/11/17-alcohol (3)). Excitation of 3 α DPS/17-Z-ethylidene with 254 nm light results in Z - E isomerization of the olefin; concomitant excitation of 3 α DPS/11/17-Z-ethylidene also results in Z - E isomerization of the olefin, but with an efficiency slightly greater than that for the compound lacking the carbonyl group ($\phi_{Z \rightarrow E} = 0.087$ and 0.079, respectively). Clearly, with ca. 80% of the DPS singlets diverted to the 11-keto group, the only way intramolecularly sensitized olefin triplet isomerization can be occurring in these two substrates at a comparable efficiency is if a significant fraction of the keto singlets are being "switched" to keto triplets and then transferred to the alkene (control studies confirm that energy transfer from the DPS to the 11-keto or 17 ethylidene groups is strictly intramolecular)(Scheme 2).



Scheme 2

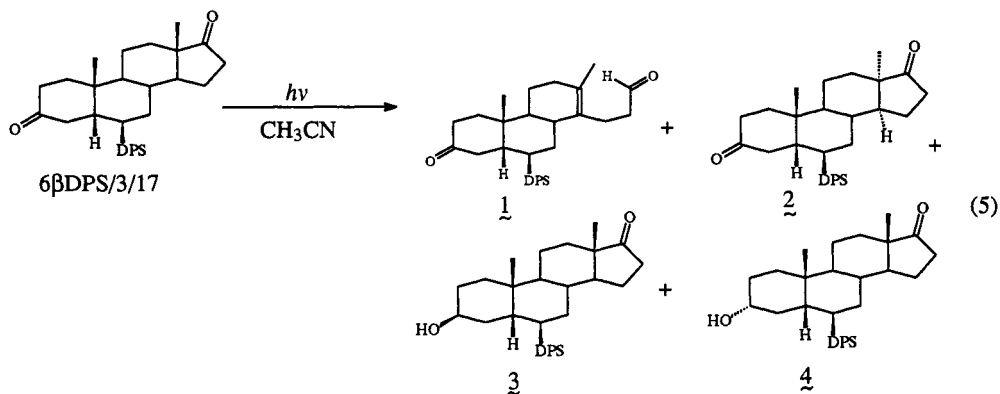
One of the more novel observations resulting from these studies is the apparent, virtually one-way photosensitized isomerization of the 17 ethylidene group. When 3 β -hydroxy-5 α -androstane-17-(Z)-ethylidene was irradiated with toluene as a sensitizer, a final product mixture consisting of 95% of the (E)-ethylidene

product was formed (equation 4). Though the photostationary state for the internally sensitized reaction has



not yet been determined, preliminary data suggest that this observation will be unique to external sensitization. We currently attribute the phenomenon to steric inhibition of the approach of the sensitizer to the more encumbered *Z* isomer. Finally, consistent with the above chemistry deriving from the olefin triplet state, we find that the direct irradiation of 3β-hydroxy-5α-androstan-17-(*Z*)-ethylidene leads to a product (in addition to *Z*-*E* isomerization) not observed under intra- or intermolecular sensitization conditions. When isolated and identified we expect this product will be a singlet derived 1,3 H shift isomer of the starting material.(9)

As noted earlier, the 3DPS/11/17 and 3DPS/6/17 compounds provided D---A₁--A₂ and D--A₁----A₂ models, respectively. We have extended these studies to the A₁--D----A₂ system by preparing 6β-(dimethylphenylsiloxy)-5β-androstan-3,17-dione (6βDPS/3/17). Photolysis of the antenna in this compound with 266 nm laser light results in the formation of two primary photoproducts (equation 5). These have been identified as the aldehyde, 6β-(DPS)-3-oxo-13,17-seco-5β-androst-13-en-17-al (**1**) and the epimer 6β-(DPS)-5β,13α-androstan-3,17-dione (**2**), both generated from α cleavage of C17 in ring D. In addition, an isomeric mixture of the alcohols, 6β-(DPS)-3β-hydroxy-5β-androstan-17-one (**3**), and its 3α isomer (**4**) was also detected. The structural identification of the products is based on ¹H and ¹³C NMR and mass spectral data.

