

off-white oily solid (88%). Distillation of the acid gave a colorless liquid (128 mg; 77%):  $[\alpha]_D = +17.7$  (*c* 2.37, EtOH) [lit.<sup>49</sup>  $[\alpha]_D = +17.87$  (*c* 5.30, EtOH)]; <sup>1</sup>H NMR  $\delta$  1.22 (d, *J* = 6.9 Hz, 3 H, CH<sub>3</sub>CHCOOH), 2.67–2.86 (m, 2 H, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 7.23–7.35 (m, 5 H, aromatic), 11.08 (br s, 1 H, COOH); <sup>13</sup>C NMR  $\delta$  16.6, 39.4, 41.4, 126.5, 128.5, 129.1, 139.2, 182.9; IR (thin film) 3400, 1703 cm<sup>-1</sup>. HRMS (EI) calcd for C<sub>10</sub>H<sub>12</sub>O<sub>2</sub>: 164.08376. Found: 164.08382.

(b) Heterocycle **39** (100 mg, 0.331 mmol) was deacylated under conditions identical to those described above for **36**. TLC showed the reaction to be complete in 30 min, and methyl chloroformate (28  $\mu$ L, 0.36 mmol) was added; the resulting mixture was allowed to stir at room temperature for 4 h. Workup as described for **36** preceded drying of the organic layer (MgSO<sub>4</sub>), filtration, and evaporation of solvent to afford **1** (530 mg, 76%). The aqueous layer was acidified with HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub>. Drying of the organic layer (MgSO<sub>4</sub>), filtration, and evaporation of solvent gave **37** (48 mg, 85%).

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**Supplementary Material Available:** Crystallographic data for **1** and **11** (14 pages). Ordering information is given on any current masthead page.

## Triethylamine-Photosensitized Reduction of a Ketone via a Chemical Sensitization Mechanism<sup>1</sup>

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**Abstract:** Photolysis of acetonitrile solutions of  $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one (**1**), or its  $\beta$ -methoxy analogue (**5**), and triethylamine (TEA) with 254-nm light leads to reduction of the 17-keto group with high stereoselectivity. By contrast, Norrish type I products are exclusively observed when the photolysis is carried out in cyclohexane, and products from both  $\alpha$ -cleavage and reduction are observed in ether or THF. Excitation of TEA in acetonitrile results in the photoionization of the amine to form a radical cation and a solvent radical anion. Several possible mechanisms for reduction of ground-state ketones by these species, or radicals derived therefrom, are outlined. The limiting quantum efficiency for reduction of **1** is 0.17. The results observed in cyclohexane are explained by singlet-singlet energy transfer from the TEA excited state to the ketone, while both photoionization and energy transfer appear to be operating in the ethereal solvents.

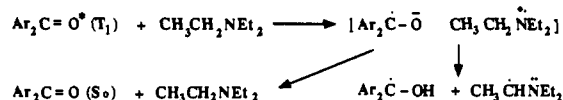
The photoreduction of aromatic ketones by aliphatic amines has been a subject of extensive investigation.<sup>2-4</sup> Early studies by Cohen and co-workers,<sup>5-7</sup> as well as more recent studies,<sup>8-11</sup> have demonstrated that a radical ion pair is generated through electron transfer from the ground-state amine to the photoexcited ketone, followed by proton transfer from the amine radical cation to the ketyl species (Scheme I). Tertiary amines, such as triethylamine (TEA), have frequently been used in these reactions.<sup>12,13</sup>

However, amines are themselves readily excited in the near UV, and although the photophysics of aliphatic amines has been thoroughly investigated,<sup>14-16</sup> very little attention has been paid to the photochemical consequences of amine excitation in the presence of other functionalities, such as ketones.<sup>17,18</sup> We now report a new mechanism for the photoreduction of ketones involving photoexcitation of an amine followed by ionization of the amine (i.e., for triethylamine: formation of TEA<sup>•+</sup>). Photoinduced reductions wherein the target functionality reacts through ground-state chemistry have been referred to as proceeding through "chemical sensitization",<sup>19,20</sup> as exemplified by the benzophenone-sensitized photoreduction of aryl-*N*-alkylimines,<sup>19,21a</sup> dibenzoyl ethylene,<sup>21b</sup> and acridine.<sup>21c</sup>

### Results and Discussion

**Photoreduction of Steroidal Ketones via Excitation of TEA.** When  $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one (**1**) and TEA are irradiated

**Scheme I.** Mechanism for Reduction of a Ketone Excited State by an Amine



with 254-nm light, using a ca. 10:1 ratio of amine to ketone such that the TEA absorbs 99% of the incident light,<sup>22</sup> one obtains

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<sup>†</sup>Purdue University.

