distillation, leaving 0.21 g of crude material, which was shown by gc to consist of two components in a 4:1 ratio. The products were isolated by preparative gc and were found to be the *cis*- and *trans*-2-ethylidenecyclohexanones isolated above.

Photolysis of 5,7-Octadienal (2). A 1% solution of **2** (40 mg) in benzene was irradiated in a Rayonet photochemical reactor using 3500-A lamps. The photolysis was followed for 84 hr, in which time most of the starting material had disappeared. No products were detected at any time which might have been 3-cyclooctenone (**1**) or 2-vinylcyclohexanone (**5**). Under the same conditions both **1** and **5** gave essentially the same photomixtures as observed with the Hanovia system in a shorter period of time.

Mass Spectra. Mass spectra of the major compounds encountered in this work are tabulated in Table I. The values of peaks in abundance greater than 1% are given as percentage of the base peak.

Acknowledgment. The mass spectrometer used in this work was purchased with a National Science Foundation equipment grant (GP 5234).

Photochemistry of Quercetin Pentamethyl Ether

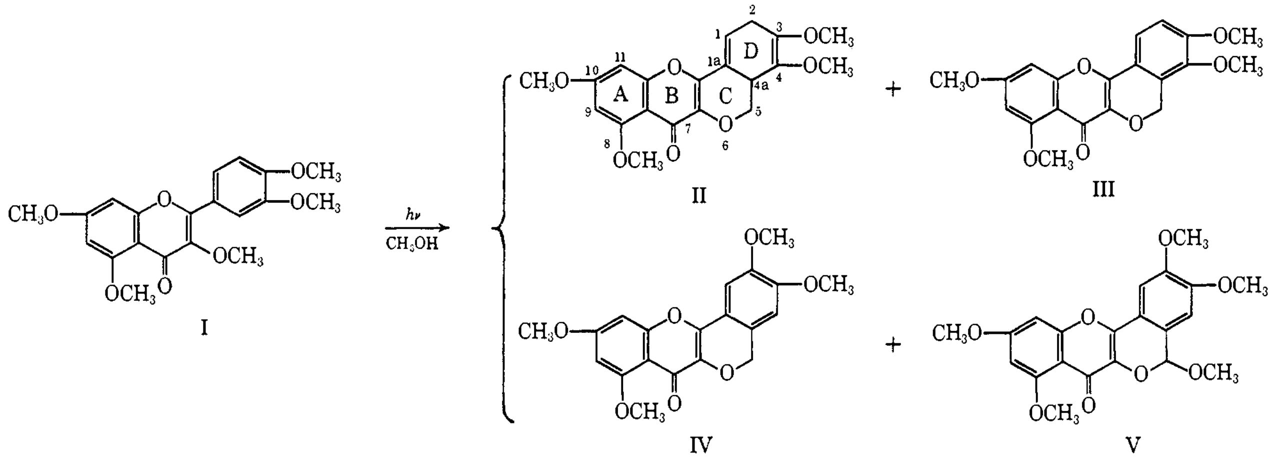
Anthony C. Waiss, Jr., Robert E. Lundin, Alson Lee, and Joseph Corse

Contribution from the Western Regional Research Laboratory, Agricultural Research Service, U. S. Department of Agriculture, Albany, California 94710.

Received May 25, 1967

Abstract: Ultraviolet (350 mμ) irradiation of quercetin pentamethyl ether (I) in methanol gave four photoproducts: lumimethylquercetin (II), α-photomethylquercetin (III), β-photomethylquercetin (IV), and methoxy-β-photomethylquercetin (V). The structures of these compounds were established by spectroscopic and chemical means. Possible mechanisms, one of which involves a novel photocycloaddition process, are proposed.

Flavonoid compounds[1] occur widely in plants and are often exposed to sunlight for long durations of time. The possibility that these compounds may act as photodynamic transferring agents (sensitizers or quenchers) for specific chemical transformations in plants is worthy of consideration.[2] The photochemistry of flavonoid compounds has not been investigated. Since quercetin is one of the better known flavonoids occurring in many plant families, its pentamethyl ether was chosen to initiate our program on a systematic study of the photochemistry of the flavonoids.



Results and Discussion

This report deals with the isolation and characterization of the four crystalline products, II, III, IV, and V, isolated from the photochemical reaction of quercetin pentamethyl ether (I) in methanol irradiated at 350 mμ and postulates possible mechanisms for their formation.

The first fluorescent compounds, lumimethylquercetin (II, R_f 0.67),[3] was isolated in 16% yield, mp 198–200°, from the irradiation product mixture by adsorption and chromatographic separations on silica gel. Mass spectroscopic and chemical analyses indicated that although II has the same molecular weight and empirical formula as its parent compound I, it contains only four methoxy groups. Evidence for the presence of a conjugated carbonyl function in V was provided by its ultraviolet spectrum [$\lambda_{\max}^{\text{MeOH}}$ 344 and 264 mμ (ε

---

(1) For recent reviews on the chemistry of flavonoid compounds see (a) T. A. Geissman, "The Chemistry of Flavonoid Compounds," The MacMillan Co., New York, N. Y., 1962, and (b) F. M. Dean, "Naturally Occurring Oxygen Ring Compounds," Butterworth & Co. (Publishers), Ltd., London, 1963.

