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Long-Range Through-Bond Photoactivated σ Bond Cleavage in Steroids. Intramolecular Sensitized Debromination[1]

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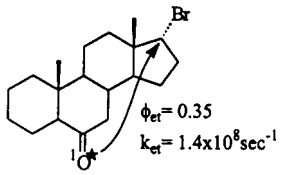
ABSTRACT



The photolysis of 17α-bromo-3α-(triphenylsilyloxy)-5α-androstane (2; 3αTPSO/17αBr) and 17α-bromo-3α-(triphenylsilyloxy)-5α-androstan-6-one (3; 3αTPSO/6ketone/17αBr) is described. Irradiation of 2 with 266 nm light leads to debromination via intramolecular transfer of triplet excitation energy with a quantum efficiency of 0.0011. Photolysis of 3 with both 266 and 308 nm light leads to debromination with quantum efficiencies of ca. 0.0066. The debromination of 3 is attributed to activation via the ketone excited singlet state, with singlet energy transfer from C6 to C17 ca. 35% efficient and occurring with a rate constant of 1.4 × 10^8 s^{-1}.

Recently, there have been a number of reports that confirm the capability of the steroid skeleton to function as a "photonic wire", thereby facilitating relatively long-range through-bond intramolecular energy transfer.[2−6] In our own studies, we have employed photochemically active moieties as the terminal excited-state energy acceptors, with π systems (e.g., ketones and alkenes) filling this role. However, there has also been extensive interest in the photochemical activation of carbon−halogen bonds through interaction with distal chromophores in rigid systems. These include chloronorbornenes (and analogues thereof)[7] and chlorobenzobicyclics.[8−12] We now report that the steroid framework will also facilitate distal cleavage of a σ, i.e., C−Br, bond. It should be noted that the *inter*molecular sensitization of carbon−halogen cleavage is well known. Though it is typically initiated through electron-transfer chemistry, sen-

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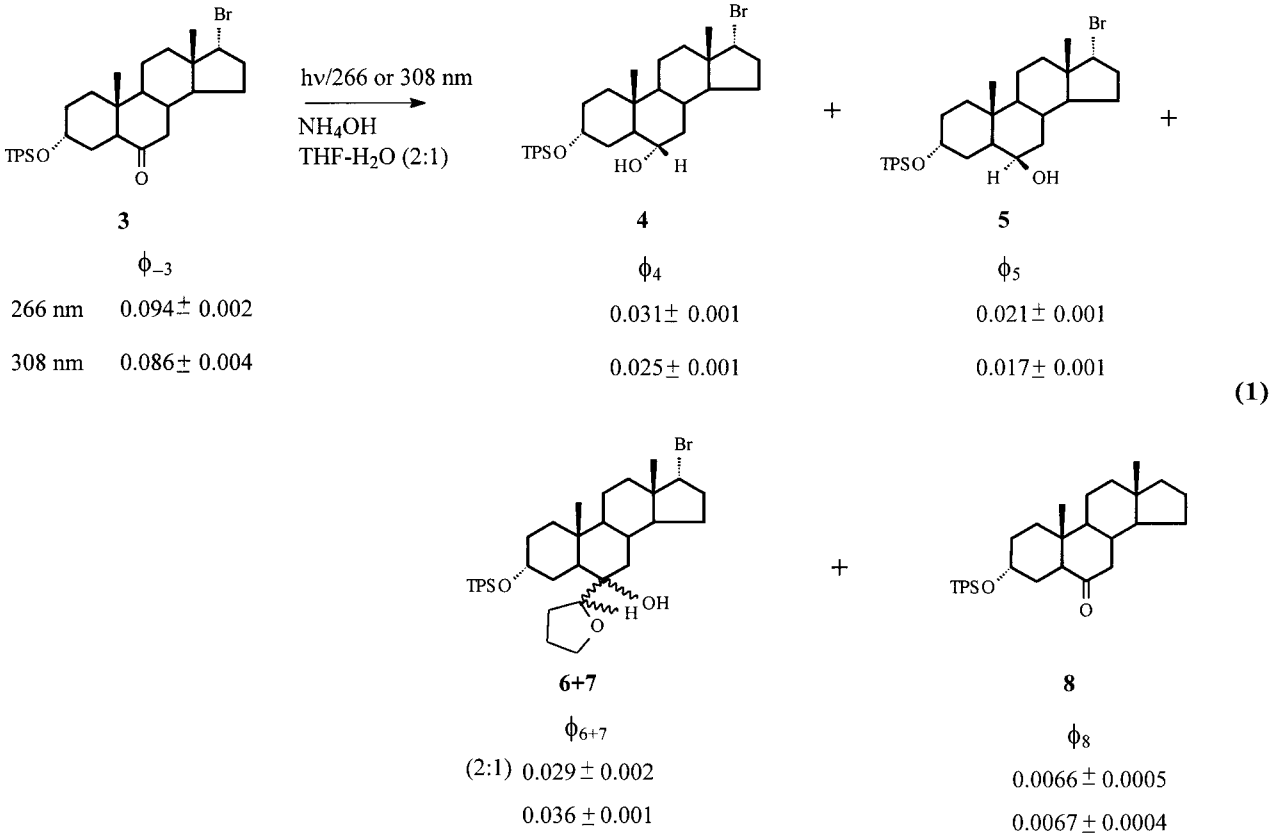