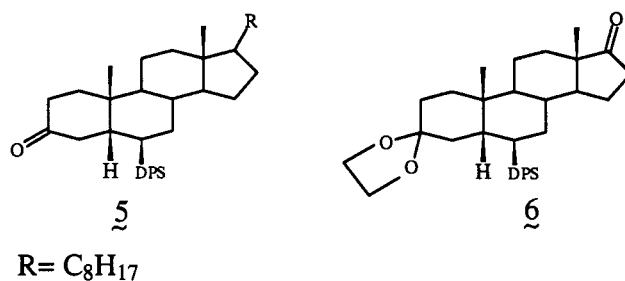


266 nm 1:2:(3+4) = 1:2.5:0.2
 308 nm 1:2:(3+4) = 1:2.3:0.3

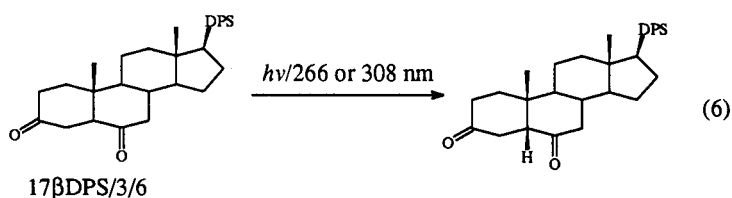
Noteworthy for **1** are the characteristic 17-CH=O and allylic CH₃ resonances at δ 9.70(s) and 1.65(s), respectively, and ¹³C resonances at δ 212 and 202 ppm corresponding to the 3 C=O and the 17-CH=O functionalities, respectively (the 17-C=O resonance, appearing at δ 221 in the starting material, is absent). The presence of both the 3- and 17-keto groups in **2** is evidenced by the ¹³C resonances at δ 212 and 222, respectively. However, the 19-CH₃ group resonance appears at δ 1.04 ppm, markedly upfield shift relative to the resonance at δ 1.24 ppm in the starting material. This change is characteristic of the conversion to a *cis* fusion of rings C and D.(3,4) Though the isomeric alcohols could not be separated, the ¹³C resonances at δ 71.3 (β) and 72.1 (α) ppm are consistent with a mixture of C3 alcohols (C17 alcohol resonances are typically at δ 80-85 ppm) with the characteristic resonance for the 17-C cyclopentanone still found at δ 222.4 ppm.

The fact that the photochemistry at C17 is unquenchable by *cis*-piperylene confirms that this photochemistry is singlet derived, independent of whether activation is through the antenna or by direct excitation of the carbonyl chromophores. Consistent with this is the observation that the addition of TEA, an excellent triplet reductant, has virtually no effect on the photochemistry. Therefore, the 6 β DPS/3/17 system closely approximates what was observed for the 3DPS/6/17 series in that intraSSET to C17 is an ultimate consequence of DPS excitation. There is thus the expected dual fluorescence for 6 β DPS/3/17 when excited with 254 nm light. From the reduced aryl fluorescence ($\phi_f = 1.1 \times 10^{-3}$) relative to that ($\phi_f = 5.3 \times 10^{-3}$) for the simple DPS substituted steroid, 3 β -DPS-5 α -androstane-17 β -ol, one can calculate an efficiency of intraSSET to one or the other of the carbonyl groups of ca. 79%. One can't say from these data how much of this energy ends up localized at C17 but the photochemical quantum efficiencies are informative in this respect. Direct photolysis of the ketone chromophores with 308-nm light from a YAG/dye laser gives the same products, and in a virtually identical ratio, to that observed with antenna excitation (cf. eq. 6). However, 308 nm excitation is clearly more efficient, e.g. at 266, ϕ_1 and $\phi_2 = 2.0 \times 10^{-2}$ and 7.0×10^{-2} ; at 308, these values are 4.4×10^{-2} and 13×10^{-2} . It thus appears that antenna excitation gives C17 excited singlet states with ca. 50% of the efficiency of direct carbonyl excitation.

One can rationalize the substantial reduction in fluorescence, and lower quantum efficiencies at 266 vs 308 nm, by proposing that intraSSET proceeds initially from the DPS to the more proximate C3 carbonyl group. Energy loss might then occur in the transmission of excitation from C3 to C17 (note that some chemistry is observed at C3). However, the 6 β DPS/3 and 6 β DPS/17 analogs (**5** and **6**) have been prepared and both also show carbonyl photochemistry upon excitation into the antenna. The C17 monoketone gives the expected epimer and aldehyde α cleavage products with quantum efficiencies comparable to that for 6 β DPS/3/17. Furthermore, the aryl fluorescence of 6 β DPS/17 ($\phi_f = 1.1 \times 10^{-3}$) is reduced to the same extent as that for the diketone. There is thus relatively efficient "communication" between the 6DPS group and the C17 ketone, much as has been previously noted between the C6 and C17 ketones, and it is unclear how important the C3 ketone is in energy transmission to C17. The C3 monoketone has been photolyzed in cyclohexane and found to give a mixture of C3 alcohols.



A_1 in the 3DPS/11/17 system is sterically shielded by an angular methyl group at C18 and is notoriously unreactive. The 17DPS/3/6 series also represents a D--- A_1 -- A_2 system but with a reactive A_1 acceptor which could affect the nature of the A_1/A_2 interaction. Towards these ends we have prepared 17 β -DPS-5 α -androstane-3,6-dione (17 β DPS/3/6) and studied its excited state properties. Photolysis with 266 nm laser light in acetonitrile gives the epimerization product at C5, i.e., 17 β -DPS-5 β -androstane-3,6-dione, as the major product. Enals are also formed in minor amounts as evidenced by their characteristic resonances in nmr spectra of the reaction mixture. The same product is formed with 308 nm light, cf. equation 6.



The first hint that 17 β DPS/3/6 is unusual came from its fluorescence spectrum in acetonitrile which shows little ketone fluorescence and appreciable aryl emission. Likewise the singlet lifetime for this molecule was found to be comparable to a model 17DPS system lacking the ketones. These data suggest that the DPS group and the 3/6 diketone are not communicating through normal intraSSET. Further evidence for this comes from the photochemical reaction quantum efficiencies which are 0.057 and 0.032 for the 266 nm and 308 nm irradiation, respectively, i.e. antenna excitation is more efficient than direct irradiation of the ketones! When *cis*-piperylene was employed to probe multiplicity a virtually flat ($k_q\tau = 3.8$) line was found for the 266 nm photolysis whereas a steep ($k_q\tau = 525$) and curved (fraction of triplet = 89%) quenching plot was obtained with 308 nm light. The same phenomenon is observed in cyclohexane and a similar wavelength effect is seen in the monoketone series, 17 β DPS/3. These data are totally different from any seen in the 3 or 6 DPS substituted series and are still under investigation.

Acknowledgments. We are grateful to Dr. Alex Siemiarczuk, Photon Technology Inc. for measuring the singlet lifetimes of 3 α DPS/17-Z-ethylidene and 3 α DPS/11/17-Z-ethylidene. This research has been funded by the National Science Foundation, Grant CHE-9311828.

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