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Contrasting Photosolvolytic Reactivities of 9-Fluorenol vs 5-Suberenol Derivatives. Enhanced Rate of Formation of Cyclically Conjugated Four π Carbocations in the Excited State[1]

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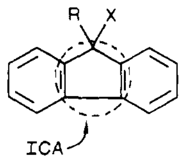
Abstract: The photosolvolysis of 9-fluorenol (**1**) and several of its derivatives, as well as related systems, has been studied in aqueous methanol and acetonitrile solutions. The primary aim of this study was to examine the effect of the internal cyclic array (ICA) of these compounds in promoting photosolvolysis with respect to the number of π electrons available in the ICA. It was observed that 9-fluorenol derivatives photosolvolyze much more efficiently than any of the related systems studied in this work. In contrast, ground-state 9-fluorenol derivatives are the least reactive systems with respect to solvolysis. Quantum yields for methyl ether formation for photosolvolysis in 50% MeOH–H_2O are reported for **1–3**. Rate constants for solvent-assisted photodehydroxylation (k_s) are calculated on the basis of the proposed mechanism of heterolytic C–OH bond rupture in the primary photochemical step and are in the range $(1.3–1.6) \times 10^{10}$ s^{-1} for **1–3**.

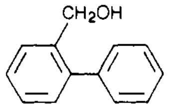
Photosolvolytic reactions have been studied for a number of years and remain a topic of current interest.[3] Recently, we have found that benzylic carbocations may be photogenerated from the corresponding alcohol precursors, in which the leaving group is the hydroxide ion.[4-7] These reactions were exceptional in that hydroxide ion is normally a poor leaving group in the ground state, but it appears to be an excellent one in the excited state when the appropriate chromophore and solvent system are used. Otherwise, these compounds are generally photostable: they do not undergo significant homolysis because formation of an incipient hydroxyl radical is generally not favorable.[8] With the hydroxide ion as the leaving group, we have documented acid catalysis of solvolysis,[4,7] as well as an example of an adiabatic photosolvolytic process in 9-xanthenol.[6] However, there were numerous systems which do not photosolvolyze.[9] Thus it was exceptional that 9-fluorenol photosolvolyzed[1] efficiently in aqueous MeOH since this system clearly lacked any obvious electron-donating group to drive the reaction. In this paper, we report the results of an investigation which attempts to delineate the reasons behind the photosolvolytic reactivity of 9-fluorenol and several of its derivatives. The results of this work give new insights into the understanding of the relative stability of charged, cyclically conjugated systems (as intermediates) in the excited state for which very little information is presently available and in which direct experimental probe of their relative stability is at present experimentally inaccessible.

Results

Product Studies. 9-Fluorenol (**1**) and several of its derivatives (**2–6**) were investigated for photosolvolytic reactivity in aqueous solution. Fluorene (**7**)—which is photostable in deoxygenated aqueous solution—was used for comparative purposes in fluorescence and lifetime measurements. In order to examine the effect of the internal cyclic array (ICA: defined as the ring system joining the two fused benzenes, as shown in **1–7**) in promoting solvolysis, several additional compounds (**8–11a,b**) were also prepared. Thus, 2-phenylbenzyl alcohol (**8**) and benzhydrol (**11b**) may be regarded as resembling **1** but without the possibility of forming an ICA on solvolysis. The 5-suberenol systems **9** and **10** may be regarded as the next members of a homologous series after the fluorene derivatives **1–6** since these possess an extra pair of π-electrons in the ICA and on solvolysis would generate a cyclically conjugated ICA of six π electrons, compared to four π electrons for **1–6**. 5-Suberol (**11a**), on the other hand, lacks the possibility of forming a *cyclically conjugated* ICA on solvolysis but still possesses an ICA nevertheless.



1: R = H; X = OH
2: R = Ph; X = OH
3: R = CH_3; X = OH
4: R = H; X = OAc
5: R = H; X = Br
6: R = H; X = OMe
7: R = X = H



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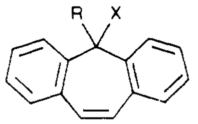
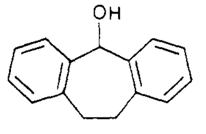
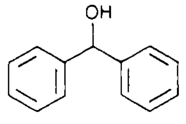


9: R = H; X = OH
10: R = CH_3; X = OH



11a



11b

Photolysis of **1–5** (10^{-3} M, 254 nm, argon-saturated solution, Rayonet RPR 100 reactor, 5–30 min) in aqueous MeOH or aqueous CH_3CN (ACN) solutions, depending on the substrate, resulted in efficient solvolysis. Thus, **1** and **2** gave the corresponding methyl esters as the only product in low (<20%) conversion experiments on photolysis in 50% (v/v) MeOH–H_2O (eq 1). Photolysis in 10–50% ACN–H_2O gave no observable reaction in the same irradiation time. For **4** and **5**, photosolvolysis was carried out in 50% ACN–H_2O. For 9-bromofluorene (**5**) the only product was **1** even at high conversion (>40%), whereas a low yield (~20%) of **14** was observed along with the major product **1** (80%) on photolysis of **4**. For **1** and **2** at conversions greater than ~20%, increasing yields of radical-derived products were observed and became the only products at ~100% conversion (Figure 1). From this plot, it seems clear that the products

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(1) A preliminary account of this work has appeared: Wan, P.; Krogh, E. *J. Chem. Soc., Chem. Commun.* **1985**, 1027.

(2) Natural Sciences and Engineering Research Council of Canada University Research Fellow, 1984–1989.

(3) Cristol, S. J.; Bindel, T. H. *Org. Photochem.* **1983**, *6*, 327.

(4) Turro, N. J.; Wan, P. *J. Photochem.* **1985**, *28*, 93.

(5) Wan, P. *J. Org. Chem.* **1985**, *50*, 2583.

(6) Wan, P.; Yates, K.; Boyd, M. K. *J. Org. Chem.* **1985**, *50*, 2881.

(7) Wan, P.; Chak, B. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1751.

(8) Kochi, J. K. In *Free Radicals*: Kochi, J., Ed.; Wiley: New York, 1973; Vol. II, Chapter 23.

(9) Wan, P. Unpublished results.

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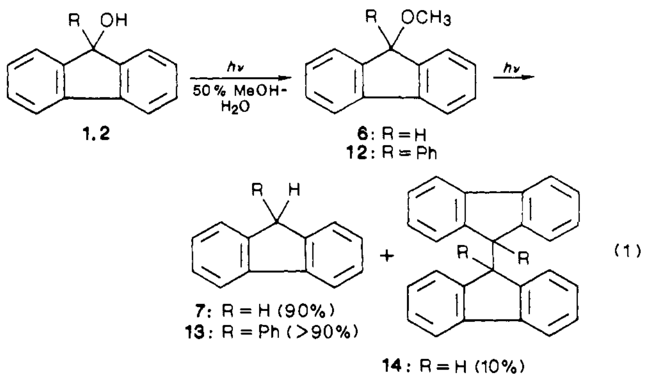


1.2

6: R=H
12: R=Ph

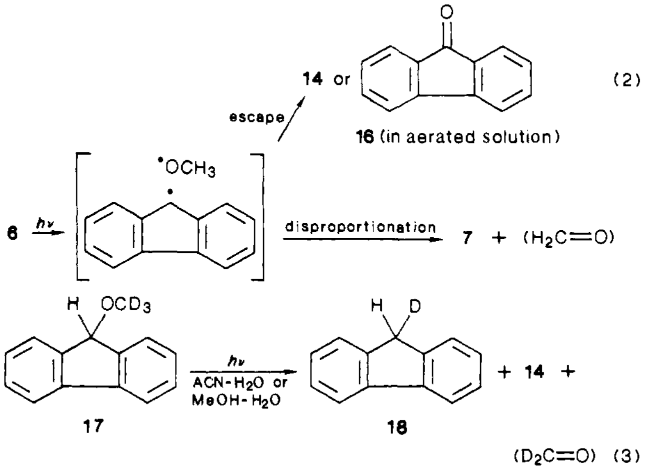
7: R = H (90%)
13: R = Ph (>90%)

14: R=H (10%)
15: R= Ph (not observed)

(1)

fluorene (7) and bifluorene (14) arise via secondary solvolysis of the initially formed methyl ether 6. This was confirmed by independent photolysis of 6 in MeOH-H_2O or ACN-H_2O, which gave only 7 (90%) and 12 (10%) at all conversions and no evidence for the possible solvolysis product 1. For 2, only 13 was observed on extended photolysis (eq 1).

That 6 failed to undergo photosolvolysis was unexpected at first considering that both 1 and 4 photosolvolyzed. However, a recent report by Tomioka et al.[10] has shown that photolysis of 6 and other 9-fluorenyl ethers in *aerated* alcohol solvents results in homolysis of the C-OR bond followed by either trapping of the 9-fluorenyl radical by dissolved oxygen (to give 9-fluorenone (16)) or disproportionation of the radical pair (to give 7 and $H_2C{=}O$) (eq 2). In our study, the ratio of 7 to 14 (90:10) remained unchanged on photolysis of 6 in deaerated MeOH-H_2O or ACN-H_2O. This suggests that 7 also arises via disproportionation of the initially generated radical pair, as opposed to abstraction of a hydrogen atom from solvent. This pathway was confirmed by photolysis of the trideuteriomethyl ether derivative 17 in aqueous MeOH or ACN, which gave 9-deuteriofluorene (18) as the exclusive photoreduction product, in addition to 14 (eq 3).