(2) Flavone is known to be a sensitizer for *cis–trans* isomerization of stilbene (G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Cowan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Am. Chem. Soc.*, **86**, 3197 (1964)) and light-induced *trans–cis* conversion of β-D-glucosyl O-hydroxycinnamic acid in leaves has been reported (F. A. Haskins, L. G. Williams, and H. J. Gorz, *Plant Physiol.*, **39**, 777 (1964)).

(3) All tlc analyses reported here were performed on starch-bound silica gel eluted with 20% 2-propanol in ethyl acetate.

Table I. Chemical Shifts[a] (τ), Multiplicity, and Coupling Constants (Hz) of Numbered Compounds Observed in Chloroform-*d* (TMS) Solutions

	H_1	H_2	H_4	H_{4a}	H_5	H_7	H_9	H_{11}	OCH_3
I	2.30 d,d-9.0, 2.5	3.05 d-9.0	. . .	2.31 d-2.5	(OCH_3)	. . .	3.68 d-2.5	3.51 d-2.5	6.06 (9 H) 6.10 (6 H)
II	3.67[b] Hidden	6.95 m	. . . . . .	5.29 d-7.0	6.26[b] Hidden	. . . . . .	3.79 d-2.5	3.65 d-2.5	6.11 (3 H); 6.32 (3 H) 6.16 (3 H); 6.34 (3 H)
III	2.61 d-8.5	3.12 d-8.5	(OCH_3)	. . . . . .	4.74 s	. . . . . .	3.73 d-2.5	3.55 d-2.5	6.08 (6 H); 6.11 (3 H) 6.15 (3 H)
IV	2.90 s	(OCH_3)	3.41 s	. . . . . .	4.90 s	. . .	3.80 d-2.5	3.55 d-2.5	6.03 (3 H) 6.14 (9 H)
V	2.84 s	(OCH_3)	3.24 s	. . .	4.07 s	. . .	3.80 d-2.5	3.51 d-2.5	5.99 (3 H); 6.07 (3 H) 6.10 (6 H); 6.41 (3 H)
VI	4.21 m	7.00 m	(OCH_3)	5.49 m	6.2–6.3 Hidden	6.70 s	3.90 d-2.5	3.85 d-2.5	6.23 (6 H); 6.32 (3 H) 6.36 (3 H)
VII	3.52 m	6.71 m	(OCH_3)	5.25 m	6.24 m	. . . . . .	3.69 d-2.5	3.60 d-2.5	6.06 (3 H); 6.46 (3 H) 6.10 (3 H)
VIIIa	2.40 d-9.0	3.14 d,d-2.5,9.0	3.55 d-2.5	. . .	4.93 s	. . .	3.30 Broad s	3.30 Broad s	6.12 (3 H) 6.17 (3 H)
IX	2.98 s	. . .	3.37 s	. . .	5.00 s	6.61 s	3.85 d-2.5	3.21 d-2.5	6.02 (3 H); 6.17 (6 H) 6.11 (3 H)

[a] The nmr spectra were taken in $CDCl_3$ (TMS) solutions using either the Varian A-60 or HR100 spectrometer.[21] [b] Values obtained from double-irradiation experiments.

14,800 and 20,200)]. Lithium aluminum hydride reduction of II produced a deoxy derivative VI which gave only negligible absorption above 300 mμ. The nmr spectrum of lumimethylquercetin (Figure 1a) is best interpreted by comparing it with the spectrum of the deoxy derivative VI (Figure 1b). Besides the appearance of a methylene peak at τ 6.70, which is typical of flav-2-enes,[4] the nmr spectrum of VI revealed that a proton at τ 4.21 appearing as apparent doublets of triplets had shifted diamagnetically out of its hidden position (τ 3.67) in lumimethylquercetin. The upfield shifts of the two *meta* protons (τ 3.65 and 3.79 to 3.85 and 3.90) and of the vinyl proton (τ 3.67 to 4.21) were attributed to the removal of the carbonyl function which was closely associated with these protons. The above evidence permits structure II (2,4a-dihydro-3,4,8,10-tetramethoxy-7-oxo[2]benzopyrano[4,3-*b*][1]-benzopyran) to be proposed for lumimethylquercetin. The plausibility of the assigned structure was affirmed by the application of the nuclear magnetic double resonance technique. The decoupled spectrum of H_{4a} at τ 5.29 (Figure 2a) with irradiation of H_5 at τ 6.26 clearly establishes that the *t*-hydrogen at C_{4a} is coupled to one of the protons at C_5. Because of steric strain in the molecule, as visualized in molecular models, it is possible that one of the hydrogens at C_5 may be located at such an angle (~90°) with H_{4a} so that there is no apparent coupling between them.[5] The relationship between the C_2 methylene (τ 6.95) to the

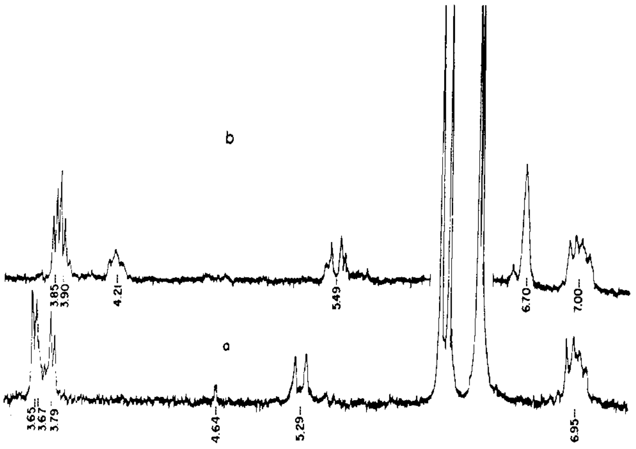


Figure 1. 100-MHz nmr spectra of (a) II and (b) VI in $CDCl_3$ (τ units).

