Hz, 6 H), 1.09–1.64 (m, 6 H) 2.00–2.14 (m, 1 H), 2.20 (s, 3 H), 2.68–2.86 (m, 1 H).

The second was **8-d_3**: ir 2950 (s), 2920 (s), 2870 (m), 2850 (m), 2275 (vw), 2200 (w), 2100 (w), 1675 (vs), 1590 (m), 1465 (m), 1360 (s) cm^{-1}; nmr (220 MHz) δ 0.85 (br s, 6 H), 1.09–1.50 (m, 5 H), 2.00–2.32 with s at 2.19 (m, 5 H), 2.54–2.78 (m, 1 H).

3-Methoxymethyl-3-methyl- and 4-Methoxymethyl-4-methyl-1-cyclopenten-1-yl Methyl Ketone-d_3 (25 and 13-d_3). Ketone **39** was converted to the unsaturated nitriles **34b-d_3** and **35b-d_3** as above. These nitriles had vpc retention time and nmr spectra (except for absent methoxy signal) identical with **34b** and **35b**. Ketones **25** and **13-d_3** were prepared following the general procedure and purified on column A. The first obtained was **25**: ir 3050 (w), 2955 (m), 2860 (m), 2710 (w), 2240 (w), 2180 (m), 2045 (m), 1675 (vs), 1620 (m), 1360 (m), 1120 (s) cm^{-1}; nmr (220 MHz) δ 1.09 (s, 3 H), 1.56 (ddd, $J_1 = J_2 = 3, J_3 = 5$ Hz, 1 H), 1.79 (ddd, $J_1 = J_2 = 3, J_3 = 5$ Hz, 1 H), 2.21

(s, 3 H), 2.47 (dd, $J_1 = J_2 = 3$, Hz, 1 H), 3.14 (s, 2 H), 6.31 (m, 1 H).

The second was **13-d_3**: ir 3050 (w), 2950 (m), 2925 (m), 2840 (m), 2725 (w), 2240 (w), 2170 (m), 2045 (m), 1675 (vs), 1620 (m), 1370 (m), 1230 (m), 1125 (s) cm^{-1}; nmr (220 MHz) δ 1.06 (s, 3 H), 2.04–2.68 with s at 2.20 (m, 7 H), 3.10 (s, 2 H), 6.44 (m, 1 H).

Photochemical and γ-Ray-Induced Reactions of Nucleic Acid Constituents. Dealkylation of 8-α-Hydroxyalkyl Purines
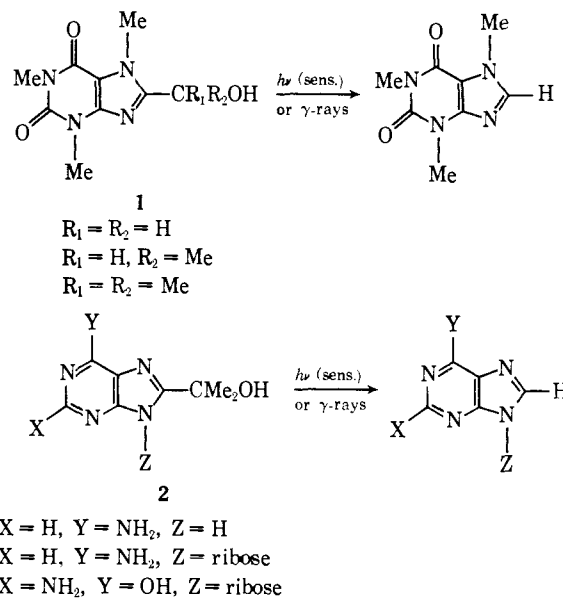
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Contribution from the Department of Organic Chemistry, The Weizmann Institute of Science, Rehovot, Israel. Received November 27, 1973

Abstract: The photosensitized dealkylation of 8-α-hydroxyalkyl purines with ultraviolet light (λ >290 nm) leads to the regeneration of the original purines in yields of up to 100%. A mechanism involving an electron transfer from the excited sensitizer to the purine molecule is proposed. The dealkylation of 8-α-hydroxyalkyl purines could also be achieved by the γ radiolysis of their aqueous solutions.