16 (in aerated solution)

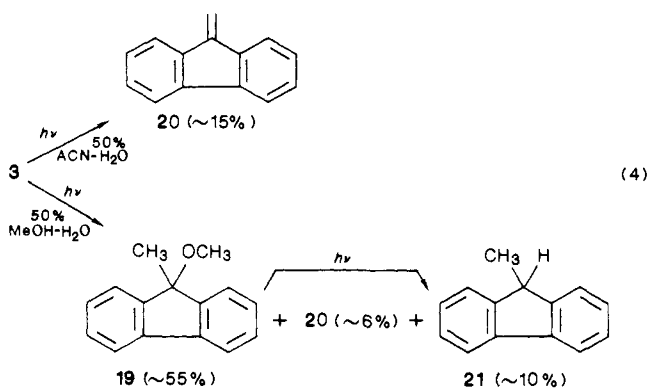
(2)

17

18

(3)

Photolysis of 3 in 50% MeOH-H_2O gave the corresponding ether 19 and 9-methylenefluorene (20) (eq 4), along with increasing amounts of 21 on continued photolysis. As was demonstrated for the photosolvolysis of 1, it is assumed here that 21 arises from secondary photolysis of 19. When 3 was photolyzed in 10-50% ACN-H_2O, only 20 was observed. In contrast, photolysis of 3 over the same time period in pure ACN gave a complicated mixture of products, one of which (~15%) was 20, as identified by its characteristic UV absorption spectrum and the ^1H NMR singlet at δ 6.0. The other products observed were not identified. That 3 gave only 20 on photolysis in 10-50% ACN-H_2O whereas both of 1 and 2 gave no reaction in this solvent under the same photolysis sime is consistent with formation of 9-fluorenyl cation intermediates on photolysis of these compounds in aqueous solution. That is, formation of 20 most likely arises via E1 elimination of photogenerated 9-methyl-9-fluorenyl cation in 10-50% ACN-H_2O. In 50% MeOH-H_2O, competing nucleophilic trapping by MeOH (and also by water, see below) becomes the major reaction pathway.



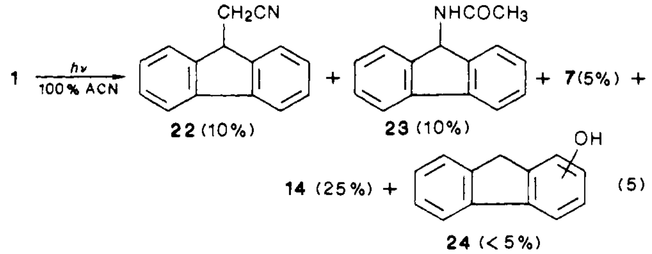
20 (~15%)

(4)

19 (~55%)

21 (~10%)

Product studies of 1 were also carried out in pure ACN and pure MeOH solutions, to examine the effect of the absence of water on photosolvolytic efficiency. As was noted above, photolysis of 1 in 10-50% ACN-H_2O resulted in essentially no observable reaction except on prolonged photolysis. However, photolysis in pure ACN (same photolysis time) resulted in extensive decomposition of 1, to give mostly the 9-fluorenyl radical derived products shown in eq 5, as deduced by GC/MS and preparative TLC, coupled with ^1H NMR. Initial C-OH homolysis followed by recombination of the radical pair can give back 1 or the hydroxyfluorenes 24 (presumed to consist of a mixture of 2- and 4-hydroxyfluorenes). Escape of the 9-fluorenyl radical would give 14. Abstraction of a hydrogen atom from the solvent ACN by the 9-fluorenyl radical would give 7 and and a cyanomethyl radical, which on recombination with another 9-fluorenyl radical accounts for 22. Formal heterolysis of the C-OH bond followed by trapping of the 9-fluorenyl cation by ACN and subsequent hydrolysis by residual water in the solvent would give acetamide 23, which is the minor photosolvolysis product observed in pure ACN. The addition of water to ACN (e.g., in 80% H_2O-ACN) nearly completely eliminates the above homolysis pathway, which is consistent with promotion of formal C-OH bond heterolysis, followed by trapping of the 9-fluorenyl cation by solvent water. Photolysis in pure MeOH did result in formation of methyl ether 6 via photosolvolysis, but the yield was reduced as compared with that in aqueous MeOH solvents, and the product mixture was accompanied by minor amounts of 7 and 24 (even at low conversion), indicating that homolysis of the C-OH bond competes to some extent. Increasing the mole fraction of water suppressed contribution of the homolytic pathway in favor of the formal heterolytic one, as manifested by a cleaner photosolvolytic reaction.



22 (10%)

23 (10%)

24 (< 5%)

(5)

2-Phenylbenzyl alcohol (8) and benzhydrol (11b) did not undergo photosolvolysis in 50% MeOH-H_2O under conditions that lead to extensive solvolysis of 1, and >95% of the substrate was recoverable after photolysis. On prolonged irradiation, 8 slowly isomerized to 3-phenylbenzyl alcohol.[11] These results suggest

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(10) Tomioka, H.; Nakamura, H.; Izawa, Y. *J. Chem. Soc., Chem. Commun.* 1983, 1070.

(11) The mechanism of this isomerization probably involves benzvalene intermediates. The isomerization is solvent independent and resembles the photoisomerization of 2-phenyltoluenes and related compounds,[12] which are believed to proceed via benzvalene intermediates.

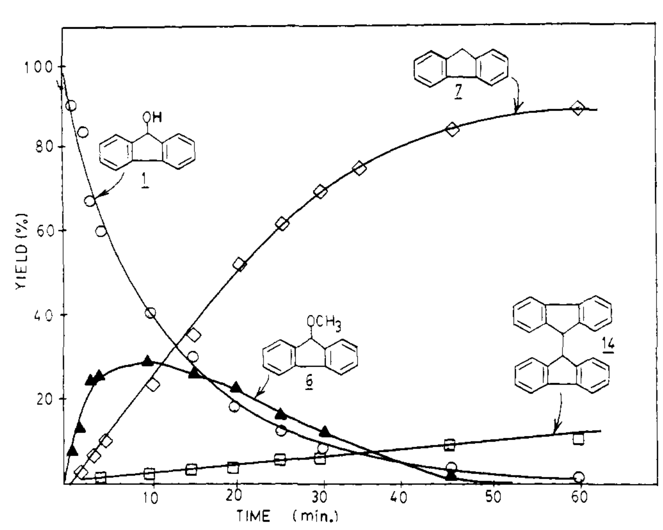
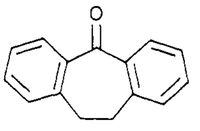


Figure 1. Plot of the product distribution vs time of the photolysis of **1** in 50% MeOH-H_2O.

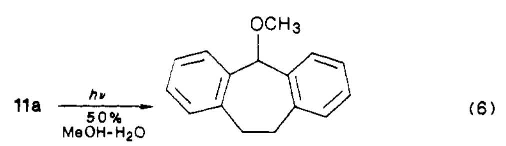
that removing the possibility of conjugation of the ICA to give a four π cation on solvolysis also removes the driving force for photosolvolysis in these systems.

The 5-suberenol derivatives **9** and **10** are precursors of dibenzotropylium ions on solvolysis. Both of **9** and **10** solvolyze readily (thermal reactions) in acidic aqueous alcoholic media (pH < 2) where all of **1–5** are stable. In neutral 50% MeOH-H_2O, both of **9** and **10** are thermally stable. Photolysis of **9** and **10** under conditions which lead to extensive photosolvolysis of **1** resulted in no observable reaction, and >95% of the materials could be recovered unchanged. Neither homolysis or heterolysis was observed. On prolonged photolysis (~30 min), **9** gave low yields of 5-suberone (**25**) (~20%).[13] It is clear that the presence of six π electrons in the ICA in **9** and **10** fails to provide any driving force for photosolvolysis in contrast to its high solvolytic reactivity in the ground state.



25

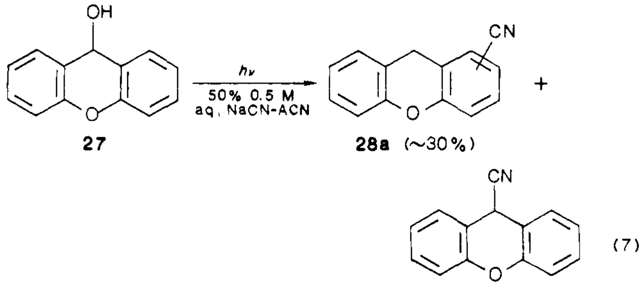
5-Suberol (**11a**) lacks the possibility of forming a *cyclically conjugated* ICA on solvolysis. This alcohol was found to solvolyze thermally in dilute acid solution (pH < 2) but was stable in neutral solution. Photolysis of **11a** in neutral 50% MeOH-H_2O resulted in clean conversion to the corresponding methyl ether **26** (eq 6).



26 (20-50%)

Conversions were lower than for **1** under the same conditions, but the yields were clearly substantial (~20–50%), *without* observable secondary photochemistry. The observation that **11a** photosolvolyzes in aqueous solution supports the notion that the presence of six π electrons in the ICA of **9** and **10** actually *hinders* photosolvolysis and the presence of four π electrons (in **1–5**) *enhances* photosolvolysis.