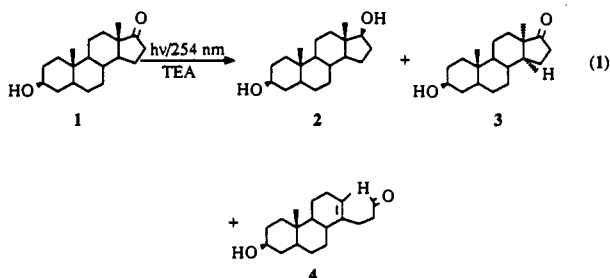
<sup>‡</sup>University of Notre Dame.

**Table I.** Solvent Effects on Photoreactions of the Ketone **1** Initiated by Photoexcitation of TEA<sup>a</sup>

solvent	yield, <sup>b</sup> %			ratio 2/(3 + 4)	loss of <b>1</b> , %
	2	3	4		
cyclohexane <sup>d,e</sup>	c	45.6	6.3		70.4
Et <sub>2</sub> O <sup>d</sup>	6.8	60.4	23.1	0.081	78.7
THF <sup>d</sup>	14.5	35.9	5.4	0.35	76.8
MeCN	79.0	2.2	c		74.7

<sup>a</sup> Photoreactions were conducted on solutions of [**1**] = 13.9 mM and [TEA] = 145 mM with 254-nm light at 28 °C for 20 min. <sup>b</sup> Yields were determined by GLC analysis relative to an internal standard and are based on recovered starting ketone. <sup>c</sup> None detectable. <sup>d</sup> An unknown (4–12%) was also detected with a long GLC retention time. <sup>e</sup> [**1**] = 7.7 mM; [TEA] = 72.5 mM.

products resulting from Norrish type I  $\alpha$ -cleavage (**3**, **4**)<sup>23,24</sup> and/or the alcohol (**2**) resulting from ketone reduction,<sup>24</sup> with the product ratio strongly dependent on the solvent (eq 1). Thus, photolysis



in degassed acetonitrile overwhelmingly generates 5 $\alpha$ -androstane-3 $\beta$ ,17 $\beta$ -diol (**2**),<sup>25</sup> whereas photolysis in cyclohexane exclusively generates the epimer, 3 $\beta$ -hydroxy-5 $\alpha$ ,13 $\alpha$ -androst-17-one (**3**), and the aldehyde [3 $\beta$ -hydroxy-13,17-sec-5 $\alpha$ -androst-13-en-17-aldehyde (**4**)]. Photolysis in ether or THF gives both  $\alpha$ -cleavage and reduction products.

A particularly interesting point is that adding 10% water into acetonitrile solution completely quenches photoreduction and initiates  $\alpha$ -cleavage of the ketone **1**, although the loss of **1** is very low with respect to other solvent systems over the same time period of irradiation. The data for various solvent systems are summarized in Table I.

The methylated ketone, 3 $\beta$ -methoxy-5 $\alpha$ -androst-17-one (**5**), shows similar photochemical behavior to its alcohol precursor.

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(14) Muto, Y.; Nakato, Y.; Tsubomura, H. *Chem. Phys. Lett.* **1971**, *9*, 597–599.

(15) Halpern, A. M. In *Chemistry of Amino, Nitroso, and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: New York, 1982; Vol. 1, pp 155–180 and earlier papers cited therein.

(16) Beecroft, R. A.; Davidson, R. S. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1063–1067.

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(22) In acetonitrile at 254 nm,  $\epsilon(\text{TEA}) = 47 \text{ M}^{-1} \text{ cm}^{-1}$  and  $\epsilon(\mathbf{1}) = 6 \text{ M}^{-1} \text{ cm}^{-1}$ .

(23) For a review of Norrish type I cleavage, see: Weiss, D. S. *Org. Photochem.* **1981**, *5*, 347–420.

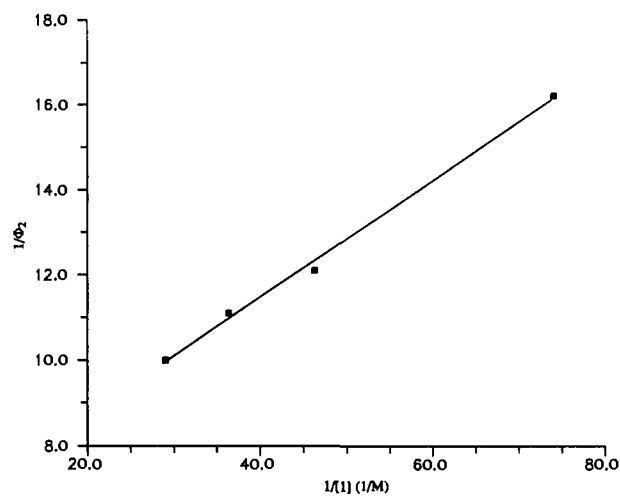
(24) For analogous chemistry in related steroids, see: Wu, Z. Z.; Morrison, H. *J. Am. Chem. Soc.* **1989**, *111*, 9267–9269. Wu, Z. Z.; Morrison, H. *Tetrahedron Lett.* **1990**, 5865–5868.

