earlier procedure. With the more reactive aromatics, *p*-dimethoxybenzene and naphthalene, additional competitions employing 2:1 or 5:1 molar ratios of benzene to *p*-dimethoxybenzene or naphthalene were also run.

Peroxide-Initiated Reactions. Chloroacetonitrile, (5 mmol), toluene (10 mmol), and the peroxide (5 mmol) were dissolved in acetonitrile (100 mL), degassed with nitrogen, and heated. The *OO-tert*-butyl isopropyl peroxycarbonate reactions were refluxed (80 °C) for one week whereas the di-*n*-propyl peroxydicarbonate reactions were placed in a constant temperature bath at 60 °C for 6 h. In both cases iodometric analysis indicated that unreacted peroxide was negligible at the end of the reaction. Product analysis was carried out directly or after partial evaporation of the solvent and reactants.

Determination of Isomer Distributions. The meta and para isomers of (methylphenyl)acetonitrile and (fluorophenyl)acetonitrile could not be separated by capillary column GC. The isomer distributions could be determined however by using GC, IR, and NMR methods.

In the case of (fluorophenyl)acetonitrile the GC could separate the ortho isomer, but the meta and para isomers gave a single peak. Examination of the infrared spectra of the authentic compounds showed that a peak at 1140 cm^{-1} could be assigned to the meta isomer while a peak at 1160 cm^{-1} was unique to the para isomer. Absorbances were determined from a series of four standards containing different ratios of (*m*- and (*p*-fluorophenyl)acetonitrile and a calibration curve for absorbance to concentration ratios constructed. The meta:para ratio for the (fluorophenyl)acetonitrile produced by the photochemical reaction of fluorobenzene and chloroacetonitrile was determined from the calibration curve by running the IR spectrum of the preparative GC sample.

NMR was used to determine the isomer distribution of the products from the toluene photolyses. GC analysis of the products gave the (*m*- and (*p*-methylphenyl)acetonitrile products together in one peak, and (*o*-methylphenyl)acetonitrile along with phenylpropionitrile together in another peak. These products were collected together in a single preparative GC sample and analyzed by NMR. The methylene protons from the ortho isomer were resolved from those of the combined meta and para isomers as well as from phenylpropionitriles and could be integrated to find the fraction of ortho isomer. The meta to para isomer ratio was determined by preparing standard solutions of the pure isomers. These solutions were mixed in varying ratios until one was obtained which gave an NMR spectrum matching that of the signal from the reaction mixture. Alternately separation of the tolylacetonitriles could be accomplished on two different columns. Column 1 separated the meta isomer from the combined ortho and para isomers, whereas column 2 separated the ortho isomer from the other two. Once the meta and ortho isomers were determined, the para isomer was calculated by subtracting the ortho isomer determined by column 2 from the ortho + para isomers of column 1 and also by subtracting the meta isomer determined by column 1 from the meta and para isomers of column 2.

Acknowledgment. The authors are grateful to Dr. Gary Schuster, Dept. of Chemistry, University of Illinois for helpful discussions and suggestions as well as for generous usage of laser flash photolysis equipment. We also wish to thank G. Farran of Stroink Pathology, Bloomington, IL, for usage of a fluorescence spectrometer. We are grateful to Lucidol Pennwalt, Buffalo, NY, and PPG Co., Barberton, OH, for generous peroxide samples.

Registry No. C_6H_6, 71-43-2; C_6H_5F, 462-06-6; $C_6H_5CH_3$, 108-88-3; $C_6H_5OCH_3$, 100-66-3; $C_{10}H_8$, 91-20-3; *p*-$C_6H_4(OCH_3)_2$, 150-78-7; $ClCH_2CN$, 107-14-2.