Interestingly, no nucleophilic trapping product was observed for any of **1–3** when photolyzed in either 50% 0.25 M NaCN-ACN or 50% 0.25 M NaBr-ACN. We have shown that 50% 0.25 M NaCN-ACN is a relatively nucleophilic medium, as we have isolated high yields of the corresponding cyano derivative on photolysis of 2,6-dimethoxybenzyl alcohol (DMBA).[7] The possibility that cyanide (or bromide) ion has a high propensity only for photogenerated methoxybenzyl carbocations was considered but ruled out since photolysis of 9-hydroxyxanthene (**27**) in 50% 0.25 M NaCN-ACN gave ~30% cyanoxanthene **28a** (presumed to be mixture of the 2- and 4-isomers) and ~20% of 9-cyanoxanthene (**28b**) (eq 7). The observed relative yields of **28a** and **28b** are somewhat dependent on the H_2O-ACN ratio. The mechanism of this reaction clearly involves formation of the 9-xanthylium cation as the intermediate, as has been established for other 9-xanthenol derivatives studied in this laboratory.[6] When 5-suberol (**11a**) was photolyzed under identical conditions, only a trace (~5%) of 5-cyanosuberane was observed, which was identified by its ^{1}H NMR, IR, and its mass spectra. McClelland et al.[15] have measured the lifetime of photogenerated 9-xanthylium cation in aqueous solution to be 8 × 10^{-5} s. The lifetime of 9-phenyl-9-xanthylium cation has also been measured (4.3 × 10^{-2} s).[16] The 5-suberanyl cation (from **11a**) would be anticipated to be *less* stable than the 9-xanthylium cation and McClelland[17] has estimated a lifetime for this cation to be ~3 × 10^{-8} s, which is about the same as for bis(4-methylphenyl)methyl cation.[15] Since cyanide ion is not known to attack photogenerated carbocations at the diffusion-controlled rate but at ~10^8 M^{-1} s^{-1},[17] it is clear that the yield of cyanide-trapping product observed depends critically on the *lifetime* of the cation itself. In other words, cyanide ion must compete with H_2O for cation (see section on ^{18}O-exchange studies), which has a concentration of ~28 M in the solvent system used. The photogenerated 9-fluorenyl cation is expected to be *less* stable than the 5-suberanyl cation, and hence, an even lower yield of cyanide-trapping product is anticipated. Under our experimental conditions, the yield is too low for detection.



^{18}O-Exchange Studies. When **1** and **11a** (natural abundance materials) were photolyzed for the same length of time (using a merry-go-round appratus; Rayonet reactor with 254-nm lamps) in a solvent consisting of 50% (v/v) ACN-H_2O (water portion enriched with 20% ^{18}O) for 20 min, the recovered substrates were found to be enriched with ^{18}O, as determined by mass spectrometry, to the extent of 11 ± 2% for **1** and 6 ± 1% for **11a**. The ratio of percent ^{18}O incorporation (for **1**:**11a**) was 1.8, which compares with a ratio of 2.1 for quantum yield of methyl ether formation of these substrates in 50% MeOH-H_2O (calculated from the results of Table 1). The two ratios agree favorably, as would be expected, for a mechanism involving carbocation in-

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(12) (a) Abramovitch, R. A.; Takaya, T. *J. Chem. Soc., Chem. Commun.* **1969**, 1369. (b) Mende, U.; Laseter, J. L.; Griffin, G. W. *Tetrahedron Lett.* **1970**, 3747.

(13) The mechanism for formation of 5-suberone (**25**) (10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-one) from **9** is believed to arise via initial photodeprotonation from the 5-position, to give the 5-hydroxy-5-suberenyl (eight π antiaromatic) carbanion, which on subsequent protonation at the 10-position gives the enol of **25**. The photogeneration of the parent 5-suberenyl carbanion in aqueous solution has been reported by us recently,[14] and it seems reasonable that a similar reaction is available for **9**. It is worthy to note that instead of photosolvolyzing—which would generate a cyclically conjugated six π carbocation—**9** prefers to undergo deprotonation to give a cyclically conjugated eight π carbanion intermediate. The details of this rather surprising process will be reported in due course.

(14) Wan, P.; Krogh, E.; Chak, B. *J. Am. Chem. Soc.* **1988**, *110*, 4073.

(15) McClelland, R. A.; Kanagasabapathy, V. M.; Steenken, S. *J. Am. Chem. Soc.* **1988**, *110*, 6913.

(16) McClelland, R. A.; Banait, N.; Steenken, S. *J. Am. Chem. Soc.* **1989**, *111*, 2929.

(17) McClelland, R. A. Private communication.

Table I. Product Quantum Yields (Φ_p) for Photosolvolysis of **1–5** and **8–11** in 50% MeOH (or ACN)–H_2O^a

compd	Φ_p^b	compd	Φ_p^b
1	0.15, 0.10,^{c} ~0.17^d	**8**	0.00^g
2	0.15	**9**	0.00^h
3	0.12	**10**	0.00^i
4	0.04^e	**11a**	0.07
5	0.14^e	**11b**	0.00^i
6	~0.2^f		

[a] Determined with the photosolvolytic reaction of 2,6-dimethoxybenzyl alcohol in 50% MeOH–H_2O as the secondary actinometer (Φ_p = 0.31).[7] λ_{ex} = 254 nm. Estimated error is ±10% of the quoted values. [b] Unless otherwise noted, quoted quantum yields are for methyl ether formation in 50% MeOH–H_2O (water at pH 7). [c] In 100% MeOH. [d] In 100% ACN. Quantum yield is for loss of substrate. [e] Quantum yield for 9-fluorenol (**1**) formation in 50% ACN–H_2O. [f] Quantum yield for loss of substrate (products are **7** and **14**). [g] Photosolvolysis not observed but slow photoisomerization to 3-phenylbenzyl alcohol occurs in all solvents. [h] Photosolvolysis not observed but formation of **24** becomes significant on extended photolysis.[13] [i] Photosolvolysis not observed and substrate can be recovered unchanged.

Table II. Product Quantum Yields (Φ_p) for Photosolvolysis of **1** in 50% ROH–ACN, 50% 0.50 M NaCN–ACN, and 0.50 M NaBr–H_2O^a

solvent^b	product^c	Φ_p
MeOH	$FlOCH_3$	0.15
EtOH	$FlOCH_2CH_3$	0.13
i-PrOH	$FlOCH(CH_3)_2$	0.09
t-BuOH	$FlOC(CH_3)_3$	0.06
NaCN–H_2O^d	FlCN	0.00^f
NaBr–H_2O^e	FlBr	0.00^g

[a] Quantum yields calculated relative to the run in 50% MeOH–H_2O (Φ_p = 0.15). Estimated errors ±15% of quoted value. [b] 50% (v/v) ROH–H_2O unless otherwise noted. [c] Fl = 9-fluorenyl. [d] 50% 0.50 *M* NaCN–ACN (pH ≈ 10). [e] 50% 0.50 *M* NaBr–ACN (pH ≈ 7). [f] No detectable FlCN (or isomer) by NMR. [g] No detectable FlBr (or isomer) by NMR.

termediates. When 9-fluorenol-^{18}O (20% enriched) was photolyzed in aqueous ACN, loss of ^{18}O was observed. Thus, after 5 min of photolysis the recovered substrate contained 11% ^{18}O, and after 10 min only 6% ^{18}O remained. All of the above ^{18}O exchanges are not observed in the dark, as shown by control experiments.

Product Quantum Yields. Product quantum yields (Φ_p) for photosolvolysis of **1–3** and **8–11a** in 50% MeOH–H_2O (water portion at pH 7) and of **4** and **5** in 50% ACN–H_2O were measured with the photosolvolytic reaction of DMBA in MeOH–H_2O as the secondary actinometer (λ_{ex} = 254 nm; Φ_p = 0.31).[7] The results are tabulated in Table I. The highest photosolvolysis quantum yield was observed for **1** in 50% MeOH–H_2O. The photosolvolysis of **1** was also carried out in several additional 50% ROH–H_2O mixtures (R = Et, *i*-Pr and *t*-Bu), in 50% 0.25 M NaCN–ACN and in 50% 0.25 M NaBr–ACN; the corresponding Φ_ps are tabulated in Table II. The observed Φ_ps decrease with increasing bulk of the alcohol nucleophile (Table II), which is in accord with previous results observed for the photosolvolysis of DMBA.[7] Product quantum yields for photosolvolysis of **1** in 50% MeOH–H_2O were also measured as a function of pH by adjusting the pH of the aqueous portion of the solvent mixture with either NaOH or H_2SO_4, as required. A plot of Φ_p vs pH (where the quoted pH is that of the aqueous portion) is shown in Figure 2, with plots of the pH dependence of photosolvolysis of DMBA[7] and 3-methoxybenzyl alcohol[7] also included for comparison purposes. A previous study from our laboratory[7] shows that acid catalysis of photodehydroxylation is observed only for those alcohols with relatively low Φ_ps in pH 7, e.g., 3-methoxybenzyl alcohol. Those alcohols with significantly higher Φ_ps at pH 7 (e.g., DMBA) failed to show acid catalysis down to pH ≈ 0. The absence of any pH effect in the photosolvolysis of **1** over the pH range 0–14 is consistent with its significant reactivity at pH 7.