(25) This reaction proceeds with rather high efficiency and stereoselectivity and may prove to be a useful synthetic methodology for the reduction of cycloalkanones. Extended irradiation times (75 min) gave a small amount of the 17 $\alpha$ -isomer, 5 $\alpha$ -androstane-3 $\beta$ ,17 $\alpha$ -diol (**5**) (ratio of **2:5** = 15.2:1.0).

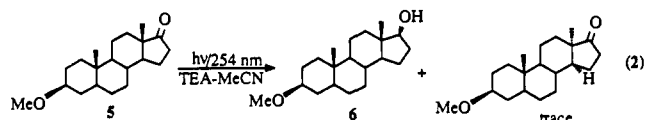
**Table II.** Solvent Effects on Photoreactions of the Ketone **1** under Photoexcitation of **1**<sup>a</sup>

solvent	yield, <sup>b,c</sup> %			ratio 3/4	loss of <b>1</b> , %
	2	3	4		
Et <sub>2</sub> O	2.4 (0)	45.2 (44.6)	11.4 (13.7)	4.0 (3.3)	26.2 (43.8)
THF	2.0 (0)	77.3 (72.2)	18.3 (18.8)	4.2 (3.8)	27.0 (44.0)
MeCN	2.0 (0)	74.0 (65.4)	16.4 (17.5)	4.5 (3.7)	29.1 (51.5)

<sup>a</sup> Photoreactions were conducted on solutions of [**1**] = 55 mM and [TEA] = 361 mM with 300-nm light at 28–32 °C for 25 min. <sup>b</sup> Yields were determined by GLC analysis relative to an internal standard and are based on recovered starting ketone. <sup>c</sup> The data in parentheses are in the absence of TEA.

**Figure 1.** Stern–Volmer plot for reduction of **1** initiated by photoexcitation of TEA in acetonitrile at room temperature.

Thus, photoexcitation of TEA in acetonitrile at 254 nm initiates reduction of **5** to form 3 $\beta$ -methoxy-5 $\alpha$ -androst-17 $\beta$ -ol (**6**, eq 2).



By contrast with the above, direct excitation of the ketone **1** with 300-nm light in the presence of TEA does not afford much reduction or demonstrate significant solvent-dependent photochemical behavior. Irradiation of **1** (55 mM) and TEA (360 mM) in acetonitrile, THF, or ether gives predominantly the  $\alpha$ -cleavage products, **3** (yield, ca. 45–77%) and **4** (ca. 11–18%), as well as a small amount of the reduction product **2** (ca. 2%). These results are not much different from those one observes in the absence of TEA, wherein photolysis in each of the three solvents generates only the  $\alpha$ -cleavage products,<sup>26</sup> with a ratio for **3** to **4** of 3.3–3.8, slightly less than in the presence of TEA (4.0–4.5). These results confirm that the singlet excited state of **1** reacts primarily through rapid singlet-state-derived  $\alpha$ -cleavage rather than intersystem crossing to the triplet where reduction by the amine could be anticipated. The data in the presence and absence of TEA are summarized in Table II.

The source of the hydrogens involved in the reduction of the ketones was explored by photolysis of **5** and TEA in CD<sub>3</sub>CN using 254-nm excitation. The reaction gives a GLC trace identical to that observed in CH<sub>3</sub>CN. Mass spectral analysis of the reduction product (**6**) generated in the CD<sub>3</sub>CN shows ca. 5% deuterium incorporation.

(26) Wehrli, A.; Schaffner, K. *Helv. Chim. Acta* **1962**, *45*, 385–389. Schaffner, K.; Jeger, O. *Tetrahedron* **1974**, *30*, 1891–1902, and references cited therein.

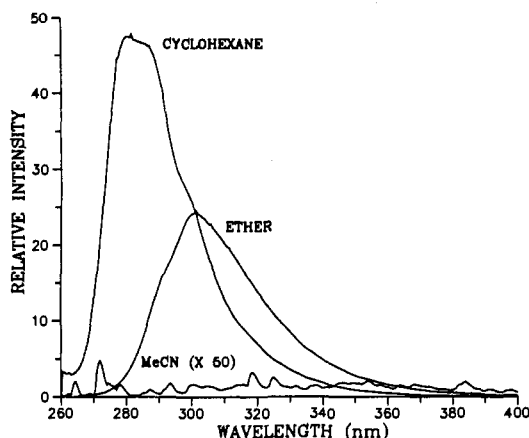


Figure 2. Corrected fluorescence spectra of TEA in several solvents at room temperature.