Photochemical reactions of purines from nucleic acids with a variety of organic compounds (*e.g.*, alcohols and amines) led to the substitution of the appropriate moiety for the H-8 hydrogen atom in the purine system.[1] It has further been shown that both adenine and guanine moieties in nucleic acids undergo similar photochemical reactions to yield photoproducts represented by **2** in Scheme I.[2] These modifications in the purines represent a new type of lesion in nucleic acids, the biological significance of which may depend on the existence of an appropriate repair system in the irradiated organism. In the case of pyrimidines, it is well established that the enzymic photoreactivation process involves the splitting of thymine dimers in irradiated DNA into the original monomeric moieties,[3] and preliminary studies with models indicated that the reaction may proceed through a photosensitization process.[4] It was felt that the study of photochemical reactions which will result in the

Scheme I

1

$R_1 = R_2 = H$
$R_1 = H, R_2 = Me$
$R_1 = R_2 = Me$

2

X = H, Y = NH$_2$, Z = H
X = H, Y = NH$_2$, Z = ribose
X = NH$_2$, Y = OH, Z = ribose

restoration of the original purines from the light-modified ones may lead to a useful model for a photoreactivation process involving the repair of lesions in the purine moieties of irradiated nucleic acids. The development of a general photochemical procedure for the repair of lesions in the various moieties of DNA is also hoped for in the course of this study. The present publication includes a detailed description of photochemical reactions which result in the restoration of the

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(2) R. Ben-Ishai, M. Green, E. Graff, D. Elad, H. Steinmaus, and J. Salomon, *Photochem. Photobiol.*, **17**, 155 (1973).

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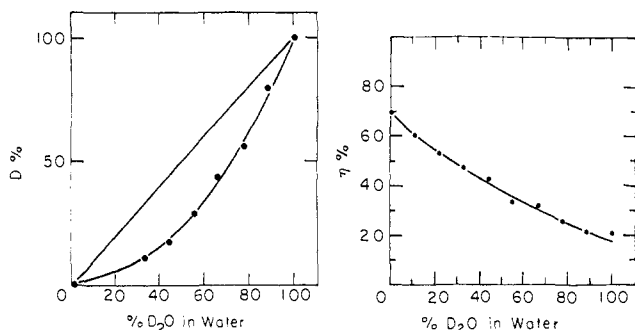
Figure 1. Influence of D_2O on the photoreactivity of caffeine-8-CMe_2OH and on the incorporation of deuterium during K_4Fe-$(CN)_6$ photoinitiated dealkylation ($\lambda_{incid} > 290$ nm): (left) yield of 8-D-caffeine in the final product; (right) conversion of starting material.

original purines from the appropriate purine photoproducts (*i.e.*, the 8-α-hydroxyalkyl purines).[5]

Results and Discussion

Irradiation of C-8-α-hydroxyalkyl purines and purine nucleosides, *e.g.*, 8-substituted caffeine and adenosine, in the presence of photosensitizers, such as hydroquinone or *N,N*-dimethylaniline, resulted in the dealkylation of the side chain at the 8 position, leading to the regeneration of the original purine. The reactions can be represented as in Scheme I.