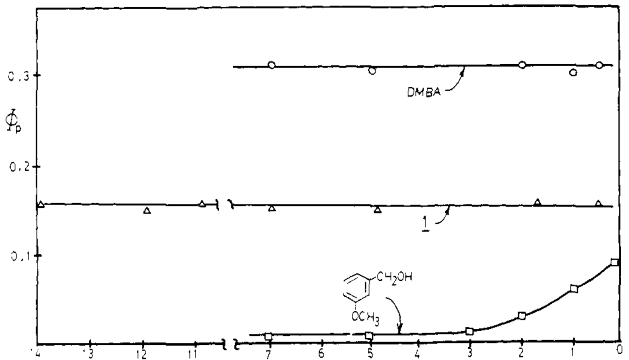


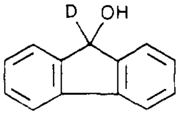
Figure 2. Plot of the quantum yield of methyl ether formation (Φ_p) as a function of pH for **1**, DMBA, and 3-methoxybenzyl alcohol.

Table III. Fluorescence Lifetimes As Measured by Time-Correlated Single-Photon Counting^a

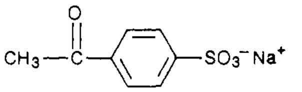
compd	τ (80% H_2O–ACN)	τ (100% ACN)
1	<0.3^b	0.35 ± 0.1
2	<0.3^b	0.30 ± 0.1
3	<0.3^b	0.30 ± 0.1
7	5.6 ± 0.1^c	6.7 ± 0.1^c
9	0.84 ± 0.05	2.3 ± 0.1
10	2.06 ± 0.05	2.16 ± 0.05
11a	4.9 ± 0.1^c	6.6 ± 0.1^c

[a] Unless otherwise noted, the excitation was via a mode-locked, sync-pumped, cavity-dumped dye laser (at 266 nm). All fluorescence decays were single exponential after deconvolution. Lifetimes via laser excitation were measured at the Center For Fast Kinetics Research, Austin, Texas. [b] Estimated upper limit based on measured lifetime in 100% ACN. [c] Lifetimes measured with a H_2-filled thyrtron-triggered spark lamp at 260 nm.

Isotope Effects. As additional probes of the mechanism of photosolvolysis, both solvent deuterium and α-deuterium isotope effects on Φ_p were measured for **1**. The solvent isotope effect was measured by carrying out photolyses in 50% H_2O–MeOH and in 50% D_2O–MeOD and comparing the extent of reaction by GC and ^1H NMR. The conversion was kept low (<20%) to avoid secondary photochemistry. In this way, Φ_{H_2O}/Φ_{D_2O} was 1.32 ± 0.05, where Φ_{H_2O} and Φ_{D_2O} are the product quantum yields for methyl ether formation in H_2O–MeOH and D_2O–MeOD, respectively. For comparison purposes, the photodecomposition of 9-methoxyfluorene (**6**) was also studied in the 50% H_2O–ACN and D_2O–ACN. No difference in relative reactivity was observed. The α-deuterium isotope effect was measured by comparing the photosolvolytic reactivity of **1** with 9-deuterio-9-fluorenol (**29**) in 50% H_2O–MeOH, which gave Φ_H/Φ_D = 1.21 ± 0.06, where Φ_H and Φ_D are the product quantum yields for methyl ether formation of **1** and **29**, respectively.



29



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Fluorescence Spectra and Lifetimes. Steady state fluorescence spectra were recorded on a Perkin-Elmer MPF 66 spectrofluorimeter with a substrate concentration of ~10^{-4} M. Fluorene (**7**) is known to be a strongly fluorescent molecule (λ_{max} = 305 nm) and photostable in deoxygenated solution. A fluorescence quantum yield (Φ_f) of 0.7[18] has been reported for **7** in polar as well as in nonpolar solvents. We have found that water has a moderate quenching effect on fluorene (**7**) emission relative to pure ACN. If we assume that Φ_f = 0.7 in 100% ACN, then Φ_f = 0.6 in 80% H_2O–ACN. This slight quenching effect was also observed in the measured fluorescence lifetimes (Table III), going from 6.7 ns in 100% ACN to 5.6 ns in 80% H_2O–ACN. Substitution at

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(18) Murov, S. L. *Handbook of Photochemistry*; M. Dekker: New York, 1973.

the 9-position by OH in **1** (or in **2** and **3**) greatly reduced the fluorescence emission ($\Phi_f < 0.01$) ($\lambda_{max} = 325$ nm) in both 100% ACN and in 80% H_2O–ACN, compared with that of **7**. However, emission of **1** is about 1 order of magnitude *stronger* in 100% ACN than in 80% H_2O–ACN. These observations are consistent with chemical deactivational pathways now open to **1** (compared to **7**) and the fact that the presence of water enhances one of these pathways, viz., photosolvolysis. In 80% H_2O–ACN, the emission was barely detectable with our instrument at the highest sensitivity. With continued irradiation of the cuvette sample in the instrument compartment, the emission intensity increased, indicative of formation of more fluorescent photoproducts. This effect was even more dramatic when the solvent used was 50% MeOH–H_2O or 100% MeOH. In these cases, the growth in emission intensity occurred much more quickly; the emission spectrum of an exhaustively irradiated sample being identical with that of fluorene (**7**).

Fluorescence lifetimes of **1**–**3** were measurable in 100% ACN with picosecond laser excitation and were found to be ~0.3 ns, whereas in 80% H_2O–ACN neither picosecond laser excitation or excitation with a standard H_2 spark lamp gave measurable lifetimes. It was concluded that the lifetimes in this solvent were too short for the instrument employed, and an upper limit of 0.1 ns was estimated. Since Φ_f in 100% ACN was about a factor of 10 more intense than in 80% H_2O–ACN, assuming that k_f remains constant in the two solvent systems, we calculate $\tau \approx 30$ ps in predominately aqueous solution.[19]

Fluorescence emissions from **9**–**11a** were readily detectable since they are much more strongly emitting than **1**–**6**. The fluorescence emission of **9** ($\lambda_{max} = 330$ nm; $\Phi_f \approx 0.1$) has a slightly more structured appearance than the absorption or excitation band. A similar observation was noted for **10** but not for **11a**. This is indicative of a more rigid S_1 state in both of **9** and **10** compared with the ground state.[20–22]

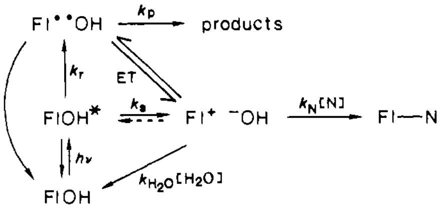
Fluorescence lifetimes of **9**–**11a** were measured in both 100% ACN and in 80% H_2O–ACN and are tabulated in Table III. Both **9** and **11a** are quenched by H_2O whereas **10** is not affected to any measurable extent. Fluorescence quenching of **9** is due to photodeprotonation of the dibenzylic proton in aqueous solution,[14] a pathway clearly not available to **10**. In addition, it also does not photosolvolyze. The quenching observed for **11a** is attributable to photodehydroxylation in aqueous solution.

Triplet-State Sensitization. Sodium 4-acetylbenzenesulfonate (**30**) ($E_T \approx 74$ kcal mol^{-1})[23] was used as the water-soluble triplet sensitizer for reaction of **1** ($E_T \approx 68$ kcal mol^{-1})[24] at $\lambda_{ex} = 300$ nm in 50% MeOH–H_2O. These experiments yielded no photoproduct, and the substrate could be recovered unchanged. We conclude therefore that the triplet state of **1** is nonreactive in aqueous MeOH and that it is the S_1 state which is responsible for photosolvolysis.

Discussion

Mechanism and Rates of Photodehydroxylation. The photosolvolytic behavior of **1**–**3** and **11a** closely resembles that observed for other benzylic-type alcohols studied in our laboratory,[4–7,25] all of which are known to proceed via initial heterolysis (photodehydroxylation) from S_1, to give an ion pair. Acid catalysis of photosolvolysis observed for several of these benzylic systems[4,5,7] was taken as strong evidence in support of initial heterolysis, as opposed to initial homolysis followed by fast electron transfer, which cannot be catalyzed by protons. In addition, the demonstrated adiabatic nature of reaction in the 9-xanthenols[6] added further support for initial heterolysis raising the possibility that adiabaticity may also be a general feature in all photodehydroxylations.

Scheme I



The results of product studies in alcoholic solvents and in the presence of cyanide ion, as well as the ^{18}O-exchange studies, indicate that the photosolvolysis of 9-fluorenols **1**–**3** and 5-suberol (**11a**) involves carbocations intermediates. Derivatives **4** and **5** probably behave similarly. A mechanistic possibility that must now be addressed is whether the carbocation is formed via a simple heterolysis of the C–OH bond, or via initial homolysis followed by fast electron transfer (ET). The latter pathway has been shown to occur in the photochemistry of simple alkyl halides by Kropp and co-workers.[26] A recently reported[27] value for the oxidation potential of 9-fluorenyl radical of −0.76 V (in ACN) along with an estimated[28,29] value of the oxidation potential of hydroxide ion of ~+1.7 V gives $\Delta G \approx -23$ kcal mol^{-1} for conversion of Fl• •OH to Fl^{+-}OH (Fl = 9-fluorenyl) in ACN. In aqueous solution, the process should be even more exothermic. Thus, thermodynamic arguments cannot be used to rule out the ET pathway.