The quantum efficiency for reduction of **1** to **2** ( $\Phi_2$ ) upon photoexcitation of TEA in acetonitrile using 254-nm light increases with increasing ketone concentration (at constant [TEA]). A linear plot of  $1/\Phi_2$  vs  $1/[1]$  is presented in Figure 1 and gives a limiting quantum efficiency of 0.17. The TEA concentration is not a factor so long as the concentration is high enough for >99% of the 254-nm incident light to be absorbed. For example, at 17.2 mM **1**  $\Phi_2$  is 0.083 and 0.080 for [TEA] = 145 and 253 mM, respectively. The quantum efficiency for the reduction of **5** was determined with the ketone and TEA concentrations at 15 and 356 mM, respectively. The value of 0.087 is virtually identical to that (0.092) observed for **1** under these conditions.<sup>27</sup>

**Photophysical Studies on TEA.** It has been noted above that the photochemistry initiated by TEA is strongly solvent dependent. One observes an analogous strong solvent dependence for TEA fluorescence. TEA fluorescence in cyclohexane is centered at 282 nm and is rather efficient ( $\Phi_f = 0.68$ ), while in ether the emission efficiency is not only reduced ( $\Phi_f = 0.35$ ) but also red shifted to 302 nm. The most dramatic effect is seen in acetonitrile, where TEA becomes totally nonfluorescent (see Figure 2).

Similar observations have been made by others<sup>14,16,28</sup> and the divergence between cyclohexane and ether has been attributed to solvation of a Rydberg excited state by the latter solvent.<sup>14,28</sup> The loss of fluorescence of the tertiary amine in acetonitrile has been noted,<sup>16,29</sup> and the quenching of *N,N*-diethylmethylamine emission in hexane by acetonitrile has been shown to be diffusion controlled and attributed to a charge-transfer interaction.<sup>30</sup> The anticipated<sup>16</sup> complete photoionization of TEA in pure acetonitrile is supported by the observation of a transient attributed to the TEA<sup>•+</sup> using flash photolysis ( $\tau = 14 \mu\text{s}$ ).<sup>29</sup>

We have repeated these flash photolysis studies using an excimer laser with 248-nm excitation. TEA in acetonitrile gave rise to two transients at room temperature. One showed an absorption that monotonically increased from 500 to 280 nm, was invariant across the decay profile, and is consistent with the absorption previously assigned as TEA<sup>•+</sup>.<sup>29</sup> The absorption of TEA itself, and the lack of sensitivity of the detection system, restricted observations at shorter wavelength. The other transient was observed to absorb in the range 700–800 nm. Both the initial absorbances of the shorter wavelength transient monitored at 330 nm and the longer wavelength transient monitored at 750 nm were plotted as a function of relative laser energy. Both plots were linear, indicating that the transients are not due to multiphotonic processes. At temperatures below 263 K, the absorption at 750

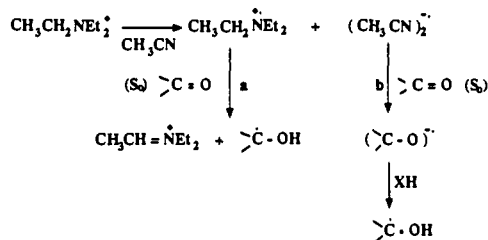
(27) This result confirms that hydrogen bonding of the 3-ol functionality of **1** to TEA plays no role in this chemistry (a concern expressed by a referee). Likewise, the <sup>1</sup>H NMR chemical shifts for the methyl resonances of TEA (55 mM) were monitored in CD<sub>3</sub>CN in the presence of varying concentrations (13–53 mM) of **5** and found to be invariant.

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**Scheme II.** Possible Chemical Sensitization Mechanisms for Reduction of a Ketone upon Photoexcitation of Triethylamine



nm weakened relative to that observed at room temperature, and a new transient appeared at 550 nm.

The appearance of the 550- and 750-nm transients and their temperature-dependent behavior are consistent with the previous assignment<sup>31</sup> of the solvent monomer anion ( $\text{CH}_3\text{CN}^{\bullet-}$ ) for the 550-nm transient and the solvent dimer anion ( $(\text{CH}_3\text{CN})_2^{\bullet-}$ ) for the 750-nm transient. The detection system was limited by the photomultiplier response and available monitoring light for analyzing the infrared transient. The solvent dimer anion has been observed in absorption as extending into the infrared beyond a maximum at 1450 nm.<sup>31</sup> In the current experiments, the 750-nm decay was used to monitor the tail of this absorption peak. The two electron scavengers, carbon tetrachloride and nitrous oxide, virtually eliminate the 750-nm signals, substantiating the assignment of this transient as a solvent anion. The 330-nm transient was also affected by these two reagents but to a lesser degree. Taken together, the three transient absorptions are consistent with the interpretation that the 248-nm excitation of TEA in acetonitrile photoionizes TEA with the formation of the TEA radical cation and a photoelectron which forms an anion with two acetonitrile molecules at room temperature.