Progress of the reactions was followed by tlc, and quantitatively by glpc and nmr, in particular by following the appearance of the nmr signal of the H-8 proton of the product (at the τ 2 region), together with the disappearance of the signals of the C-8 side chain of the starting material (at the τ 8.5 region). Products were isolated by a modified "dry column chromatography,"[6] and identified by comparison with authentic samples by the usual procedures. Reactions were generally performed in methanol or in water, and were also found to proceed upon exposure to sunlight or visible light, as well as to γ-rays in aqueous solutions. Quantum yields of up to 1.1×10^{-2} have been measured by ferrioxalate actinometry.[7] It is noteworthy that under the reaction conditions, the 8-α-hydroxylalkyl purines are generally stable toward ultraviolet light of $\lambda > 260$ nm in the absence of photosensitizers. However, the addition of the appropriate photosensitizer leads to high yields of dealkylation. No reaction could be observed in the dark, even in boiling methanol. Small amounts of 8-alkyl purines were formed as by-products of some of the photodealkylation reactions. It has been observed that, under the reaction conditions, the 8-alkyl purines are stable to ultraviolet irradiation in the presence of photosensitizers, as well as to exposure to γ-rays. The reactions studied are summarized in Table I. It is noteworthy that the structure of the 8-α-hydroxylalkyl side chain affects the yields of the purine in these reactions, since under similar reaction conditions, the amount of restored caffeine increases in the order of α-hydroxymethyl < α-hydroxyethyl < α-hydroxyisopropyl.

A study of the *N,N*-dimethylaniline-sensitized dealkylation of 8-α-hydroxyisopropylcaffeine (with light of λ

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Table I. Photodealkylation of 8-α-Hydroxyalkyl Purines[a]

8-Substituted purine	Photosensitizer	Product (yield %)[b] Purine	Product (yield %)[b] 8-Alkyl purine
Caffeine-8-CH_2OH		Trace	
	Carbazole	12	Trace
	N,N-Dimethylaniline	30	4
Caffeine-8-$CHMeOH$		Trace	
	Carbazole	12	Trace
	N,N-Dimethylaniline	35	6
Caffeine-8-CMe_2OH		7	
	Carbazole	71	8
	N,N-Dimethylaniline	81	10
	N,N-Dimethylaniline[c]	40	Trace
	Phenothiazine	23	Trace
	Indole	18	5
	Histidine	14	Trace
	$K_4Fe(CN)_6$	95	Trace
	$K_4Fe(CN)_6$[c]	34	
	Hydroquinone	91	6
	Quinhydrone	57	6
	o-Catechol	41	5
	Dihydrochloranil		
	KI[d]	100	
	e	100	
Adenine-8-CMe_2OH			
	Carbazole	15	41
	N,N-Dimethylaniline	10	34
	$K_4Fe(CN)_6$	19	7
	Hydroquinone	49	17
	e	15	
Adenosine-8-CMe_2OH		Trace	
	Carbazole	38	11[g]
	N,N-Dimethylaniline	80	17[g]
	N,N-Dimethylaniline[f]	32	
	$K_4Fe(CN)_6$	88	
	Hydroquinone	95	Traces
	KI[d]	92	
	e	50	
Guanosine-8-CMe_2OH			
	Hydroquinone	69	

[a] Unless otherwise specified, all reactions were carried out in methanol using Hanovia 450-W high-pressure mercury vapor lamps as the light source, and Pyrex filters ($\lambda > 290$ nm). Irradiation time was usually 22 hr. [b] Yields are based on total amount of starting purine. [c] Visible light (4×20 W fluorescent lamp GEC). Irradiation time *ca.* 200 hr. [d] Corex filter ($\lambda > 260$ nm). [e] With γ-rays, using a ^{60}Co source (Gammacell 220, Atomic Energy of Canada Ltd. Ottawa); dose rate, 12,000 rads/min; irradiation time, 24–90 hr. [f] In sunlight; exposure 5–12 days. [g] Identified by nmr.