(1)

sitization by energy transfer from both aromatic and ketone donors has been reported.[13−16]

Our initial efforts focused on 17α-bromo-3α-(triphenylsilyloxy)-5α-androstane (**2**, 3αTPSO/17αBr). We reported earlier that a donor (dimethylphenylsiloxy; DPSO) group at C3 can transfer both singlet[2a−c] and triplet[1,2d,f] energy to acceptors at C17. The latter, in particular, requires the exchange mechanism which, with the rates observed at the ca. 13 Å separation of the C3 and C17, necessitates that through-bond interaction (TBI) facilitated transfer be operative.[1] The DPSO group, chosen as the antenna in the earlier work because of its favorable properties,[17] was, in this study, replaced by the TPSO group because of its diminished sensitivity to acid.[18,20,21]

Irradiation of **2** (6 mM) at 266 nm[22] in the presence of NH_4OH (12 mM; to serve as an HBr scavanger) in degassed THF−H_2O (2:1) gave a product mixture consisting of a small amount of the debromination product **1** (3α-(triphenylsilyloxy)-5α-androstane)[23] admixed with uncharacterized isomers of **2** involving transformations of the TPSO group. The quantum efficiency for formation of **1** was determined to be 0.0011 while that for disappearance of the starting material was 0.064. That debromination was induced by intramolecular triplet sensitization was confirmed by the photolysis of **2** (6 mM) in the presence of 6 mM 3α-hydroxy-5α-androstan-17α-bromide (3αOH/17αBr) and, in a second experiment, in the presence and absence of 1.2 mM *cis*-piperylene. No debromination of the 3αOH/17αBr was observed,[24] and the debromination of compound **2** was quenched by 80% by the diene.[25]

Though this chemistry demonstrated that steroid-mediated triplet sensitization of C−Br cleavage had been accomplished, its low efficiency (a minimum[26] of 1% assuming that the φ_{isc} for the TPSO group is ca. 8%)[1,18] prompted us to determine whether the presence of a ketone at C6 might facilitate energy transfer. In earlier work we observed a significant enhancement of both singlet[2a−c,e] and triplet[1,2e,f]