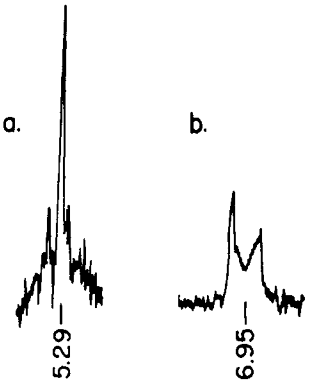
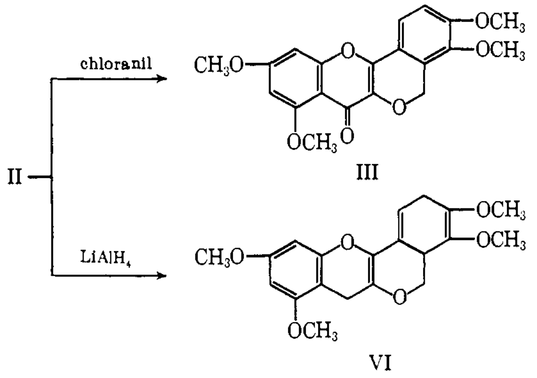


Figure 2. 100-MHz nmr spectra of II (a) at H_{4a} with irradiation at H_5 (τ 6.26), (b) at H_2 with irradiation at H_1 (τ 3.67).



---

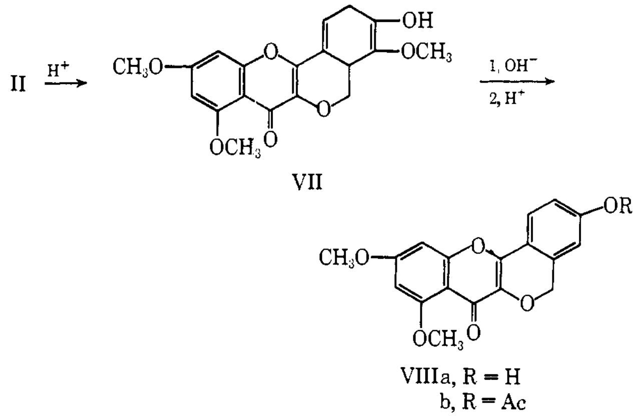
(4) Unpublished results from L. Jurd and A. C. Waiss, Jr.

(5) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

vinyl proton (at C_1) is demonstrated similarly (Figure 2b) by the irradiation of the later proton at τ 3.67.

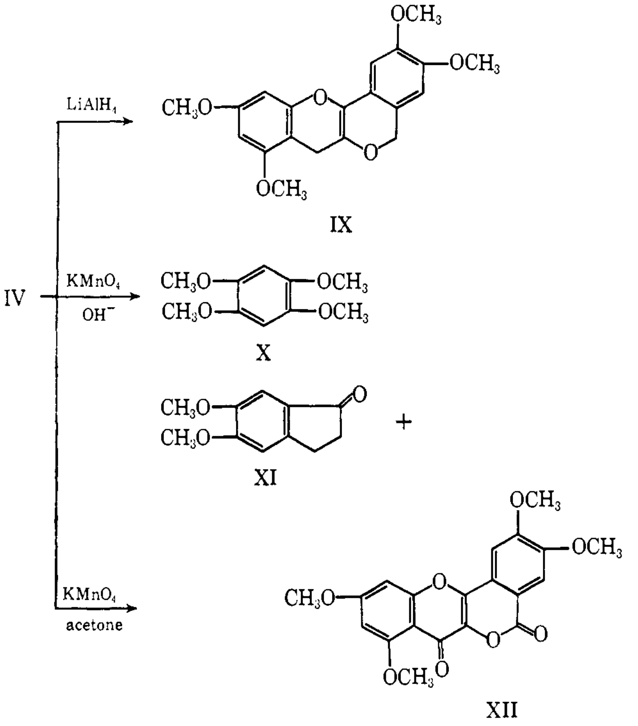
Chloranil oxidation of lumimethylquercetin (II), which gave α-photomethylquercetin (III) in 65% yield, lent additional support for the structural assignment. The structural elucidation of III was rather straightforward. It analyzed for $C_{16}H_6O_3(OCH_3)_4$, absorbed at 365 mμ (19,500), and had a simple nmr spectrum (Table I) showing two *meta*-coupled protons, two single aromatic (*ortho*) protons, a benzylic methylene singlet, and four methoxyl groups. Except for the two *ortho* protons the nmr spectrum of α-photomethylquercetin (VI) is very similar to that of β-photomethylquercetin (VII); *vide infra.*

Conversion of lumimethylquercetin (II) to the flavone VIIIa gave further support to its structural assignment. Being an enol ether, II was readily hydrolyzed with acid to the enolic derivative VII. The ultraviolet absorptions of II and VII were virtually identical; however, nmr and modified Zeisel O-methyl analyses indicated only three methoxy groups in the latter compound. Treatment of VII with sodium hydroxide solution followed by acidification yielded flavone VIIIa. The structure of flavone VIIIa was established in the usual manner by chemical, ultraviolet, and nmr analyses. The phenolic nature of compound VIIIa was attested by a bathochromic shift (47 mμ) in the ultraviolet by the addition of sodium hydroxide[6] and by the formation of a monoacetate, VIIIb.