Product Studies of the Photocycloaddition Reactions of 5-Chloro- and 5-Fluorouracil Derivatives and Olefins. An Interesting and Useful Effect of Fluorine on Regioselectivity

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Received October 12, 1983

The acetone-sensitized photochemical cycloadditions of 1,3-dimethyl-5-chlorouracil (**1a**), 5-chlorouracil (**1b**), 1,3-dimethyl-5-fluorouracil (**4**), and 5-fluorouracil (**7**) have been studied. The 5-chlorouracil systems **1a** and **1b** gave complex, acidic product mixtures on attempted photocycloaddition to enol acetates. Only tetramethylethylene underwent clean photocycloaddition with **1a** and **1b**, affording a mixture of cycloadduct and 1,3-dimethyl-5-(1,1,2-trimethyl-2-propenyl)-2,4(1*H*,3*H*)-pyrimidinedione (**3**). By contrast, 5-fluorouracil derivatives **4** and **7** underwent clean photochemical cycloaddition to isopropenyl acetate, cyclopentenyl acetate, and cyclohexenyl acetate to form endo,exo mixtures of the head-to-tail photoadducts. In its photocycloaddition to simple olefins, 5-fluorouracil showed a much higher preference for formation of the head-to-tail photoadduct than do other simple uracil derivatives or cyclohexenone. The reaction of 5-fluorouracil with isobutylene, methylenecyclopentane, methylenecyclohexane, and methylenecycloheptane gave nearly exclusively the head-to-tail regioisomer. The ratio of head-to-tail to head-to-head isomers for the reaction of 5-fluorouracil with 1-methylcyclopentene, 2-methyl-2-butene, and propene was 89:11, 85:15, and 76:24, respectively. Extensive ^{19}F NMR data are reported for the photocycloadducts.

The initial impetus for investigating the photocycloaddition chemistry of 5-chloro- and 5-fluorouracil was to employ the adducts as intermediates in the synthesis of 5-functionalized uracils and uridines as noted in the accompanying paper.[1] A prelude to applying the above strategy to uracil functionalization was a study of the photochemical cycloaddition of the 5-halouracils with enol acetates; these results are reported herein.[2a] More interestingly, the photochemical cycloaddition of 5-fluorouracil with simple olefins showed an unexpectedly high

(1) Kaminski, V. V.; Wexler, A. J.; Balchunis, R. J.; Swenton, J. S. *J. Org. Chem.*, following paper in this issue.

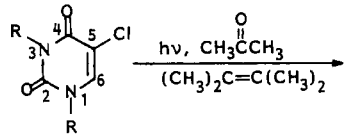
(2) Some of this material has been reported in preliminary form: (a) Wexler, A. J.; Balchunis, R. J.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1975**, 601. (b) Wexler, A. J.; Swenton, J. S. *J. Am. Chem. Soc.* **1976**, *98*, 1602.

0022-3263/84/1949-2733$01.50/0

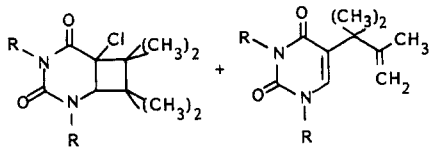
degree of regioselectivity.[2b] Uracil and its 5- and 6-methyl derivatives had been shown earlier to undergo high-yield photocycloaddition reactions with olefins.[3] However, the formation of difficultly separable regioisomeric photoaddition products with simple olefins detracted from the synthetic utility of the process.[4] The possibility that photocycloadditions of 5-fluorouracil could eliminate the regioisomeric mixtures obtained from the simple uracils studied previously prompted a detailed study of 5-fluorouracil photocycloaddition chemistry which is also reported herein.

Photocycloadditions of 5-Chlorouracil Derivatives

There are few examples of bimolecular photocycloaddition reactions of α-halo-α,β-unsaturated carbonyl compounds with olefins.[5] Surmising that a 5-iodo- or 5-bromouracil would give cleavage of the carbon–halogen bond[6] under irradiation conditions, the photocycloaddition chemistry of 1,3-dimethyl-5-chlorouracil was examined first. Acetone-sensitized irradiation of **1a** in the presence



1a, R = CH_3
b, R = H

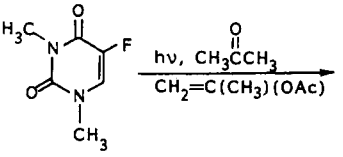


2a (33%) 3a (35%)
b (30%) b (20%)