Although acid catalysis of photosolvolysis could not be demonstrated for **1**–**3** and **11a** in the present study, several observations argue for initial heterolysis in the reaction of these substrates: (i) Fluorescence quenching of S_1 (both steady-state and transient measurements) observed for **1**–**3** and **11a** on addition of water is consistent with promotion of heterolysis on increasing the polarity of the solvent. (ii) The observation of elimination product **20** *without* any side products on photolysis of **3** in aqueous solution is consistent with elimination from the ion pair and *not* from a radical pair. The radical pair is known to give several additional side products in addition to **20**, as observed from irradiation in pure ACN. (iii) The solvent isotope effect observed for **1** also argues for a simple heterolytic cleavage step. The lower yield of methyl ether product observed in 50% D_2O–MeOD (compared to that of H_2O–MeOH) can best be accomodated by a mechanism in which the primary photochemical step is loss of hydroxide ion assisted by proton transfer from solvent water. In a mechanism involving initial homolysis followed by fast ET, the solvents H_2O and D_2O should have little differential effect on the initial homolytic cleavage. For example, we have already seen that there is no observable solvent isotope effect for the photodecomposition of 9-methoxyfluorene (**6**), the mechanism of which clearly involves initial homolysis. The subsequent electron-transfer step should be essentially H_2O–D_2O independent since the difference in solvent polarity between these two solvents is negligible.[30] The trapping

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[19] The method used here for estimating τ is essentially identical with that used by Cristol and Stricker for estimating the lifetimes of several benzobicyclo[2.2.2]octadienes: Cristol, S. J.; Aeling, E. O.; Strickler, S. J.; Ito, R. D. *J. Am. Chem. Soc.* **1987**, *109*, 7101.

[20] Werner, T. C. In *Modern Fluorescence Spectroscopy*; Wehry, E. L., Ed.; Plenum Press: New York, 1976; Vol. 2, Chapter 7.

[21] Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, 1978.

[22] Cowan, D. O.; Drisko, R. L. *Elements of Organic Photochemistry*; Plenum Press: New York, 1976.

[23] Estimated on the basis of the known E_T of acetophenone derivatives.[18]

[24] Estimated on the basis of the known E_T of fluorene (**7**).[18]

[25] It should be noted that Ullman and co-workers (Lin, C.-I.; Singh, P.; Ullman, E. F. *J. Am. Chem. Soc.* **1976**, *98*, 6711 and 7848) have reported the solvolysis of benzyl alcohols in bichromophoric systems which have a quite different mechanistic behavior. In these systems, reaction is initiated by electron transfer from a donor chromophore to the benzyl alcohol. Such a mechanistic possibility is not applicable to our substrates.

[26] Kropp, P. J. *Acc. Chem. Res.* **1984**, *17*, 131. It should be pointed out that there is no evidence to indicate that the homolysis followed by ET pathway is generally applicable to the photobehavior of benzylic halides or other types of C–X bonds such as C–OH.

[27] Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132.

[28] Wubbels, G. G.; Kalhorn, T. F.; Johnson, D. E.; Campbell, D. *J. Org. Chem.* **1982**, *47*, 4664.

[29] Frank, A. J.; Grätzel, M.; Henglein, A. *Ber. Bunsenges Phys. Chem.* **1976**, *80*, 593.

[30] Weast, R. C., Ed.; *CRC Handbook of Chemistry and Physics*, 56th ed.; CRC Press: Cleveland, 1975; p E55.

Table IV. Estimated Rate Constants for Solvent-Assisted Photodehydroxylation from S_1 (k_s)[a]

compd	τ	k_s (s^{-1})
1	~30 ps[c]	1.6×10^{10}
2	~30 ps[c]	1.6×10^{10}
3	~30 ps[c]	1.3×10^{10}
9	0.84 ns[b]	$<10^6$ [d]
10	2.06 ns[b]	$<10^6$ [d]
11	4.9 ns[b]	4.6×10^7

[a] In 50% $MeOH-H_2O$. [b] Lifetimes measured in 80% H_2O–ACN, but they do not change appreciably in 50% $MeOH-H_2O$. [c] Calculated on the basis of the measured lifetime in 100% ACN (see the text). [d] Estimated upper limit. No photosolvolysis observed for these compounds at pH 7.

of photogenerated cations by MeOH and MeOD should only display a secondary effect.[33] Thus, the observed substantial solvent isotope effect for the quantum yield of methyl ether formation in the two solvent systems of 1.32 is too large for the ET mechanism. However, the magnitude of this solvent isotope effect is almost the same as that observed for dimethoxybenzyl alcohol photosolvolysis,[7] where initial heterolysis has been established more convincingly.

A working mechanism for reaction of **1**–**3** and **11a** in aqueous solution consistent with the above arguments and general results of this study is shown in Scheme I (shown for FlOH = **1**), where the primary photochemical event which leads to solvolysis is C–OH heterolysis (k_s; solvent-assisted photodehydroxylation). We have no direct evidence that this photodehydroxylation step is adiabatic in these compounds, but because the reaction of the 9-xanthenols has been shown to be adiabatic,[6] we cannot rule out adiabatic return to FlOH* via recombination of $(Fl^+)^*$ with OH^- (or H_2O). Significant adiabatic return to FlOH* would result in non-first-order decay of FlOH*, but this valuable test for adiabatic return is not useful in these systems due to the difficulty encountered in measuring fluorescence lifetimes of FlOH* in aqueous solution. The predominant mode of return of Fl^+ to FlOH is believed to be via k_{H_2O}, i.e., capture of Fl^+ (or $(Fl^+)^*$) by solvent H_2O, which has been demonstrated to occur by the ^{18}O-exchange studies. In addition, capture by external nucleophiles N would give Fl–N. A *competing* primary pathway from FlOH* is C–OH bond homolysis (k_r). This pathway is significant in 100% ACN and is less so in 100% MeOH. However, in essentially aqueous solutions, it is believed to be insignificant. Homolysis of the C–OH bond is probably nonadiabatic (as there is no literature precedent to suggest otherwise). Once formed, it will either (i) recombine on the ground-state surface to give back FlOH (or an isomer); (ii) react with solvent, which could lead to several products; or (iii) escape the solvent cage to combine with other $Fl^\bullet$ to give bifluorene (**14**).

Assuming that k_s is the predominant pathway for formation of $Fl^{+-}OH$, the quantum-yield expression for methyl ether formation in 50% $MeOH-H_2O$ (Φ_p) is given by eq 8, where k_{MeOH}

$$\Phi_p = \left(\frac{k_{MeOH}[MeOH]}{k_{MeOH}[MeOH] + k_{H_2O}[H_2O]}\right)k_s\tau \qquad (8)$$

is the second-order rate constant for trapping of Fl^+ by MeOH and τ is the singlet lifetime of FlOH*. A further simplifying assumption that $k_{MeOH} \approx k_{H_2O}$[31] results in eq 9, taking into account

$$k_s \approx \Phi_p(0.31\tau)^{-1} \qquad (9)$$

the mole fraction of MeOH and H_2O in the solvent system. In this way, values of k_s, the rate constant for solvent-assisted photodehydroxylation, may be estimated. The results are shown in Table IV. It is clear from these data that the fluorenyl system is the most reactive with respect to photodehydroxylation (i.e., carbocation formation), followed by the suberanyl system (**11a**), with suberenyl system (**9** and **10**) being nonreactive.

Effect of Leaving Group. The results of Table I indicate that, with respect to photosolvolysis, the hydroxide ion is the best leaving group for this purpose in the fluorenyl system. This is unexpected based on what is known about the relative leaving-group abilities (in ground-state solvolyses) of the leaving groups studied in this work. However, the leaving-group effects observed for the fluorenyl system should not be taken as general for all photosolvolytic reactions since this system is complicated by the ease of competing homolysis, as exemplified by 9-methoxyfluorene (**6**), which undergoes homolysis in all solvents. The absence of solvolysis of **6** in aqueous solution can be rationalized by noting the favorability of homolysis to give a relatively stable 9-fluorenyl radical and a methoxy radical. The study by Tomioka et al.[10] of a range of 9-alkoxyfluorenes also indicates that photohomolysis of the C–O bond is extremely facile in these alkoxy-substituted substrates. On the other hand, homolysis in 9-fluorenol (**1**) would give the hydroxyl radical, which is much less stable than methoxyl,[8] in addition to 9-fluorenyl, which is common to both systems. The low photosolvolysis quantum yield observed for **4** (FlOAc) in 50% H_2O–ACN is probably due to a competing homolysis which efficiently leads back to substrate on recombination, with a minor amount escaping the cage to give **14**. Unlike the situation in $Fl^{\bullet\bullet}OMe$, $Fl^{\bullet\bullet}OAc$ cannot disproportionate to give fluorene but can only recombine or escape the solvent cage. Surprisingly, when the leaving group is bromide ion (in **5**), only solvolysis is observed. According to Kropp,[26] alkyl iodides followed by alkyl bromides are most prone to react via homolysis followed by ET. It was anticipated that some radical escape would have been observed for **5** in competition with ET if the Kropp mechanism was operative. However, the clean photosolvolysis observed must indicate either a very fast ET or operation of the heterolytic cleavage pathway.