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(18) The TPSO fluorescence efficiency (0.010) and lifetime (2.1 ns) in a model system, 3α-(triphenylsilyloxy)-5α-androstane (**1**), are similar to those observed for the DPSO group (0.005 and 1.2 ns, respectively).[19]
(19) Wu, Z.-Z.; Morrison, H. *Tetrahedron Lett.* **1990**, *31*, 5865.
(20) Compound **2** was prepared by displacement of the triflate of 17β-hydroxy-5α-androstan-3-one with lithium bromide, followed by reduction with $LiHAl[OC(CH_3)_3]_3$ and silylation of the C3 α-alcohol by TPSCl. The configurations of the TPSO and bromine groups were assigned by NMR and confirmed by X-ray analysis of **3**.
(21) Satisfactory analytical and spectroscopic data have been obtained for all new compounds reported herein.
(22) Using a Continuum NY-61 Nd:YAG laser equipped with a frequency quadrupler (30 mW, 10 Hz, ca. 3.0−3.3 mJ/pulse) and with a 2× beam enlarger in front of a 1 cm square Vycor cell.
(23) Prepared from 3α-hydroxy-5α-androstan-17-one by Wolff−Kishner reduction of the ketone and silylation of the alcohol.
(24) Nor was there debromination of the 3αOH/17αBr by 266 nm light when this compound was irradiated by itself, thus ensuring that the photochemistry of **2** is initiated by light absorption by the TPSO antenna.
(25) Interestingly, the TPSO chemistry was unquenched by piperylene.
(26) This is a minimum value since the extent of recombination of the initially created radical or ion pairs cannot be determined from the data in hand.

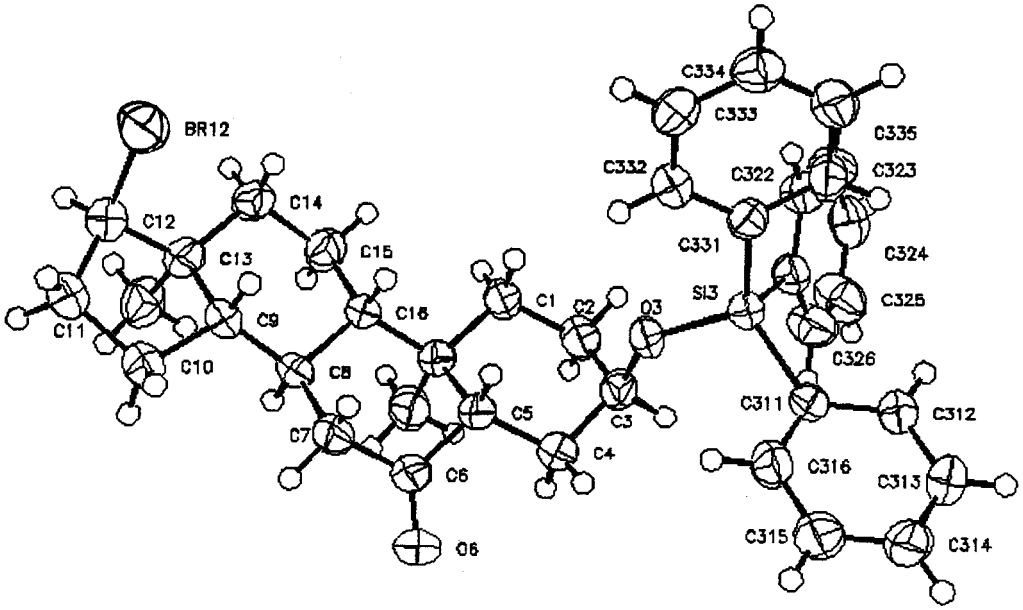
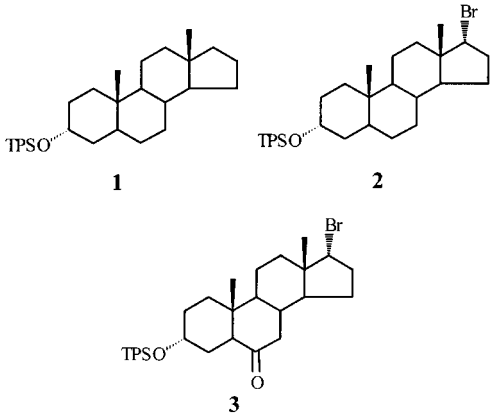


Figure 1. X-ray structure of **3**.

energy transfer to C17 after initial intraSSET from a C3 aryl antenna to a C6 carbonyl group (triplet energy transfer occurring after intersystem crossing by the ketone). Toward these ends, we prepared 17α-bromo-3α-(triphenylsilyloxy)-5α-androstan-6-one (**3**, 3αTPSO/6ketone/17αBr)[27] and confirmed the structure by X-ray analysis (Figure 1).