The occurrence of α-photomethylquercetin (III) in the irradiation product mixture was first suspected when a small impurity band at τ 4.74 was observed in the nmr spectrum of lumimethylquercetin (Figure 1a). This resonance band corresponds exactly to the absorption by the C_6-methylene of α-photomethylquercetin derived from chloranil oxidation of II. Further chromatographic separation of later fractions of II gave a small yield of III. Since the R_f of pure III is 0.66 as compared to 0.67 of II, the two spots of II and III are not resolved by tlc of the product mixture. The complete separation of II and III was very difficult.

β-Photomethylquercetin[7] (IV), the lowest R_f (0.39) fluorescent photoproduct, was isolated as pale yellow needles, mp 209–210°, in 31% yield. It analyzed for $C_{16}H_6O_3(OCH_3)_4$, absorbed at 375 mμ (ϵ 21,800) in the ultraviolet, and gave a positive flavone test.[8] The nmr spectrum of IV (Table I) indicated also the loss of a methoxy group from I and the appearance of a new methylene singlet at τ 4.90. The ABX pattern in the D ring of I had collapsed to two *para*-proton singlets at τ 2.90 and 3.41, while the *meta*-protons of the A ring remained comparatively unchanged.



Lithium aluminum hydride reduction of β-photomethylquercetin (IV) produced the deoxo derivative IX showing a methylene singlet (C_7) at τ 6.61 in the nmr spectrum. Potassium permanganate oxidation of VII in basic solution gave *m*-hemipinic acid (X) while mild oxidation in acetone yielded a mixture of *m*-meconin (XI) and lactone XII. The authenticity of *m*-meconin and *m*-hemipinic acid was proven by comparison with synthetic samples,[9] and the structure of lactone XII was shown by elemental analysis ($C_{20}H_{16}O_8$) and infrared (1730 cm^{-1}, lactone), ultraviolet (362 and 345 mμ), and nmr (absence of τ 4.90 peak) spectroscopic data.

Attempts to find a lumimethylquercetin analog of β-photomethylquercetin (*i.e.*, simple photocycloaddition product) led us to the exploration of all fluorescent products, even those in minute quantities. Further chromatographic separation of early fractions of IV gave a small yield (*ca.* 1%) of another crystalline product. There is little doubt that this compound (V) is the 5-methoxy derivative of β-photomethylquercetin. The appearance of an aliphatic methoxy band at τ 6.41, accompanied by the transformation of the C_6 benzylic methylene (τ 4.90 in β-photomethylquercetin) absorption into a one-proton singlet paramagnetically shifted to τ 4.07, lent heavy support to the structural proof for V. Expectedly, V analyzed for $C_{21}H_{20}O_8$ and absorbed at 364 mμ (ϵ 20,800) in the ultraviolet. Because of its relatively small quantity, V appears only as a faint blue fluorescent spot (R_f 0.45) in the tlc of the photoproduct mixture.