Quenching experiments were done on the two room temperature transients in acetonitrile solutions of TEA by monitoring at 330–350 and 750 nm. The decays of the transients were roughly second order under the laser operating conditions. Half-lives ranged from several hundreds of nanoseconds for the 750-nm transient to several microseconds for the 330-nm transient; however, weak tails of the transient absorptions extended beyond 100  $\mu\text{s}$ . The relatively high absorbances (0.2–0.3) necessary to see good signals in the infrared led to nonuniform concentrations of the transient,<sup>32</sup> which, in turn, led to a distorted second-order decay. Attempts were made to see evidence of first-order components in the 330- and 750-nm decay traces on addition of aliquots of **1** (0.4–3 mM) to acetonitrile solutions of 12.5 mM TEA. No such components could be definitively identified, but there was a general decrease in the initial absorbance of the two transients, and the second-order rate constants increased somewhat at higher concentrations of **1**. Since none of the decay traces cleanly followed any simple kinetics, and since the 750-nm signals were weak, no mechanistic conclusions could be inferred from this analysis. In fact, the high pulse energies needed to see the transients and the relatively high absorbances at 248 nm likely contribute to the dominant second-order decay and, furthermore, could mask a slow pseudo-first-order quenching of one or both of the transients by **1**. However, such a pseudo-first-order quenching is indicated by the double-reciprocal plot from the steady-state results (Figure 1).

**Mechanistic Discussion.** The solvent effects reported in Table I are readily rationalized by reference to the TEA emission studies. In cyclohexane, TEA photosensitizes the singlet-state  $\alpha$ -cleavage chemistry of **1** by singlet–singlet energy transfer. This process is also responsible for  $\alpha$ -cleavage in ether, and one obtains a ratio of 3:4 in this solvent which is similar to that (3.3:1.0) observed by photoexcitation of **1** with 300-nm light.<sup>33</sup> Amine-sensitized

(31) Bell, I. P.; Rodgers, M. A. J.; Burrows, H. D. *J. Chem. Soc., Faraday Trans. 1* **1977**, *73*, 315–326.

(32) Boag, J. W. *Trans. Faraday Soc.* **1968**, *64*, 677–685.

(33) This experiment was done in ether because of the limited solubility of **1** in cyclohexane. No alcohol is detectable. The presence or absence of TEA has virtually no effect on the product ratio with 300-nm excitation.

ketone fluorescence has been observed<sup>17</sup> and proceeds via diffusion-controlled (exchange mechanism) energy transfer.<sup>17</sup>

As one might have anticipated, the situation is quite different in acetonitrile, where one observes virtually complete reduction. Singlet energy transfer to millimolar concentrations of a ketone is clearly not expected to compete with photoionization and the concomitant formation of the TEA radical cation and the acetonitrile radical anion. Both of these radical ions are potential reductants, TEA via the donation of a hydrogen atom to ground-state **1** to form an iminium ion ( $\text{Et}_2\text{N}^+=\text{CHCH}_3$ ) and the dialkylhydroxycarbonyl radical and  $(\text{CH}_3\text{CN})_2^{\cdot-}$  through formation of a ketyl species (cf. paths a and b in Scheme II, respectively). Donation of an  $\alpha$ -hydrogen atom to the ketone by  $\text{TEA}^{+\cdot}$  finds analogy in the recent observations of facile  $\alpha$ -C-C bond homolysis in some amine radical cations<sup>13</sup> and there is precedent for reduction by the acetonitrile radical anion.<sup>34,35</sup> The proton source (XH) in path b may be the solvent or  $\text{Et}_3\text{NH}^+$  formed by hydrogen atom abstraction from the solvent by  $\text{TEA}^{+\cdot}$ .

Both paths a and b would produce the linear double-reciprocal plot shown in Figure 1. As noted above, the existence of this linear dependence under the normal, low-intensity photolytic conditions contrasts with our inability to observe first-order quenching by the ketone of either of the transients seen under flash photolytic conditions. One must conclude that conditions peculiar to the higher intensity laser studies create the dominant second-order decay which is observed for the transients and mask the expected first-order quenching one expects after addition of the ketone or yet a different transient is involved in the reduction. One such additional transient would be the  $\alpha$ -amino carbonyl radical,  $\text{CH}_3\text{CHNEt}_2^{\cdot}$ , which could form via proton abstraction from  $\text{TEA}^{+\cdot}$  by TEA.<sup>36</sup> This radical could transfer a hydrogen atom to the ketone to form the dialkylhydroxycarbonyl radical. Such  $\alpha$ -amino radicals are also good reducing agents (an oxidation potential of 1.0V vs SCE has been estimated)<sup>36,37</sup> and would be capable of directly converting the ketone to the ketyl radical anion.<sup>38,39</sup>

In summary, we have observed the photoreduction of steroidal ketones upon excitation of triethylamine. The reactions are unique to acetonitrile and occur concomitantly with the reported photoionization of the amine in this solvent. Several possible reductants can be postulated, and further studies on both the mechanism of this reaction and its potential application to other functionalities are in progress.