Isotope Effects for Photodehydroxylation. The solvent isotope effect for the quantum yield of methyl ether formation in 50% $MeOH-H_2O$ (vs 50% $MeOD-D_2O$) was found to be 1.32 ± 0.05 for **1**. If it is assumed that the singlet lifetimes of the substrate in the two media ($MeOH-H_2O$ and $MeOD-D_2O$) are nearly equal[33] and that secondary isotope effects from nucleophilic attack of Fl^+ by H_2O (vs D_2O) and MeOH (vs MeOD) are negligible,[33] then we can estimate that $k_{H_2O}/k_{D_2O} \approx 1.3$, which is the kinetic solvent isotope effect for photodehydroxylation. The magnitude of this effect is consistent with heterolytic C–OH bond cleavage assisted by solvent and not with a simple C–OH bond homolysis step since the latter would be expected to exhibit only a small secondary isotope effect (arising from the difference in C–OH and C–OD bond strengths).

The α-deuterium isotope effect of methyl ether formation ($\Phi_H/\Phi_D = 1.21 \pm 0.06$) in 50% $MeOH-H_2O$ may be converted to a kinetic isotope effect if the fluorescence lifetimes of both **1**

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[31] Ritchie and co-workers[32] have reported relative nucleophilicities of MeOH and H_2O and other nucleophiles toward several relatively stable carbocations. The reported N_+ values for water and MeOH are 0.0 and 0.5, respectively (logarithmic scale), in their respective pure solvents, whereas it is 3.8 for CN^- and 4.5 for ^-OH. To simplify our calculations, we have assumed that MeOH and H_2O are equally nucleophilic for the photogenerated cations in this work. However, it is easy to show that use of Ritchie's N_+ values for relative rates of MeOH and H_2O attack in the calculations does not in fact change the ordering of the calculated relative reactivities reported in Table IV. In addition, it is arguable whether the subsequently calculated rate constants would be more accurate, since it is not known to what degree the difference in nucleophilicity between MeOH and H_2O is carried over for much less stable cations.

[32] Ritchie, C. D. *Acc. Chem. Res.* **1972**, *5*, 348.

[33] We have measured the lifetimes of a number of reacting benzyl alcohol systems in both H_2O and D_2O and the difference in lifetimes is at most ~10%. In addition, deuterium isotope effects on singlet lifetimes are usually not large unless perdeuteration is involved.[34] Furthermore, of the benzyl alcohols we have lifetime data for, the lifetime is slightly longer in D_2O than in H_2O. Thus if the assumption of similar lifetimes is not strictly valid for **1**, it means that our estimate for the kinetic isotope effect (k_{H_2O}/k_{D_2O}) is now a *lower* limit. In terms of the relative nucleophilicity between H_2O and D_2O (or MeOH or MeOD) for cation, we are not aware of any direct measurements for trapping of photogenerated carbocations by these nucleophiles, but it is reasonable to assume[15] that for relatively unstable carbocations the isotope effect would be a secondary one. For much longer lived carbocations such as 9-xanthylium,[15] there is the possibility of general-acid catalysis in water addition, which should show a primary isotope effect.[17]

[34] Swenton, J. S. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C. Eds.; Elsevier: Amsterdam, 1975; Vol. 1, Chapter 5.

and **29** are known, and the assumption is made that the secondary isotope effect from nucleophilic attack of Fl^+ and α-D-Fl^+ by H_2O and MeOH is negligible. Assuming the latter, simplification first gives the expression $k_H/k_D \approx \Phi_H\tau_D/\Phi_D\tau_H$, where k_H and k_D are the rate constants for solvent-assisted photodehydroxylation of **1** and **29**, respectively, and τ_H and τ_D are their respective lifetimes. We have found[35] that α-deuterium substitution (at the 5-position) of both **9** and **11a** lenghthens the lifetime by at most 5% in aqueous solution. Thus the ratio τ_D/τ_H is expected to be very close to unity for **1** and **29**. Hence, we calculate $k_H/k_D \approx 1.2$. A normal α-secondary isotope effect (typically $k_H/k_D \approx 1.3$)[36] is expected if a reaction involves a change from sp^3 to sp^2 hybridization in the transition state, and an inverse effect is expected for the opposite direction. Thus, the observed value of 1.2 is consistent with both C–OH bond heterolysis and homolysis as the primary photochemical step.

Effect of ICA on Carbocation Formation. The primary aim of this study was to delineate the effect of the ICA on photosolvolytic reactivity of dibenzannelated alcohols. The results indicate that there exist a simple "electron-count" rule to predict the relative reactivity of these systems. The rule works by simply counting the maximum contributing number of electrons in the ICA in the incipient carbocation. An electron count of four π is the most favorable, followed by a system in which complete conjugation through the ICA is not possible but possessing a cyclic array nevertheless is. The least reactive system is that in which the incipient carbocation has six π electrons in the ICA. An electron count of four π electrons appears to be particularly favorable as the *9-fluorenols are the most reactive compounds known to date in photodehydroxylation* on the basis of their estimated rate constants (k_s) for reaction, being even more reactive than dimethoxybenzyl alcohols, which have estimated k_5 values of up to 1.9×10^9 s^{-1}.[37]

In the ground state, the order of solvolytic reactivity of the dibenzannelated alcohols studied in this work is the 5-suberenols **9** and **10** > 5-suberol (**11a**) ≫ the 9-fluorenols **1**–**3**. The reactivity trend is exactly reversed to that observed in the excited singlet state. The observed trend in the *ground state* is in accord with what is expected based on Hückel's $4n + 2$ rule for aromaticity and the $4n$ rule for antiaromaticity developed by Breslow.[38] Woodward and Hoffmann,[39] Zimmerman,[40] and Dewar[41] have each developed theoretical predictions for the outcome of ground- and excited-state pericyclic reactions. However, photochemical reactions which give rise to cyclically conjugated charged intermediates have not been addressed in these treatments. We propose that $4n$ π carbocations (e.g., 9-fluorenyl carbocation) have some degree of aromatic stabilization[42] in the excited state (as opposed to its antiaromatic destabilization in the ground state) and that it is this effect which is primarily responsible for the observed reactivity trend in the excited state of these systems. This implicitly assumes that these photodehydroxylations are adiabatic. Although no direct evidence is available at this stage for the systems studied in this work, the known adiabaticity of the 9-xanthenols[6] is encouraging. In addition, recent results of flash-photolysis work[47] (see section below) also indirectly suggest an adiabatic reaction.

Flash-Photolysis Studies. We have recently carried out flash-photolysis studies of 9-fluorenol (**1**) in aqueous MeOH solution using nanosecond laser excitation[47] and have identified both the 9-fluorenyl cation and 9-fluorenyl radical as intermediates. The 9-fluorenyl cation absorption (~640 nm) band increase in intensity with added water at the expense of the 9-fluorenyl radical (~500 nm). These results corroborate the observations made in this study, viz., that solvent polarity has a pronounced effect on the efficiency of the photosolvolysis pathway. Also measured in this study[47] was the quantum yield of 9-fluorenyl cation formation that reaches the thermally equilibrated ground state ($\Phi \approx 0.03$). The *total* photochemical yield of carbocation can be calculated by the product $k_s\tau$ (see Scheme I and eq 8), which gives ~0.5. The large difference in the two cation yields indicates that most of the photogenerated cations are quenched by nucleophiles *before* ever reaching the ground state. This result is consistent with an adiabatic reaction.

Experimental Section

General Procedures. ^1H NMR spectra were recorded on a Perkin-Elmer R32 or Bruker WM250 instruments in $CDCl_3$ (TMS internal standard). UV spectra were obtained on a Perkin-Elmer Lamda 4B spectrophotometer. Mass spectra were taken on a Finnigan 3300 instrument. Melting points were obtained on a Koefler hot-stage microscope and are uncorrected. Gas chromatography was carried out with a Varian 3700 instrument with a Hewlett-Packard 3390A integrator. Photolyses were carried out in Suprasil quartz cuvettes or 200-mL quartz tubes using a Rayonet RPR 100 photochemical reactor.

Materials. Alcohols **8** and **11b** were purchased from Aldrich Chemical Co. and used as received. Alcohols **1**, **9**, **11a**, and **27** were made via $NaBH_4$ reduction of the corresponding ketones, obtained from Aldrich. The α-deuteriated alcohol **29** was made via $LiAlD_4$ reduction of 9-fluorenone. Alcohols **2**, **3**, and **10** were synthesized from the corresponding ketones and the appropriate organolithium or Grignard reagent. 9-Acetoxyfluorene (**4**) was prepared from **1** by treatment with acetyl chloride in pyridine. 9-Bromofluorene (**5**) was prepared from **7**, with *N*-bromosuccinimide in CCl_4. The ethers **6** and **17** were prepared from **5** by reaction with the appropriate alcohol (reflux in the alcohol for several hours).