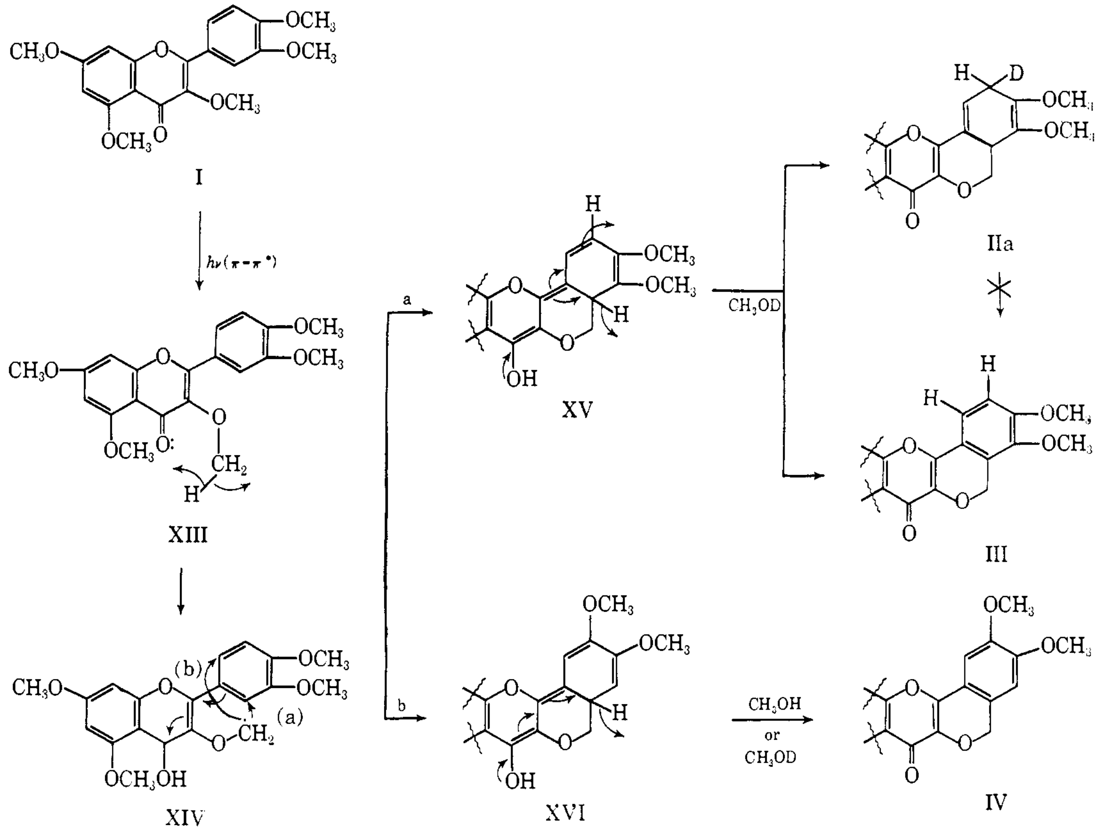
---

(6) L. Jurd in ref 1a, p 126.

(7) Described in our earlier communication [A. C. Waiss, Jr., and J. Corse, *J. Am. Chem. Soc.*, **87**, 2068 (1965)] as photomethylquercetin.

(8) J. Shinoda, *J. Pharm. Soc. Japan*, **48**, 214 (1928).

(9) G. A. Edwards, W. H. Perkin, Jr., and F. W. Stoyle, *J. Chem. Soc.*, 195 (1925).



Attempted Quenching Experiments. The fluorescence and phosphorescence emission spectra of quercetin pentamethyl ether (I) in EPA (ether–isopentane–ethanol, 5:5:2) were broad and structureless.[10] The singlet and triplet energies, nevertheless, could be approximated to 75 (E_s) and 56 (E_t) kcal/mole, and the fluorescence emission band was about 20 times more intense than that of phosphorescence. In order to establish the multiplicity of the reactive intermediate in the photochemical reaction an equimolar concentration (2.7×10^{-3} *M*) of anthracene ($E_t = 42$ kcal/mole) was added to the methanolic solution for irradiation assuming that it would quench triplet intermediates of I. The addition of this triplet quencher, however, produced no significant change in the rate of disappearance of I. This rate was approximated by taking aliquots of the reaction mixture at intervals during irradiation and comparing the integrated nmr signals of H_1 and H_{4a} of the remaining starting material to that of the singlet (τ 1.55) produced by *p*-dinitrobenzene, the internal standard,[11] in each aliquot.

On another attempt, oxygen gas at atmospheric pressure was passed continuously through the methanolic solution during irradiation. In this instance no change of reaction rate was observed; however, the only isolated products were α- and β-photomethylquercetin (III and IV).

When the irradiation was carried out in deoxygenated benzene solution, the photoreaction was observed to proceed at approximately twice the rate of that in methanolic solution, and again only α- and β-photomethylquercetins were obtained. No lumimethylquercetin was detected even in the nmr spectrum of the crude photoproduct mixture. Similar results were obtained in a vigorously degassed benzene solution of which last trace of oxygen was removed by vacuum transfers over triethylaluminum.

The detailed mechanism of the photochemical reactions of quercetin pentamethyl ether (I) is a complex one. It is possible, however, to speculate on certain important features of this reaction with the limited information at hand. First, it is reasonable to assume that the primary photochemical process is the promotion of the ground state (S_0) of I to an excited singlet (S_1) involving a π–π^* transition, since the ultraviolet absorption of I shifts hypsochromically in less polar solvents[12] (345 mμ in methanol to 322 mμ in cyclohexane). The high intensity of fluorescence (~20 times) relative to phosphorescence, indicating a relatively low rate of intersystem crossing, appears to indicate that the lowest excited singlet exists in the π–π^* state.[13] Because the rate of internal conversion of S_1(n–π^*) to the lower lying S_1(π–π^*) state is presumably very rapid (~10^{12} sec^{-1}), any quercetin pentamethyl ether excited to the S_1(n–π^*) state would be too short-lived to be significant.

The lack of inhibition of the reaction by triplet quenchers, namely O_2 and anthracene, and low intensity of phosphorescence as compared to fluorescence, led us to the conclusion that the primary reactive intermediate is most probably also in the S_1(π–π^*) state. This conclusion is valid, of course, only if the rate of intramolecular photoaddition is sufficiently slow to allow triplet quenching to be effective.[14]

---

[10] The fluorescence and phosphorescence spectra were kindly provided by Professor J. S. Bradshaw.

[11] S. Barcza, *J. Org. Chem.*, 28, 1914 (1963).

[12] M. Kasha in "Light and Life," W. D. McElroy and B. Glass, Ed., Johns Hopkins University Press, Baltimore, Md., 1961.

[13] D. M. Hercules in "Fluorescence and Phosphorescence Analysis," D. M. Hercules, Ed., Interscience Publishers, Inc., New York, N. Y., 1966, p 23.