> 290 nm) in various solvents indicated that the reaction is very slow in benzene, methylene chloride, or acetonitrile, while the addition of increasing amounts of methanol led to higher yields of the restored purine. In order to establish the role of the solvent in these reactions, we investigated the photodealkylation of 8-α-hydroxyisopropylcaffeine in water in the presence of $K_4Fe(CN)_6$ as photosensitizer. By gradual addition of D_2O, we observed a decrease in the degree of conversion of the starting material, together with an increased incorporation of deuterium to yield 8-D-caffeine. However, the D–H distribution at the C-8 atom noticeably differs from the D–H ratio in the solvent mixture (as depicted in Figure 1). Irradiation in pure D_2O leads to 8-D-caffeine as the sole photoproduct.[8] The incor-

(8) An alternative pathway for the formation of 8-D-caffeine during the reaction in D_2O-H_2O mixtures would involve two consecutive stages. The first would consist of the photosensitized dealkylation of the starting material leading to 8-H-caffeine, while during the second subsequent deuteration by D_2O would occur. This pathway can be ruled out, since under the reaction conditions (including work-up), we observed very little C-8 deuteration ($\leq 5\%$) of 8-H-caffeine in the D_2O-H_2O mixture.

poration of deuterium into the restored purine as well as the observed isotope effect indicate that a proton transfer from the solvent is involved in the reaction mechanism.

In the reported reaction, most of the incident light (λ >290 nm) is absorbed by the sensitizer. In an attempt to understand the pathway from the light absorption step by the photosensitizer to the restoration of the original purine, we investigated the mode of the transfer of energy from the excited sensitizer to the 8-substituted purine. We observed that photosensitizers possessing high triplet energies, such as acetophenone, failed to initiate the reactions, and that the reactions were quenched only partially by triplet quenchers, such as cis-piperylene. Furthermore, hydroquinone, although possessing a relatively low triplet energy[9] as compared to purines,[10] was found to be very effective as photosensitizer. These observations led us to conclude that the reaction, most probably, does not involve a transfer of triplet energy.

Most of the aromatic sensitizers which are efficient in the photodealkylation process possess relatively low ionization potentials (N,N-dimethylaniline 8.18 eV, phenothiazine 7.02 eV),[11] and are described in the literature as good electron donors, either in their ground state (e.g., phenothiazine), or in their excited state[12] (e.g., carbazole[13] and indole[14,15]). Furthermore, N,N-dimethylaniline is known to give exciplexes in the presence of suitable electron acceptors,[16] while polyvinyl-carbazole is reported to develop electrical conductivity[17] due to the formation of a mobile positive charge in the polymer following a light-induced charge transfer to a nitroaromatic acceptor.[18]

In accordance with these data we considered the possibility of a charge-transfer process from the photosensitizer to the 8-substituted purine. This, however, does not meet the general consensus, according to which purines might rather act as weak electron donors.[19] Although purines are known to be reducible by polarography,[20] and caffeine has been reported to act as an acceptor,[21] precise determinations of electron affinities which would contribute to a better understanding of the role of nucleic acid bases in electron-transfer reactions[22] are still scarcely found in the literature. From the only

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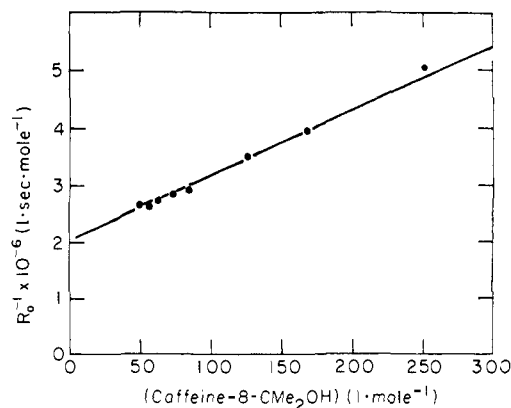
Figure 2. N,N-Dimethylaniline-sensitized photodealkylation of caffeine-8-CMe$_2$OH. Dependence of the initial rate of reaction upon the initial substituted purine concentration.

computed estimations available, namely the coefficients of the LEMO, no significant conclusions can be drawn concerning the possible donation to purines by a very good electron donor (with low coefficient of the HOMO[23]).