5-Suberenol (9) (5*H*-Dibenzo[*a*,*d*]cyclohepten-5-ol). To 10 g (49 mmol) of 5-suberenone dissolved in 200 mL of cold MeOH was added 1.0 g (2 equiv) of $NaBH_4$. After 2 h of stirring, the solution was quenched with 100 mL of a saturated NH_4Cl solution and extracted with CH_2Cl_2, to yield a solid which was recrystallized from ligroin: mp 122 °C (lit.[48] mp 122.5–124 °C); yield 8.2 g (80%); ^1H NMR δ 2.42 (d, J = 6 Hz, 1 H), 5.34 (d, J = 6 Hz, 1 H), 7.04 (s, 2 H), 7.2–7.7 (arom, 8 H); mass spectrum (EI) (m/z) 208 (M^+).

5-Methyl-5-suberenol (10) (5-Methyl-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol). To a prepared solution of methyl magnesium bromide (1.5 equiv) in 50 mL of anhydrous ether under N_2 and cooled to –5 °C was added 5.0 g (24 mmol) of 5-suberenone dissolved in 100 mL of ether. After 1 h at reflux the reaction was quenched by diluting with 100 mL of a saturated NH_4Cl solution and then extracted with ether, to yield a solid material recrystallized from hexane: mp 118–120 °C (lit.[49] 113.5–115 °C); yield 3.8 g (71%); ^1H NMR δ 1.6 (br, 3 H), 2.4 (br, 1 H), 6.98 (s, 2 H), 7.2–8.0 (arom, 8 H); mass spectrum (CI) (m/z) 222 ($M^+ + 1$).

9-(Trideuteriomethoxy)fluorene (17). To 3.0 mL of MeOH-d_4 (Aldrich NMR grade, 99.5 atom % D) was added 250 mg (1.0 mmol) of **5**. After 48 h at reflux, the solvent was evaporated to yield a viscous oil which solidified on standing. The crude product was recrystallized from petroleum ether: mp 38–40 °C; yield 150 mg (76%); ^1H NMR δ 5.58 (s, 1 H) 7.2–7.7 (arom, 8 H); mass spectrum (CI) (m/z) 200 ($M^+ + 1$).

9-Deuterio-9-fluorenol (29). To 3.0 g (17 mmol) of **16** dissolved in 50 mL of anhydrous ether was added 0.22 g (1.4 equiv) of $LiAlD_4$. After 2 h of stirring under reflux, the reaction mixture was poured onto 100 g of an ice–water mixture acidified with 10% HCl and was extracted with ether, to yield a solid material recrystallized from ligroin: mp 155–156 °C; yield 2.6 g (84%); ^1H NMR δ 1.95 (s, 1 H), 7.2–7.7 (arom, 8 H); mass spectrum (CI) (m/z) 184 ($M^+ + 1$).

Product Studies. Dark Reactions. None of the compounds studied in this work showed any tendency to react in the dark with the exception

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(35) Wan, P.; Krogh, E. Unpublished results.

(36) Streitweiser, A., Jr.; Jagow, R. H.; Fahey, R. C.; Suzuki, S. *J. Am. Chem. Soc.* **1958**, *80*, 2326.

(37) Wan, P.; Chak, B.; Krogh, E. *J. Photochem. Photobiol., A* **1989**, *46*, 49.

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of the suberenols, **9** and **10**, and xanthenol **27**, which will solvolyze in the dark under acidic conditions. At neutral pH and the typically short irradiation times employed, these compounds exhibited no thermal reaction. A typical experimental procedure for a preparative dark reaction follows. A solution of 100 mg of compound in 100 mL of MeOH was diluted with 100 mL of water. The solution was stirred in the dark at room temperature for the appropriate irradiation time, (usually less than 1 h). The reactions were worked up by saturating the solution with NaCl and extracting with CH_2Cl_2. The isolated materials were analyzed by ^1H NMR spectroscopy.

Preparatory Photolysis of 1–3, 9, 11a. In a typical preparative study, 200 mg of substrate was dissolved in 100 mL of MeOH and then diluted with 100 mL of H_2O. The solution was then transferred to a quartz vessel fitted with a cooling finger and deaerated with a continuous stream of argon. The solution was then irradiated at 254 nm. After photolysis, the solution was worked up by saturating it with NaCl followed by extraction with 2 × 100 mL of CH_2Cl_2. The photosolvolysate was then analyzed by ^1H NMR and gas chromatography, from which the identity and ratios of various products were determined. Product mixtures were separated by preparative TLC. In each case, the methyl ethers were isolated and characterized by ^1H NMR and mass spectroscopy and chemical analysis for **12** and **19**, as presented below.

9-Methoxyfluorene (6): mp 42 °C (lit.[50] 43.5 °C); ^1H NMR δ 3.00 (s, 3 H), 5.53 (s, 1 H), 7.2–7.7 (arom, 8 H).

9-Methoxy-9-phenylfluorene (12): mp 91 °C; ^1H NMR δ 2.90 (s, 3 H), 7.1–7.8 (arom, 13 H). Anal. Calcd for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.10; H, 5.89.

9-Methoxy-9-methylfluorene (19): mp 86 °C; ^1H NMR δ 1.68 (s, 3 H), 2.70 (s, 3 H), 7.2–7.8 (arom, 8 H). Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.58; H, 6.68.

5-Methoxysuberane (26) (5-Methoxy-10,11-dihydro-5*H*-dibenzo[*a*,*d*]cyclohepten-5-ol): ^1H NMR δ 3.30 (s, 3 H), 2.7–3.7 (m, 4 H), 5.20 (s, 1 H), 7.1–7.5 (arom, 8 H); IR (cm^{-1}) 2800–3100 (m), 1490 (m), 1440 (m), 1100 (m), 1080 (s); mass spectrum (CI) (*m/z*) 225 (M^+ + 1). Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.73; H, 7.15.

The hydrocarbon products **7**, **13**, **14**, and **21** were isolated and characterized by comparison with the readily available authentic materials. However, 9-methylenefluorene (**20**) polymerized on attempts to isolate it from the reaction mixture. It is known to polymerize readily[51] and hence has not been characterized fully by the standard spectroscopic techniques. However, the ^1H NMR singlet of the product mixture at δ 6.0 supports the existence of the exocyclic double bond in **20**. In addition, the UV absorption spectrum observed after brief photolysis of **3** in water was almost identical with that reported for 9-ethylidenefluorene,[52] which is a stable compound. The dimeric product 9,9′-bifluorene (**14**) was observed in the photolysis of **1**, whereas the 9,9′-disubstituted-9,9′-bifluorene analogues for **2** and **3** were not observed in sufficient quantity for characterization.

The photolysis of **9** in a similar manner as above led to recovery of the starting material. On extended photolysis the ketone **25** was observed and characterized by comparison with the authentic material.

Preparatory Photolysis of 4–6. In a typical reaction 100 mg of substrate was dissolved in 60 mL of ACN and then diluted with 140 mL of H_2O. After transferring to a quartz vessel and deaerating with argon, the solution was irradiated for 10 min at 254 nm. The solution was then saturated with NaCl and extracted with 2 × 100 mL of CH_2Cl_2. The product mixtures were analyzed by ^1H NMR and GS/MS. Compound **6** was also photolyzed in a 50% MeOH–H_2O mixture.

Preparatory Photolysis of 17. A solution of 50 mg of **17** was dissolved in 50 mL of MeOH and diluted with 100 mL of H_2O. After treating in the normal manner, the solution was photolyzed for 10 min at 254 nm. Recovery of the fluorene fraction from the photolysate was accomplished by preparative TLC (silica/CH_2Cl_2). Analysis of the 250-MHz ^1H NMR indicates that deuterium has been 100% incorporated; the partially resolved 1:1:1 triplet at δ 3.84, J_{H-D} = 3 Hz, integrates as 1:8 with respect to the aromatic signal. This observation was confirmed by the mass spectral data.

Preparatory Photolysis of 27 in Aqueous NaCN. A solution of 100 mg of **27** in 70 mL of ACN was diluted with 70 mL of a 0.5 M aqueous NaCN solution. This was treated in the normal manner and photolyzed for 15 min at 254 nm. On workup, the ^1H NMR showed three singlets in the δ 4–6 region. One of these was at δ 5.7 and is due to the starting material **27**. The remaining two were at δ 5.35 and 4.20. The mixture was separated by preparative TLC (CH_2Cl_2/hexanes) to give two major bands. One of these bands ($R_f \approx 0.2$) contained only **27**. The other band ($R_f \approx 0.6$) gave an ^1H NMR spectrum which contained both of the δ 5.35 and 4.20 singlets. All attempts to separate this band into two components failed. However, the strong IR peak at 2220 cm^{-1} as well as a CI mass spectrum peak at 208 (M^+ + 1) are consistent with cyano-substituted xanthene product(s). In addition, a strong peak at 181 in the CI mass spectrum is consistent with a 9-cyanoxanthene product (**28b**) since this isomer would be expected to lose HCN readily in the CI spectrum. Thus we assign the δ 5.35 to the methine of **28b** and the δ 4.20 to the methylene peak of **28a**. Integration of the two peaks gave a ratio of 60:40 for **28a**:**28b**. The total yield of these two isomers was about 60%.