[14] Ineffective triplet quenching because of rapid rate of photochemical reaction has been reported: (a) H. E. Zimmerman and J. S.

Regardless of the exact nature of the reaction intermediate, a plausible pathway for the photochemical reaction may be postulated with the aid of deuterated solvent.

It appears likely, because of the proximity of the methoxy group to the carbonyl function, that the first step following the excitation is the hydrogen transfer from the OCH_3 to the excited carbonyl oxygen. The rebonding of XIV presumably may proceed on either of the two *ortho* positions of the D ring producing two isomeric intermediates, XV and XVI. In benzene solution these intermediates are oxidized to α- and β-photomethylquercetin (III and IV), respectively. In methanol the formation of lumimethylquercetin (II), in addition to III and IV, apparently follows from ketonization of XV.

Whether III was derived by direct hydrogen abstraction from XV or its keto form II was resolved by irradiating I in methanol-O-*d*. It was found that one deuterium was introduced in the C_2 position of Va but none in III or IV. Because of this selective introduction of deuterium one must conclude that IIa and III were derived from XV through independent pathways. Since the introduction of deuterium in IIa was nonstereospecific, as indicated by a broad unresolved peak integrating for only one proton centering at τ 6.79, α-photomethylquercetin (III) could not have been derived from stereospecific elimination of deuterium from IIa.

The formation of β-photomethylquercetin (IV), which involves the abstraction of two hydrogens from intermediate XVI, is presumably analogous to that of α-photomethylquercetin (III). Photodehydrogenation of organic compounds in vapor phase is known to proceed by vibrationally excited, "hot" ground-state intermediates,[15] which, because of relatively large intermolecular distances, cannot lose excess vibrational energy by collision with surrounding molecules but release their energy through the rupture of C–H bonds. In solutions on the other hand, photodehydrogenation is usually traced to the presence of an oxidant.[16] Although in methanolic solution oxygen tends to enhance the formation of III at the expense of II, its presence is not always necessary for the oxidative process.[17] The irradiation of I in rigorously deoxygenated (with triethylaluminum) benzene solution produces only photooxidized product III and IV. The reduced product in this reaction has not been isolated.

The formation of 5-methoxy-β-photomethylquercetin (V) is not entirely unexpected since solvent addition in photochemical reactions has been well documented.[18]

Experimental Section

Irradiation of Quercetin Pentamethyl Ether (I) in Methanol. A solution of 2.5 g (6.7 mmoles) of quercetin pentamethyl ether[19] in 2.5 l. of methanol was deoxygenated by alternate evacuating and filling with dry nitrogen. The solution was irradiated in a photochemical reactor[20,21] equipped with 16 24-w, 3500-A lamps. The progress of the reaction was followed by tlc.[4] The solvent was evaporated under reduced pressure at the end of the reaction, which usually requires 30–40 hr, and the crude product was chromatographed through 2 kg of silica gel gradiently eluted with ethyl acetate and 20% methanol in ethyl acetate. After a small forerun of starting material, lumimethylquercetin (II) was isolated (16%). Recrystallization from a methanol–chloroform mixture gave II as colorless needles, mp 198–200°, $\lambda_{\max}^{\mathrm{MeOH}}$ 344 and 264 mμ (ϵ 14,800 and 20,200), R_f 0.67,[4] *m/e* 372.

Anal. Calcd for $C_{20}H_{20}O_7$: C, 64.5; H, 5.41; OCH_3, 33.3. Found: C, 64.6; H, 5.40; OCH_3, 33.2.

β-Photomethylquercetin (IV), R_f 0.39,[4] was obtained in later chromatographic fractions, 770 mg (31%), and recrystallized from a methanol–chloroform mixture, mp 209–210°, $\lambda_{\max}^{\mathrm{MeOH}}$ 375, 261, and 243 mμ (ϵ 21,800, 18,000 and 20,200), *m/e* 370.

Anal. Calcd for $C_{20}H_{18}O_7$: C, 64.9; H, 4.90; OCH_3, 33.5. Found: C, 64.6; H, 5.04; OCH_3; 33.1.

A combination of eluent immediately after fractions containing II from four runs was rechromatographed, and α-photomethylquercetin was isolated (*ca.* 5%), mp 202–204°, $\lambda_{\max}^{\mathrm{MeOH}}$ 365, 275, and 254 (ϵ 19,500, 12,100, and 20,800), R_f 0.66,[4] *m/e* 370.

Anal. Calcd for $C_{20}H_{18}O_7$: C, 64.9; H, 4.90. Found: C, 64.8; H, 4.90.

Similar to the isolation of III, 5-methoxy-β-photomethylquercetin (V, *ca.* 1%) was obtained from forefractions of IV and recrystallized from a methanol–chloroform mixture, mp 222–225°, $\lambda_{\max}^{\mathrm{MeOH}}$ 364, 270, 262, and 240 (ϵ 20,800, 14,400, and 14,500), R_f 0.45,[4] *m/e* 450.

Anal. Calcd for $C_{21}H_{20}O_8$: C, 63.0; H, 5.04. Found: C, 62.5; H, 5.01.