We have performed a series of experiments aiming at the support of our assumption. In the first set of reactions we investigated the general mode of excitation of the 8-substituted purines. No ground-state charge-transfer complex between the purine and the sensitizer could be observed both in the uv and the nmr spectra of the reaction mixtures.[24] Similarly, no decrease in the rate of reaction was detected by raising the temperature, which presents additional support for the non-occurrence of a ground-state charge-transfer complex.[25] Upon irradiation, the change in the uv absorption of mixtures of N,N-dimethylaniline and 8-α-hydroxyiso-propylcaffeine is very different from that of the irradiated isolated sensitizer, while no change was observed under the same conditions in the spectrum of the 8-substituted purine. Additional kinetic measurements involved the study of the dependence of the initial concentration of the 8-substituted purine upon the initial rate (R_0) of the photosensitized dealkylation (see Experimental Section). A plot of the reciprocal of R_0 vs. the reciprocal initial concentration of 8-α-hydroxy-isopropylcaffeine gave a straight line, as shown in Figure 2. This indicates that the reaction involves the interaction of an excited species with a ground-state molecule.[26] This set of results as well as our observation that the reaction is favored by a polar medium suggest that the reaction may proceed through the formation of a complex between the excited photosensitizer and a ground-state 8-substituted purine molecule (exciplex).

Further support for the involvement of a charge-transfer step in the reaction path was derived from the following experiments. We observed an increased efficiency in the photosensitized dealkylation reactions in the series dihydrochloranil < o-catechol < p-hydroquinone, which can be correlated with decreasing nor-

(23) L. Brillouin in "Horizons in Biochemistry," Academic Press, New York, N. Y., 1962, p 308; A. Pullman and B. Pullman, ibid., p 567.
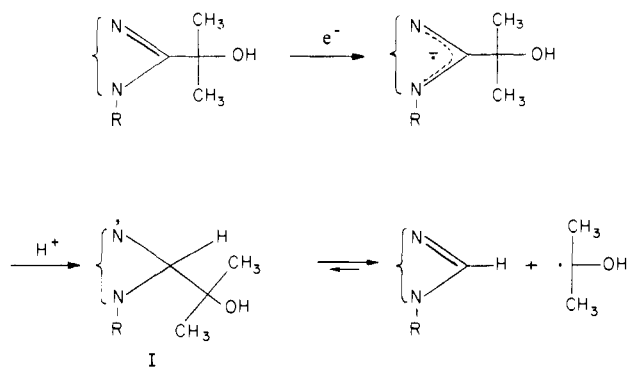
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(25) R. Forster in "Organic Charge-Transfer Complex," Academic Press, New York, N. Y., 1969, p 189.

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mal redox potentials of the appropriate quinone counterparts.[27] Thus, it appears that, within the same series, the reducing power (i.e., the electron-donating ability) of the sensitizers controls the efficiency of the dealkylation reactions. The involvement of an electron-transfer step to the 8-substituted purines was unambiguously demonstrated by exposing them to other sources of electrons, such as irradiated ferrous ions and γ-rays in aqueous solutions. Ferrous ions, especially $K_4Fe(CN)_6$, are known to generate solvated electrons with a high quantum yield under uv irradiation.[28] Upon exposure to light of $\lambda > 290$ nm [where only $K_4Fe(CN)_6$ absorbs], almost quantitative dealkylation took place. The involvement of solvated electrons in this reaction was shown by quenching the reaction with a good electron scavenger such as $NaNO_3$, at concentrations where the latter does not absorb. Similar results were obtained by replacing the ferrous salt by KI (with light of $\lambda > 260$ nm).[29] We were finally able to perform quantitative dealkylation by exposing aqueous solutions of the 8-α-hydroxyalkyl purines to γ-rays. Scavenging of OH radicals generated during radiolysis, to prevent the destruction of the purine nucleus,[30] was achieved by KI or tert-butyl alcohol.[31] This allowed a smooth dealkylation to proceed, with a G value of up to 0.2. No dealkylation occurred, however, upon saturation of the reaction mixtures with N_2O, or by the addition of other scavengers of solvated electron, such as $K_3Fe(CN)_6$, $NaNO_3$, or NaH_2PO_4. It is noteworthy that, in the presence of sodium formate, the degree of conversion of the starting material is reduced during radiolysis; this can be explained by the transformation of the solvated electron into the weaker reductive formate radical during radiolysis.[32] Our experimental results lead us to propose a pathway which involves successive electron- and proton-transfer processes during the reaction; the initial transfer of an electron to the 8-substituted purines results in the formation of a radical anion, which rapidly abstracts a proton from the solvent. The resultant free radical, which can be represented as I (in Scheme II), disproportionates to yield the original purine and a ketyl radical.[33,34] The equilib-