### Experimental Section

**Materials.** Tetrahydrofuran and ethyl ether were distilled under nitrogen from sodium benzophenone. Acetonitrile and triethylamine were distilled under nitrogen from calcium hydride. (*E*)-1-Phenyl-2-butene was purified by preparative GLC on a Varian Model 3300 gas chromatograph equipped with a thermal conductivity detector and a 25% XF-1150 column (16 ft  $\times$  0.25 in.) on 60/80 AW Chromasorb P at 175 °C. All other reagents were used as received.

**Instrumentation.** NMR spectra were obtained with a General Electric QE-300 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 1800 FT-IR spectrometer. Mass spectra were determined with a Finnigan 4000 GLC-MS spectrometer (EI/CI) equipped with a DB-1 capillary column (30 m  $\times$  0.25 mm i.d.; 0.25- $\mu\text{m}$  film thickness). Absorption spectra were recorded on a Perkin-Elmer Model Lambda 3B spectrometer. Fluorescence spectra were recorded on a component fluorometer,<sup>40</sup> and fluorescence quantum efficiencies were measured by

reference to toluene ( $\Phi_f = 0.14$  in cyclohexane).<sup>41</sup> The computer-controlled laser system used in the flash photolysis studies has been previously described.<sup>42</sup> The experiments were performed with 248-nm light from a Lambda-Physik excimer laser filled with a mixture of krypton, fluorine, and helium. The relative laser energy was monitored with a pyroelectric detector. The laser was operated so that the energy per pulse was between 10 and 100 mJ. Front-face geometry was used for the excitation/monitoring light beams. The absorbances of the solutions at 248 nm were in the range 0.2–0.3 at an optical path length of 0.2 cm. The temperature-controlled experiments<sup>43</sup> were performed with a nitrogen flow passing at various rates through copper tubing immersed in liquid nitrogen and directed onto the face of the sample cell. The cell and its holder were encased in a Dewar. Temperatures were measured with a thermocouple.

Gas-liquid chromatography analyses were performed on a Varian Model 3700 capillary instrument with flame ionization detector, coupled to a Hewlett-Packard 3390A integrator. The capillary columns used were (A) DB-1 (J&W Scientific), 15 m  $\times$  0.25 mm i.d., 0.25- $\mu\text{m}$  film thickness, and (B) DB-1 (J&W Scientific), 30 m  $\times$  0.25 mm i.d., 0.25- $\mu\text{m}$  film thickness). The internal standard was 17 $\beta$ -hydroxy-5 $\alpha$ -androstan-3-one (Aldrich). Typical condition and retention times were as follows (at 200 °C): ketone **1**, 12.05 min; alcohol **2**, 12.49 min; epimer **3**, 10.02 min; aldehyde **4**, 10.29 min; ketone **5**, 11.22 min; alcohol **6**, 11.73 min.

**Photolyses.** Photolyses were performed in a Rayonet photochemical reactor (Model RPR-100; Southern New England Ultraviolet Corp.) equipped with sockets for 16 254- or 300-nm lamps, a merry-go-round turntable, and a cooling fan. All solutions were purged with argon for at least 15 min prior to use. Photolyses involving 254-nm excitation were carried out using quartz tubes (9.0 cm  $\times$  1.1 cm o.d.), and photolyses with 300-nm light used Pyrex tubes (9.5 cm  $\times$  1.3 cm o.d.).

**Quantum Efficiency Determinations.** Quartz tubes containing 2 mL of an argon-degassed acetonitrile solution of **1** (13.5–34.5 mM) and TEA (356 mM) were irradiated at room temperature with 16 254-nm lamps for 15 min. Dark controls consisted of a quartz tube containing 2 mL of acetonitrile solution ( $[\text{I}] = 34.5$  mM and  $[\text{TEA}] = 356$  mM) wrapped with aluminum foil and placed in the Rayonet during the irradiation of the sample solution. The solutions were analyzed by GLC with an internal standard. Analysis of the dark control showed no evidence for product formation and no change in the concentration of the ketone **1**. Actinometry was performed using the *E/Z* isomerization of (*E*)-1-phenyl-2-butene, for which the quantum efficiency for formation of *Z* has been determined to be 0.20.<sup>44</sup> The amount of the *Z* isomer formed was determined by GLC on column B at 80 °C; the retention times of the two isomers were 8.12 and 8.70 min for the *E* and *Z* isomers, respectively. Conversions to the *Z* isomer were corrected for back reaction.