Lithium Aluminum Hydride Reduction of II. The mixture of 150 mg (0.4 mmole) of II, 300 mg (8.8 mmoles) of lithium aluminum hydride, and 150 ml of anhydrous ether was heated at reflux temperature for 24 hr. After the excess hydride was decomposed with ethyl acetate and methanol, the mixture was acidified with aqueous tartaric acid and extracted (three times) with 50-ml portions of ether. Methanol (3 ml) was added to the residue, obtained after evaporation of the combined ether extracts, and 80 mg (56%) of colorless needles was obtained. The deoxy derivative of II was recrystallized from an ethyl acetate–methanol mixture, mp 145–147°.

Anal. Calcd for $C_{24}H_{22}O_6$: C, 67.0; H, 6.19; OCH_3, 34.6. Found: C, 67.0; H, 6.26; OCH_3, 34.2.

Chloranil Oxidation of II. The solution of 50 mg (0.13 mmole) of II and 40 mg (0.16 mmole) of chloranil in 15 ml of xylene was heated at reflux temperature in an atmosphere of nitrogen for 20 hr. The solvent was removed under reduced pressure and the crude product was chromatographed through 10 g of silica gel eluted with 2% methanol in ethyl acetate. The pale yellow needles of III (31 mg, 62%) thus obtained was recrystallized with a mixture of ethyl acetate and chloroform. The oxidation product is identical in every respect with α-photomethylquercetin (III) isolated from the photolysis product mixture.

Acid Hydrolysis and Conversion of II to VIII. The solution of 200 mg (0.54 mmole) of II in 10 ml of 1 *N* hydrochloric acid and 10 ml of ethanol was heated in an atmosphere of nitrogen on a steam bath for 5 hr. The product was diluted with 50 ml of ice–water and extracted (three times) with 10-ml portions of chloroform. The combined chloroform extracts were dried over anhydrous sodium sulfate and evaporated to dryness under reduced pressure. The crude product, 155 mg (50%), was crystallized in 10 ml of methanol and recrystallized from a chloroform–methanol mixture to pink needles, mp 210–214°. Although the ultraviolet spectrum of the enol ether VII is identical with that of II in methanol, addition of sodium hydroxide shifts its absorption (365 mμ) bathochromically to 546 mμ.

Anal. Calcd for $C_{19}H_{18}O_7$: C, 63.7; H, 5.06. Found: C, 63.2; H, 5.15.

The solution of 100 mg (0.28 mmole) of VII in 10 ml of 6 *N* sodium hydroxide and 10 ml of ethanol in a nitrogen atmosphere was heated at reflux temperature for 8 hr and remained at room temperature overnight. The solution was acidified with 6 *N* hydrochloric acid and extracted with chloroform. The extract was washed with water and dried over anhydrous sodium sulfate. After

---

Swenton, *J. Am. Chem. Soc.*, **89**, 906 (1967); (b) M. H. Fisch and J. H. Richards *ibid.*, **85**, 3029 (1963).

(15) (a) R. Srinivasan, *ibid.*, **82**, 5063 (1960); (b) R. Srinivasan and J. C. Powers, *J. Chem. Phys.*, **39**, 580 (1963).

(16) (a) F. B. Mallory, C. S. Wood, and J. T. Gordon, *J. Am. Chem. Soc.*, **86**, 3094 (1964); (b) W. M. Moore, D. D. Morgan, and F. R. Stermitz, *ibid.*, **85**, 829 (1963); (c) G. M. Badger, R. J. Drewer, and G. E. Lewis, *Australian J. Chem.*, **16**, 1042 (1963).

(17) N. Toshima and I. Moritami, *Tetrahedron Letters*, 357 (1967).

(18) (a) P. J. Kropp, *J. Am. Chem. Soc.*, **88**, 4091 (1966); (b) J. A. Marshall and R. D. Carrol, *ibid.*, **88**, 4093 (1966); (c) W. G. Dauben and W. T. Wipke, *Pure Appl. Chem.*, **9**, 539 (1964); (d) C. C. Leznoff and G. Just, *Can. J. Chem.*, 42, 2801 (1964).

(19) J. A. Anderson, *Can. J. Res.*, 7, 283 (1932).

(20) Available from New England Ultraviolet Co., Middletown, Conn.

(21) Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

removal of solvent at reduced pressure the product was crystallized in aqueous acetic acid, 66 mg (72%), decomposed above 290°, $\lambda_{\max}^{\mathrm{MeOH}}$ 365, 265, and 249 mμ. The acetate VIIIb, prepared by heating VIIIa with acetic anhydride and potassium acetate, had mp 210–213° and $\lambda_{\max}^{\mathrm{MeOH}}$ 356, 268, and 238 mμ.

Anal. Calcd for $C_{18}H_{14}O_6$: C, 65.0; H, 4.49. Found: C, 64.9; H, 4.40.

Lithium Aluminum Hydride Reduction of IV. The reduction of IV, performed similar to that of II, gave IX in pink needles in 58% yield, mp 143–145°.

Anal. Calcd for $C_{20}H_{20}O_6$: C, 67.4; H, 5.66. Found: C, 67.3; H, 5.81.