rium could be shifted toward the dealkylation in the present case, due to both the accumulation of radical I from the electron-transfer step and the driving force to release a ketyl radical. An alternative mechanism in which radical I would be involved includes the addition of a hydrogen atom to the C-8=N-7 position of the 8α-hydroxyalkyl purine. This type of reaction has been reported previously in irradiated purines,[35] and it could be possible that sensitizers like hydroquinone would fragment by β fission,[36] yielding a hydrogen atom (and a semiquinone radical), which would then be scavenged by a ground-state purine. This possibility is ruled out, however, since H atoms generated by γ-rays failed to induce the dealkylation, and H atom scavengers did not quench the reaction. It is noteworthy that the dealkylation reactions involve a C–C bond fission, and that the efficiency of the reaction increased with enhanced stability of the "released" 8-side chain in the form of a free radical: $CH_2OH < CHMeOH < CMe_2OH$. Furthermore, 8-alkyl purines were stable under similar reaction conditions. It seems, therefore, that the stability of the released free radical is an important parameter in the driving force for the C–C bond fission.

In summary, we have developed new photochemical reactions which lead to the restoration of the original purines from the light-altered molecules, i.e., the 8-α-hydroxyalkyl purines. The reaction process involves an electron transfer in an excited state, during which the purines apparently behave as electron acceptors.[37] This process can be regarded as a photochemical repair of lesions in the purine moieties of nucleic acids. It is noteworthy that the photosensitized monomerization of pyrimidine photodimers,[4e] which imitates the light-requiring step of the enzymic photoreactivation, also involves the transfer of an electron, however, in the opposite direction.[4f] It is possible that electron-transfer processes of a similar nature are part of a more general repair system for radiation damage, the mechanism of which may include a redox turnover in the chromophore responsible for the light absorption.

Experimental Section

Experiments were carried out at room temperature in an immersion apparatus; Hanovia 450-W high-pressure mercury vapor lamps which were cooled internally with running water were used as the light source. Pyrex filters ($\lambda > 290$ nm) as well as Corex filters ($\lambda > 260$ nm) were employed. Agitation was performed by oxygen-free nitrogen bubbling during the irradiation, as well as by

Scheme II

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Table II. Photodealkylation of 8-Hydroxyisopropylcaffeine with N,N-Dimethylaniline. Yield of Caffeine Formed $vs.$ Time and Initial Rates of Reaction

Caffeine-8-CMe₂OH (initial amount, mg)	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5	6	7	8	9	10	R_0, μM l.$^{-1}$ sec^{-1}
10	10	20	30	38	48	55	62	71								0.198
15	9	17	25	33	41	48	56	62								0.255
20		14	21	28	34	39		52	58	64						0.285
30		11	16	21	27	32		42		52	63					0.342
35		7	12	17		28		38		46	55	63	72			0.352
40		7	12	16	19	25		33		42	50	58	66	74		0.364
45			10	16	18	23		31		38	44	53		68		0.378
50			10	13		19		27		33	41			62	67	0.375