Preparatory Photolysis of 11a in Aqueous NaCN. In the same manner as above for **27**, photolysis of **11a** in the presence of NaCN gave no observable reaction when photolyzed for 15 min. However, on extended photolysis (~60 min), a low yield (~5%) of 5-cyanosuberane was observed: ^1H NMR (250 MHz) δ 3.15–3.35 (m, 4 H), 5.47 (s, 1 H), 7.05–7.55 (arom, 8 H); IR (cm^{-1}) 2240 (m); mass spectrum (CI) (*m/z*) 220 (M^+ + 1), 193 (M^+ − CN).

Photosolvolysis of 1 in Alcohols. Via the same procedure as for the runs in 50% MeOH–H_2O, the following ethers were isolated by preparative TLC (silica/CH_2Cl_2–hexanes) and characterized by their ^1H NMR, as follows.

9-Ethoxyfluorene:[10] δ 1.13 (t, *J* = 7 Hz, 3 H), 3.25 (q, *J* = 7 Hz, 2 H), 5.58 (s, 1 H), 7.2–7.7 (arom, 8 H).

9-(Isopropyloxy)fluorene:[10] δ 1.18 (d, *J* = 7 Hz, 6 H), 3.80 (m, 1 H), 5.56 (s, 1 H), 7.2–7.7 (arom, 8 H).

9-(*tert*-butyloxy)fluorene:[10] δ 1.20 (s, 9 H), 5.50 (s, 1 H), 7.2–7.7 (arom, 8 H).

Photodecomposition of 1 in ACN. Photolysis of 100 mg of **1** in pure ACN for 30 min gave essentially 100% conversion to a mixture of products which were characterized by GC/MS and by the ^1H NMR of the photolysate mixture. For instance, the ^1H NMR of one fraction from preparative TLC showed δ 2.65 (d, *J* = 7 Hz, 2 H) and 4.10 (t, *J* = 7 Hz, 1 H) with an IR stretch of 2250 cm^{-1}, which was assigned to product **22**. Acetamide **23** was characterized by a methyl singlet at δ 1.78 and an IR stretch at 1670 cm^{-1} along with GC/MS data.

^{18}O-Exchange Studies. Solutions consisting of ~1 × 10^{-4} g of both **1** and **11a** were made up in 50% (v/v) ACN and H_2O (enriched with 20% ^{18}O from M.S.D. Isotopes) and photolyzed for ~20 min. The solutions were extracted with CH_2Cl_2. The percent of ^{18}O incorporation was calculated by the increase in (M^+ + 3) peak in the CI mass spectrum, compared to the intensity of this same peak in the natural abundance material. 9-Fluorenol-^{18}O (20% enriched) was made by solvolyzing **5** in 20% H_2O (20% ^{18}O) under reflux. Loss of ^{18}O label in this compound on photolysis was studied by following the decrease in intensity of its (M^+ + 3) peak in the CI mass spectrum. None of the above ^{18}O exchanges was observed in the dark, as confirmed by control experiments.

Steady-State Fluorescence and Lifetime Measurements. Fluorescence spectra (uncorrected) were measured on a Perkin-Elmer MPF 66 instrument in 1.00-cm Suprasil quartz cuvettes at 10^{-4} M at ambient (22 ± 3 °C) temperature. Solutions were purged with argon prior to measurement. Time-correlated single photon counting fluorescence lifetimes were measured either at the Center for Fast Kinetics Research (CFKR) using a mode-locked, synch-pumped, cavity-dumped dye laser, frequency doubled to provide an excitation source in the UV at 266 nm (Spectra Physics Model 574B dye laser with Spectra Physics series 3000 Nd:YAG as the pump source) or with a standard time-correlated single photon counting system using a hydrogen spark lamp as the excitation source.

Quantum Yields and pH Effects. Quantum yields for the methyl ether formation from the alcohols **1–3** at different pHs and **9** and **11a** in neutral solution were measured with the photosolvolysis reaction of 2,6-dimethoxybenzyl alcohol in 50% MeOH–H_2O as a secondary actinometer (Φ = 0.31).[7] Argon-purged solutions at 6.0 mM were photolyzed in quartz cuvettes in a merry-go-round apparatus at 254 nm in a Rayonet photochemical reactor and conversions were determined by GC after the samples were extracted with CH_2Cl_2.

Relative Reactivity in the Ground State. Solutions consisting of ~100 mg of each of **1**, **9**, and **11a** were prepared in 100 mL of MeOH, and the appropriate acid solution was added (ranging from pH 7 to ~40% H_2SO_4). The solutions were left stirring in the dark for ~1–2 h. They were then extracted with CH_2Cl_2 and the extents of reaction were determined by ^1H NMR. At pH 2 and 1, both **9** and **11a** showed reaction, with **9** solvolyzing more efficiently. However, **1** failed to react until much more strongly acidic solutions were used, e.g., 30–40% H_2SO_4.

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surements and analyses of the data produced were performed at the Center for Fast Kinetics Research at the University of Texas at Austin. The CFKR is supported jointly by the Biotechnology Research Program of the Division of Research Resources of NIH (Grant No. RR00886) and by the University of Texas at Austin. Additional lifetime measurements were carried out in the laboratory of Prof. David Holden, University of Waterloo, whom we acknowledge for his assistance. The fluorescence lifetime measurement for **11a** by Edinburgh Instruments, Edinburgh, U.K., is also acknowledged.

Studies on the Reactivity of Bicyclomycin with Amines[1]

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Abstract: The reactivity of bicyclomycin (**1**) under basic conditions has been investigated. Eight different amines were sequentially reacted with **1**. Treatment of bicyclomycin with the primary amines methylamine and ethylamine yielded the ring-cleaved products **15–18**. Correspondingly, use of the heteroaromatic amines imidazole, benzimidazole, and (*dl*)-N_α-benzoylhistidine methylamide in these experiments led to the formation of a diastereomeric mixture of the ring-opened adducts **19**, **21**, and **22**, respectively. Finally, treatment of **1** with the secondary amines morpholine, ethyl piperazinecarboxylate, and *N*-methylpiperazine furnished the novel adducts **26–28**, respectively. Analysis of the composite results suggests that a key step in the base-mediated chemical processes is the reversible ring-opening of the C(6)-hemiaminal bond to give the enone **2**. The mechanism of these reactions and the implications of these studies in relation to the mode of action of the antibiotic are discussed.

Bicyclomycin (**1**), a clinically used antibiotic, has received considerable attention in recent years.[2-4] It is a structurally unique cyclic peptide possessing pronounced activity against several strains of Gram-negative bacteria. Most proposals pertaining to the mode of action of **1** have suggested that nucleophilic species present within the peptidoglycan assembly of the bacterial cell wall play a pivotal role in the activation and subsequent binding of the chemotherapeutic agent.[5-9] Both sulfhydryl-containing proteins[5] and amidases[6-8] have been advanced as likely candidates in these transformations. Information in favor of the former species emanated from the pioneering studies of Iseki and co-workers which demonstrated that **1** reacts with methyl mercaptan at basic pH.[5a] This result, coupled with the observation that **1** covalently interacts with inner-membrane proteins of *Escherichia coli*,[5c] led to the notion that the antibacterial activity of **1** is associated with the binding of a nucleophile (i.e., a protein sulfhydryl group) to the terminal olefinic group [C(5)–C(5a)] of the drug. The initially proposed pathway for this transformation is depicted in Scheme I.[6] Alternatively, recent work by Vasquez and co-workers has led to the speculation that amidases play an integral role in the bicyclomycin activation process.[7] Moreover, the close structural correspondence of **1** to the projected structure of the diaminopimelic acid–diaminopimelic acid unit within the peptidoglycan assembly of the cellular membrane has prompted the suggestion by Williams and his group that the drug functions as a competitive substrate for a protease involved in the biosynthesis of the bacterial cell envelope (Scheme II).[6] Key steps in this hypothesis include the enzymic cleavage of the C(9)–N(10) amide bond in **1** to yield **4** and the Michael addition of a second biological nucleophile to the conjugated system **5** to generate **6**.

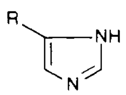
In light of these mechanistic scenarios, it is surprising that no information exists on the reactivity of bicyclomycin with amines. All previous accounts have focused on sulfur-[5a,8-10] and oxygen-containing[11] nucleophiles. In this paper, we report on the chemical reactivity of **1** with primary, secondary, and heteroaromatic amines, including a functionalized derivative of histidine. Special attention is centered on the interplay of both the type of amine used and the pH of the reaction medium on the product profile. Arguments are advanced that a critical step in the chemical activation of the drug is the reversible ring-opening of the C-(6)-hemiaminal bond of bicyclomycin to generate enone **2**. Michael addition of the amine to the α,β-unsaturated system generates a C(5a)-substituted adduct. This species can then be converted into a series of novel rearranged, ring-opened, or ring-cleaved products depending upon the reaction conditions.

Results

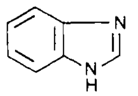
(a) Choice of Amines. The reactivity of bicyclomycin with eight different amines was assessed. The primary amines methylamine (**7**) and ethylamine (**8**), and the heteroaromatic amines imidazole (**9**) and benzimidazole (**10**) were chosen as simple models of

RNH_2

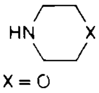
7, R = CH_3
8, R = CH_2CH_3



9, R = H
11, R = $\underset{C(O)NHCH_3}{CH_2CHNHC(O)C_6H_5}$



10



12, X = O
13, X = $NC(O)OC_2H_5$
14, X = NCH_3

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