**Preparation of 3 $\beta$ -Methoxy-5 $\alpha$ -androstan-17-one (1).** The procedure follows the general method of Aoyama et al.<sup>45</sup> To a solution of 3 $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one (582 mg, 2.0 mmol) and fluoroboric acid (42%, 418 mg, 2 mmol) in 8.0 mL of methylenechloride at 0 °C was added dropwise (trimethylsilyl)diazomethane (1 mL, 2.0 M in hexane) over 5 min under nitrogen. Three further portions of (trimethylsilyl)diazomethane (0.50, 0.25, and 0.25 mL) were then added dropwise every 20 min. After complete addition of the reagent, the mixture was stirred at 0 °C under nitrogen for 30 min. The mixture was poured into 10 mL of water and extracted with methylene chloride. The combined methylene chloride extract was dried and concentrated under reduced pressure. The residue was chromatographed with silica gel (230–400 mesh), using 10% EtOAc/hexane as eluent, to give crystalline 3 $\beta$ -methoxy-5 $\alpha$ -androstan-17-one (435 mg, yield 71%), mp 109–111 °C (lit.<sup>46</sup> 112–114 °C).

**Photolysis of 3 $\beta$ -Hydroxy-5 $\alpha$ -androstan-17-one/TEA in Acetonitrile.** Two quartz tubes, each containing 5 mL of acetonitrile solutions of TEA (330 mM) and **1** (32.7 mM), were irradiated with 16 254-nm lamps at room temperature for 55 min. The colorless photolysate was shown by GLC (on column A) to contain two major components, the starting material and the alcohol **2**, plus a trace amount of the epimer **3** (peak area ratio of 1:2:3 = 18.3:48.0:1.0). There was an 80% loss of the ketone **1**. The solvent was removed under reduced pressure, and the residue was chromatographed with silica gel (230–400 mesh), using 10% EtOAc/

(34) See: Chateaufort, J. E. *J. Phys. Chem.* **1990**, *94*, 7177–7180.

(35) The reduction is completely quenched upon addition of ca. 10% water to the acetonitrile, and one then observes only cleavage products resulting from energy transfer. Preliminary emission data indicate that water may be eliminating photoionization of the Rydberg excited state. Further studies of this effect are in progress.

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$\text{CH}_2\text{Cl}_2$  as eluent, to give recovered **1** (17 mg) and the alcohol **2** (white solid, 45 mg, 57% isolated yield). The NMR spectrum of the alcohol was identical with that reported.<sup>47</sup>

**Photolysis of 3 $\beta$ -Hydroxy-5 $\alpha$ -androstan-17-one/TEA in Ethyl Ether.** A solution of TEA (0.42 mL, ca. 300 mM) and **1** (85 mg, 32.7 mM) in 10 mL of anhydrous ether was irradiated with 16 254-nm lamps at room temperature for 55 min. The colorless photolysate was shown by GLC to contain four major components, the ketone **1**, the alcohol **2**, the epimer **3**, and the aldehyde **4**, with a peak area ratio of 1:2:3:4 = 3.6:1.0:6.8:1.9 at 67% loss of the ketone **1**. The solvent was removed under reduced pressure and the residue chromatographed on silica gel (230-400 mesh) with 5% EtOAc/ $\text{CH}_2\text{Cl}_2$  as eluent, to give recovered **1** (28 mg) and a mixture of the ketones and the aldehyde (solid, 13 mg). The mixture was shown by GLC to consist of the epimer **3** (60%), aldehyde **4** (19%), and the ketone **1** (17%). Compound **3** (3 $\beta$ -hydroxy-5 $\alpha$ ,13 $\alpha$ -androstan-17-one) was purified by further column chromatography to provide an enriched sample (ca. 80%) for spectral analysis:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$  3.56 (m, 3C- $\alpha\text{H}$ ), 2.4-1.0 (m, steroidal skeletal hydrogen), 0.96 (s, 18- $\text{CH}_3$ ), 0.62 (s, 19- $\text{CH}_3$ ). The assignment of structure rests on the characteristic upfield shift of the 19- $\text{CH}_3$  group relative to the starting material ( $\delta$  0.62 and 0.83, respectively)<sup>48</sup> and the extensive studies on photoepimerization of 17-keto steroids.<sup>26</sup> The aldehyde, 3 $\beta$ -hydroxy-13,17-seco-5 $\alpha$ -androstan-13-en-17-aldehyde (**4**), could only be obtained as a 60% pure mixture with the epimer. The proton NMR data match well with those reported<sup>49</sup> for aldehydes formed from analogous 17-keto

steroids:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ; 300 MHz)  $\delta$  9.76 (s, HC=O), 3.52 (m, 3C- $\alpha\text{H}$ ), 1.62 (s, 18- $\text{CH}_3$ ), 0.76 (s, 19- $\text{CH}_3$ ).