It is noteworthy that the TPSO moiety points away from the C6 carbonyl group, thus lessening the potential for a through-space interaction between the two groups. This arrangement is contrary to that observed for an analogous compound containing a DPSO antenna and C6 ketone (with an alkylidene group at C17).[2f] Nevertheless, a comparison of the aryl fluorescence quantum efficiencies for compounds **1**−**3** confirms that efficient intraSSET from the TPSO group to the C6 ketone is occurring. Thus, φ_f for **1** and **2** are 1.0 × 10^{-2} and 9.3 × 10^{-3}, respectively, both some 10-fold higher than that for **3** (9.5 × 10^{-4}). Using the standard expression[2] that $\varphi_{intraSSET} = [\varphi_f(\mathbf{1}) - \varphi_f(\mathbf{3})]/\varphi_f(\mathbf{1})$, one calculates that intraSSET from the TPSO group to the C6 carbonyl group is 90% efficient. (Note that the fluorescence quantum efficiencies for **1** and **2** are comparable, evidence that the C17 bromine has a minimal effect on the TPSO singlet state.[28])

Irradiation of **3**, as described for **2** above, resulted in the formation of five primary photoproducts (eq 1). Four of these are derived from ketone photochemistry, i.e., the alcohols, 17α-bromo-6α-hydroxy-3α-TPSO-5α-androstane (**4**) and



17α-bromo-6β-hydroxy-3α-TPSO-5α-androstane (**5**), and a pair of solvent photoalkylation products, **6** and **7**. The latter are presumed to be the β hydroxy, *R* and *S* tetrahydrofuryl isomers resulting from α attack, but a definitive assignment requires more extensive spectral characterization. The fifth product was the anticipated debromination product, 3α-TPSO-5α-androstan-6-one (**8**).[21,30,31] The same products were formed when **3** was photolyzed with 308 nm light.[32] Quantum efficiencies were determined for the loss of **3** and the formation of the products at both excitation wavelengths and are also shown in eq 1. It is clear that activation at C17

(27) Prepared from testosterone via initial conversion to the 17β hydroxy, 3,6 dione, conversion of the alcohol to the 17α bromide, and selective reduction and silylation at C3.

(28) The aryl emission of **1** was found to be unaffected by the presence of an equimolar concentration of 3α-hydroxy-5α-androstan-6-one (3αOH/6ketone),[29] thus confirming that there is no *inter*molecular interaction between the C6 carbonyl group and the TPSO singlet state at the concentrations (ca. 10^{-4} M) used in the emission experiments.

(29) Prepared from dehydroisoandrosterone in four steps.

(30) The structures are assigned on the basis of spectral analysis. Those for compounds **4**, **5**, and **8** were confirmed by comparison with independently prepared authentic samples.

(31) This is clearly a product resulting from homolysis of the C−Br bond. There was no evidence for the C17 alcohol one might have anticipated had heterolysis been observed. For a recent, relevant discussion, see: Lipson, A.; Deniz, A. A.; Peters, K. S. *Chem. Phys. Lett.* **1998**, *288*, 781 and references therein.

(32) Using a Luminics EX-700 Pulse Master Excimer Laser at 308 nm, 30 mW power (10 Hz, 3.5 mJ/pulse).

has been enhanced by the presence of the ketone; there is a 6-fold increase in the efficiency of the debromination reaction of **3** relative to **2**.