magnetic stirring. The γ-ray induced reactions were performed in glass tubes which were placed into a ⁶⁰Co Gammacell apparatus (Atomic Energy of Canada Ltd., Ottawa, Canada), with an air cooling device and at a dose rate measured of 12,000 rads/min. Reaction vessels were flushed with nitrogen for 15 min prior to irradiation. Typical reactions are described; other experiments were conducted under similar conditions and are summarized in Table I. Progress of the reactions was followed by tlc, nmr, as well as (in the case of caffeine) by glpc. Column chromatography was achieved by a modified "dry column" procedure.[6] Products of the reactions were compared with authentic samples by the usual procedures,[1a,b] or were characterized by their elemental analyses and appropriate physical data in the case of new compounds. Unless stated otherwise, Pyrex filters were used in the ultraviolet light-induced reactions.

Reaction of 8-α-Hydroxyisopropylcaffeine and N,N-Dimethylaniline. A mixture of 8-α-hydroxyisopropylcaffeine (0.2 g), N,N-dimethylaniline (0.2 ml), and methanol (75 ml) was irradiated for 24 hr. Excess reagents were removed under reduced pressure, and the solid residue was chromatographed on silica gel (50 g). Acetone–petroleum ether (3:17) eluted 8-isopropylcaffeine (0.02 g), mp 142–143° (from acetone–petroleum ether),[1f] which was followed by unreacted starting material (0.01 g, eluted with a 1:4 mixture). Further elution with acetone–petroleum ether (3:7) afforded caffeine (0.13 g).

Reaction of 8-α-Hydroxyisopropylcaffeine and Polyvinylcarbazole. A mixture of 8-α-hydroxyisopropylcaffeine (0.1 g), polyvinylcarbazole (4 g), and water (160 ml) was irradiated for 48 hr with vigorous stirring. After filtration and extraction with chloroform, the usual work-up and chromatography afforded 8-isopropylcaffeine (0.008 g), as well as unreacted starting material (0.05 g) and caffeine (0.03 g).

Reaction of 8-α-Hydroxyisopropyladenine and N,N-Dimethylaniline (Corex filter). A mixture of 8-α-hydroxyisopropyladenine (0.3 g), N,N-dimethylaniline (0.3 ml), and methanol (160 ml) was irradiated for 21 hr. The usual work-up and chromatography using a methanol–chloroform mixture as the eluent gave 8-isopropyladenine (0.13 g), which was eluted with methanol–chloroform (3:47), and exhibited mp 269–270° (dec from methanol), nmr (CD₃OD) τ 1.82 (s, 1 H, C-2-H), 7.62 (broad m, 1 H, (CH₃)₂CH), and 8.58 (d, $J = 7$ Hz, 6 H, (CH_3)₂CH). *Anal.* Calcd for C₈H₁₁N₅: C, 54.22; H, 6.26; N, 39.52; mol wt, 177. Found: C, 54.06; H, 6.37; N, 39.8; mol wt, 177 (mass spectrum). Further elution with methanol–chloroform (1:1) afforded unreacted starting material (0.06 g), followed by adenine (0.03 g), which was eluted with methanol–chloroform (1:9).

Reaction of 8-α-Hydroxyisopropyladenosine and Hydroquinone. A mixture of 8-α-hydroxyisopropyladenosine (0.2 g), hydroquinone (0.2 g), and methanol (160 ml) was irradiated for 21 hr. The usual work-up and chromatography led to recovered starting material (0.01 g), which was eluted with methanol–chloroform (3:22) and to adenosine (0.15 g), which was eluted with methanol–chloroform (3:17).

Reaction of 8-α-Hydroxyisopropyladenosine with Potassium Iodide. A mixture of 8-α-hydroxyisopropyladenosine (0.1 g), KI (6 g), and water (160 ml) was irradiated (Corex filter) for 24 hr. Excess reagents were removed under reduced pressure and the residue was chromatographed on silica gel (100 g) to yield adenosine (0.07 g).