**Photolysis of 3 $\beta$ -Hydroxy-5 $\alpha$ -androstan-17-one/TEA in Ethyl Ether, THF, and  $\text{CH}_3\text{CN}$  with 300-nm Light.** Photolysis of 3 $\beta$ -hydroxy-5 $\alpha$ -androstan-17-one (**1**, 55 mM) in the presence and absence of TEA (360 mM) was carried in a 2-mL anhydrous solvent (ethyl ether, THF, or  $\text{CH}_3\text{CN}$ ). Each run was done in the Rayonet photochemical reactor equipped with 15 300-nm lamps through Pyrex at room temperature for 25 min. Analysis was performed with GLC on column A at 200 °C with an internal standard.

**Photolysis of 3 $\beta$ -Methoxy-5 $\alpha$ -androstan-17-one/TEA (**5**) in  $\text{CH}_3\text{CN}$  and  $\text{CD}_3\text{CN}$ .** Two quartz tubes, one containing **5** (14 mM) and TEA (143 mM) in  $\text{CH}_3\text{CN}$  (2 mL) and the other containing **5** and TEA at the same concentrations but in  $\text{CD}_3\text{CN}$  (1 mL), were irradiated with 16 254-nm lamps at room temperature for 22 min. GLC analyses on column A showed two product peaks for each solution, with identical retention times for  $\text{CH}_3\text{CN}$  and  $\text{CD}_3\text{CN}$ : 9.31 and 11.73 min. These peaks are assigned to an epimer and the alcohol (**6**) by analogy with the photochemistry of **1**. GLC/mass spectral analyses of the alcohol showed a molecular ion at  $m/e$  306 and  $(M+1)/M$  ratios of 15.9% and 20.3% for  $\text{CH}_3\text{CN}$  and  $\text{CD}_3\text{CN}$ , respectively.

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## Reactivities of Diarylmethyl and Triarylmethyl Cations with Primary Amines in Aqueous Acetonitrile Solutions. The Importance of Amine Hydration

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**Abstract:** By use of the technique of laser flash photolysis, rate constants  $k(\text{RNH}_2)$  have been directly measured for the reactions of primary amines  $\text{RCH}_2\text{NH}_2$  ( $\text{R} = \text{CH}_3\text{CH}_2, \text{CH}_3\text{OCH}_2, \text{NCCH}_2, \text{CF}_3$ ) with diarylmethyl cations ( $\text{D}^+$ ) in acetonitrile/water solutions. In 100% acetonitrile the reactions approach the diffusion limit,  $5 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$ , although they are slower,  $k(\text{RNH}_2)$  for a given cation increasing with increasing amine basicity and for a given amine increasing with decreased electron donation from substituents in  $\text{D}^+$ . In the mixed solvents the rate constants decrease in a regular fashion with increasing water content. The changes can be large, being on the order of 10-100 proceeding from 100% acetonitrile to 100% water. Moreover, the rate-retarding effect of water is more pronounced with more basic amines, with the consequence that in water-rich solutions the reactivity order no longer parallels amine basicity. Plots of  $\log k(\text{RNH}_2)$  versus  $\text{p}K_a(\text{RNH}_3^+)$  not only are curved but also show a change in the sign of their slope on progressing from weakly basic amines (positive  $\beta_{\text{nuc}}$ ) to strongly basic ones (negative  $\beta_{\text{nuc}}$ ). This behavior is explained by a mechanism in which a hydrated amine  $\text{RNH}_2 \cdots \text{HOH}$  is unreactive and an equilibrium desolvation to form the unhydrated amine precedes reaction with the cation. Quantitative treatment is carried out, using the rate constants in 100% acetonitrile to model the reaction of the free amine. This approach reproduces the experimental data within an average of  $\pm 0.04$  log unit and results in equilibrium constants for the desolvation with the expected  $\beta = -0.2$  dependency on amine basicity. Rate constants have also been measured in 33% acetonitrile/water for a series of triarylmethyl cations ranging from 4,4'-( $\text{Me}_2\text{N}$ ) $_2\text{T}^+$  to 4,4'-( $\text{CF}_3$ ) $_2\text{T}^+$ . The  $\beta_{\text{nuc}}$  values for these are all positive, with a clear trend for  $\beta_{\text{nuc}}$  to decrease with increasing cation reactivity, this being true even for the relatively stable cations 4,4'-( $\text{Me}_2\text{N}$ ) $_2\text{T}^+$ , 4- $\text{Me}_2\text{NT}^+$ , and 4,4',4''-( $\text{MeO}$ ) $_3\text{T}^+$ . Thus, amine nucleophiles do not adhere to the  $N_+$  constant selectivity relation, even for stable cations.

The technique of laser flash photolysis is proving highly valuable for the direct study of carbocations generated under conditions where they are commonly found as reactive intermediates. We have described for example experiments where a number of triaryl-

and diarylmethyl cations were generated in aqueous acetonitrile solutions<sup>3,4</sup> and rate constants directly measured for their decay

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