To confirm that excitation energy transfer in **3** is intramolecular (as in **2**) 6 mM **3** was photolyzed in the presence of an equimolar concentration of 3αOH/17αBr with both 266 and 300 nm light. No debromination of the 3αOH/17αBr was observed in either case. Nor, in fact, was debromination observed upon the 300 nm irradiation of 3αOH/17αBr with an equimolar concentration of 3αOH/6ketone under the usual conditions, or by itself in an acetone solution.

Because intraSSET from the TPSO group to the C6 ketone is so efficient, it is reasonable to assume that the excitation energy transmitted to C17 in **3** derives solely from the carbonyl group. Both the ketone singlet (84 kcal/mol) and triplet (ca. 78 kcal/mol) excited states[33] should be capable of debrominating **3** (C−Br BDE = ca. 68 kcal/mol for isopropyl bromide).[34] To determine whether it is the ketone singlet or triplet state that is responsible for the debromination, 6 mM **3** was irradiated with 300 nm light in the presence of 1.2 mM *cis*-piperylene. No quenching of debromination to **8** was observed even though there was efficient (50−70%) quenching of the ketone photoproducts **4**−**7**. *We thus conclude that activation of the C17 C−Br bond in **3** occurs through interaction with the C6 ketone singlet state*.

The rate constant for this interaction can be estimated by measuring the singlet lifetimes of 6-keto steroids with and without a bromine at C17 (the TPSO group was removed from C3 to avoid any possible interactions of the ketone singlet with the aryl chromophore). Values of 2.5 ± 0.2 and 3.7 ± 0.2 ns were determined for the two compounds, respectively. If one assumes that the shortened lifetime in the presence of the C17 bromine is entirely due to the interchromophoric interaction, one calculates a rate constant for $k_{C6\rightarrow C17Br} = 1.3 \times 10^8\ s^{-1}$.

Alternatively, but less directly, one can determine the reduction in φ_{isc} in the two steroids caused by the C6 ketone/C−Br singlet interaction by measuring the relative amount of triplet reduction at C6 by the solvent for the two ketones. A 37% diminution in C6 reduction products is observed when there is a bromine at C17. This compares favorably with the 32% reduction observed for the singlet lifetime (see above). Assuming that $\varphi_{isc} \sim 1.0$ in the absence of the halogen, and that all the reduction in the presence of the bromine is due to energy transfer (i.e., $\varphi_{C6\rightarrow C17Br} = 0.37$), one calculates $k_{C6\rightarrow C17Br} = 1.5 \times 10^8\ s^{-1}$. The average of the two values, $1.4 \times 10^8\ s^{-1}$, may be compared to the value of $8.3 \times 10^8\ s^{-1}$ measured for triplet energy transfer from a C6 ketone to a C17 ethylidene group.[2f,35] Extending the assumption that the 37% reduction in φ_{isc} reflects a corresponding level of activation of the C17 halogen, and with the assumption that C−Br activation quantitatively leads to cleavage, one calculates that 0.0066/0.37 or ∼2% of C−Br cleavage results in product.

Apparently the ketone triplet state either lacks sufficient energy to initiate cleavage or cannot do so within its lifetime in the THF medium. Computations are in progress, but it seems likely that the mode of activation of the C−Br bond is through TBI coupling of the carbonyl n,π^* singlet state with the C−Br n,σ^* state, by analogy with the proposed mode of activation of the carbon−halogen bond in the chloronorbornenes[7] and chlorobenzobicyclics.[9]

Acknowledgment. This work was supported by the National Science Foundation through Grant CHE 9530650.

Supporting Information Available: Experimental procedures and characterization, including ^{1}H and ^{13}C NMR and HRMS data for compounds **1**−**8** and 3αOH/6ketone; X-ray crystal data for **3**. This material is available free of charge via the Internet at http://pubs.acs.org..

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(35) Studies to determine the rate constant and overall efficiency for triplet energy transfer from the C3 TPSO antenna to C17Br are in progress.