γ-Ray-Induced Dealkylation of 8-α-Hydroxyisopropylcaffeine. A mixture of 8-α-hydroxyisopropylcaffeine (0.25 g), KI (9 g), and water (135 ml) was irradiated for 16 hr. Extraction with chloroform followed by evaporation under reduced pressure and chro-

Table III. Influence of D₂O on the Photoreactivity of Caffeine-8-CMe₂OH and on the Incorporation of Deuterium during K₄Fe(CN)₆ Photoinitiated Dealkylation ($\lambda_{incid} > 290$ nm)

% D₂O in H₂O	% conversion of starting material	% 8-D-caffeine in the final product
0	70	
11	60	
22	52	
33	49	11
44	42	17
55	33	30
66	32	44
77	26	55
88	21	80
100	21	100

matography led to unreacted starting material (0.1 g) and caffeine (0.12 g). Longer irradiation time (28 hr) led to complete disappearance of the starting material, and to quantitative formation of caffeine, with a G value of 0.2. Bubbling of N₂O (25 mM) in the reaction mixture during radiolysis prevented the formation of the product, while the starting material remained intact. Alternatively, the addition of NaNO₃, K₃Fe(CN)₆, or NaH₂PO₄ prior to irradiation (10 g in each case) quenched the γ-ray-induced reaction. In the absence of KI, however, no purine product was observed, while the starting material had been totally consumed under the same conditions of irradiation.

Reaction of 8-α-Hydroxyisopropylcaffeine and K₄Fe(CN)₆ with Sunlight or Visible Light. Exposure of a mixture of 8-α-hydroxyisopropylcaffeine (0.2 g) and K₄Fe(CN)₆ (0.9 g) to sunlight for 15 days afforded traces of 8-isopropylcaffeine, as well as recovered starting material (0.06 g), together with caffeine (0.09 g). When illuminated with visible light (4 × 20 W fluorescent tubes, G.E.C.) for 200 hr, the same mixture afforded caffeine (0.05 g), as well as recovered starting material (0.13 g). In the presence of a GWC filter (λ >370 nm) and of the same source of visible light, caffeine (0.02 g) was isolated together with unreacted starting material (0.15 g) after illumination for 300 hr.

Kinetics of the Photodealkylation of 8-Hydroxyisopropylcaffeine with N,N-Dimethylaniline. Mixtures of N,N-dimethylaniline (25 μl), 8-α-hydroxyisopropylcaffeine (various quantities), and methanol (10 ml) were irradiated in Pyrex test tubes. The kinetics of each reaction mixture was followed by nmr and glpc analysis, to evaluate the amount of caffeine formed. From the graph of the caffeine concentration (C) $vs.$ time (t) obtained for each initial 8-α-hydroxyisopropylcaffeine concentration, the corresponding set of graphs of dC/dt $vs.$ t afforded $(dC/dt)_{t=0} = R_0$ by extrapolation. The plot of $1/R_0$ $vs.$ the reciprocal concentration of the 8-substituted purine affords a straight line. Our results are summarized in Table II.

Effect of D₂O on the Photosensitized Dealkylation of 8-α-Hydroxyisopropylcaffeine. Mixtures of 8-α-hydroxyisopropylcaffeine (0.015 g) and potassium ferrocyanide (0.03 g) in various D₂O–H₂O solutions (9 ml in total per run) were irradiated for 20 hr in Pyrex tubes. Extraction with chloroform and evaporation of the solvent left a residue which was analyzed by its nmr spectrum as for the degree of conversion of the starting material, as well as for the incorporation of D atoms at the C-8 position. Under the work-up conditions, no thermal C-8 deuteration was observed, while photosensitized irradiation of 8-H-caffeine in 50% aqueous D₂O led to small amounts of 8-D caffeine ($\leqslant 5\%$) under the reaction conditions. Our results are summarized in Table III.