Basic Potassium Permanganate Oxidation of IV. The mixture of 100 mg of (0.27 mmole) of IV, 474 mg (3 mmoles) of potassium permanganate, and 20 ml of 1 *N* potassium hydroxide was heated on a steam bath for 1 hr. Ethanol was added to reduce the excess permanganate and the reaction mixture was acidified with 1 *N* HCl and extracted (four times) with ether. The combined ether solution was extracted with a saturated solution of sodium bicarbonate. Acidification of the bicarbonate solution and reextraction with ether gave 14 mg of *m*-hemipinic acid (X), mp 183–190°.[9] Sublimination at reduced pressure dehydrated the acid to its anhydride, mp 176–178°.[9]

Potassium Permanganate Oxidation of IV in Acetone. The solution of 0.5 g (1.4 mmoles) of IV, 0.1 ml of acetic acid, and 0.8 g (5 mmoles) of potassium permanganate in 500 ml of acetone, freshly distilled over potassium permanganate, was stirred at room temperature for 1 hr, and the solvent was removed under reduced pressure. The residue was extracted with 100 ml of hot chloroform and upon removal of solvent 165 mg of product mixture was obtained. This crude mixture was triturated with 10 ml of methanol to rid it of *m*-meconine, and the residue was crystallized in chloroform–methanol mixture, from which 70 mg (15%) of lactone XII was obtained, mp 322–324°, $\lambda_{\max}^{\mathrm{MeOH}}$ 362, 348, 270, and 262 mμ, ν (KBr) 1730 cm⁻¹.

Anal. Calcd for $C_{20}H_{16}O_8$: C, 62.5; H, 4.20; OCH_3, 32.6. Found: C, 62.6; H, 4.25; OCH_3, 32.2.

The methanol extract of the oxidation product mixture was evaporated to dryness and chromatographed through a silica gel column (25 g eluted with ethyl acetate) giving 36 mg of *m*-meconine (XI), mp 155–157°.[9]

Irradiation of I in Oxygenated Methanol. The irradiation experiment was conducted as described in deoxygenated methanolic solution except that a slow stream of oxygen was passed through the stirred solution during irradiation.

Irradiation of I with Anthracene. The reaction was carried out under identical conditions as described in the irradiation of I in deoxygenated methanol except that an equimolar (6.7 mmoles) amount of anthracene was added to the solution.

Irradiation of I in Deoxygenated Benzene. In this experiment benzene was used as solvent instead of methanol; otherwise the reaction was performed under identical conditions.

In another experiment the benzene used in the reaction was heated and cooled under a stream of nitrogen, followed by the addition of triethylaluminum to remove last traces of oxygen, and was then vacuum transferred to the reaction flask containing I. The reaction was carried out in a sealed flask.

Acknowledgment. The authors wish to thank Professors W. G. Dauben and J. S. Bradshaw and Dr. K. L. Stevens for several stimulating discussions. We appreciate also the help of Miss N. Henderson for her assistance in our nmr analyses and L. M. White and G. Secor for elemental analyses.

Kinetics of Iodination of 1-Alkylpyrazoles. Relative Electrophilic Reactivities of 1-Substituted and 1-Unsubstituted Pyrazoles[1]

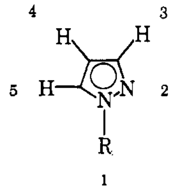
John D. Vaughan, Gary L. Jewett, and Virginia L. Vaughan

Contribution from the Departments of Chemistry of Colorado State University, Fort Collins, Colorado, and Virginia Polytechnic Institute, Blacksburg, Virginia.

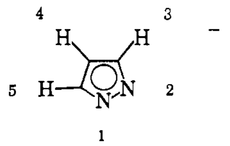
Received July 5, 1967

Abstract: The kinetics of iodination of 1-methylpyrazole, 1-ethylpyrazole, and 1-isopropylpyrazole was studied. The rate laws were found to be the same as that of aniline and the reactivities of these alkyl-substituted pyrazoles followed the inductive order. The rate of iodination of the pyrazole molecule was estimated from that of 1-methylpyrazole and compared with the rate of iodination of the anion of pyrazole. The varying sensitivities of aromatic substrates to particular bases in base-catalyzed reactions was noted and suggestions regarding the transition states of these reactions were made.

The observed rate of iodination of pyrazole (I, R = H) has been shown[2a] to be inversely proportional to the hydrogen ion concentration in aqueous media at constant ionic strength. This dependence is understood if the anion II undergoes electrophilic attack rather than the molecule itself.[2] Since pyrazole is a very weak acid ($K_a \sim 10^{-14}$), it follows that the anion of pyrazole must have far greater electrophilic reactivity than the undissociated molecule. It is of considerable theoretical interest to ascertain how much more reactive the anion is than the corresponding molecule. An indirect approach to this problem would be to determine the relative rates of iodination of 1-alkylpyrazoles. Since 1-alkylpyrazoles do not have acidic properties, only the molecule is subject to attack by the electrophile. Accordingly, one purpose of this investigation was to conduct a detailed rate study of the aqueous iodination of 1-alkylpyrazoles,



I



II

---

[1] Supported in part by a Colorado State University Faculty Grant.

[2] (a) J. D. Vaughan, D. G. Lambert, and V. L. Vaughan, *J. Am. Chem. Soc.*, **86**, 2857 (1964); (b) J. H. Ridd, *J. Chem. Soc.*, 1238 (1955).