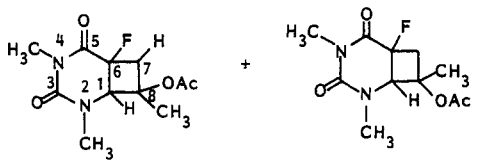
of isopropenyl acetate, vinyl acetate, or ethyl vinyl ether gave dark acidic reaction mixtures which showed a complex mixture of products. Only tetramethylethylene afforded a relatively clean reaction from which **2a** and **3a** could be isolated in good yield.[7] Since complicated reaction mixtures usually resulted from photocycloaddition reactions of 5-chlorouracil derivatives, further studies with **1a** and **1b** were abandoned.

Photocycloaddition Reactions of 5-Fluorouracil (7) and Enol Acetates

It appeared likely that one of the complications in the photocycloaddition chemistry of the 5-chlorouracil derivatives arose from cleavage of the carbon–chlorine bond at some stage in the reaction. The photochemistry of 1,3-dimethyl-5-fluorouracil (**4**) was investigated next since the carbon–fluorine bond is one of the stronger bonds in organic molecules; thus, carbon–halogen bond cleavage would be less of a factor.[8] Indeed, photosensitized reaction of **4** with isopropenyl acetate gave two products in a 2:1 ratio



4



5 (32%) 6 (16%)

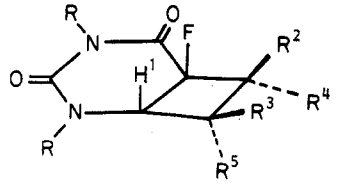
which could be separated by careful silica gel chromatography with some loss of material. Spectroscopic and analytical data showed the two products to be **5** and **6**. Especially informative was the appearance of H-1 in the ^1H NMR spectra of **5** and **6** as clean doublets at δ 4.13 (J_{HF} = 22 Hz) and δ 3.90 (J_{HF} = 19 Hz). The stereochemistry of the acetate and methyl groups was assigned on the basis of an intramolecular cyclization[1] and was supported by the positions of the methyl resonances in the ^1H NMR spectra. The endo methyl group of **5** occurred at δ 1.31 while the exo methyl group of **6** was at δ 1.78.[9]

After the successful photocycloaddition of 1,3-dimethylfluorouracil and isopropenyl acetate, the reaction of 5-fluorouracil (**7**) with other enol acetates was studied, and the results are collected in Table I. Isopropenyl acetate, cyclohexenyl acetate, and cyclopentenyl acetate underwent photochemical cycloadditions with 5-fluorouracil to give the adducts shown. While the yield of the mixture of epimeric cycloadducts was quite good, fractional crystallization or silica gel chromatography required to obtain the pure isomers resulted in lower isolated yields. However, since each adduct fragmented to the same 5-substituted uracil under basic conditions,[1] the epimeric adducts need not be separated for their intended use.

The appearance of H-1 in the ^1H NMR spectrum as a doublet (J = 19–22 Hz after a D_2O wash to remove N–H coupling) establishes the expected head-to-tail orientation for the photoadducts. For the isopropenyl acetate cycloaddition products, the major regioisomer has the methyl group endo since the methyl resonance in the NMR is shielded (δ 1.22) relative to the exo methyl group in the minor regioisomer (δ 1.56). This correlation had been noted previously for **5** and **6**. The ^{19}F NMR was indispensible for assigning the stereochemistry of the cyclohexenyl acetate and cyclopentenyl acetate cycloadducts. While the magnitude of the hydrogen–fluorine coupling constant depends on dihedral angle[11] θ, it is also a function of the electronegativity of the groups near the atoms of concern.[12] However, for a similar series of compounds, the hydrogen–fluorine coupling constants can be used to assign stereochemistry. Thus, when an alkyl substituent at C-7 is exo, the ^{19}F NMR signal is a doublet of doublets

(3) Wexler, A. J.; Hyatt, J. A.; Raynolds, P. W.; Cottrell, C.; Swenton, J. S. *J. Am. Chem. Soc.* **1978**, *100*, 512.
(4) This limitation does not apply for photochemical cycloadditions to symmetrical olefins. For example, see: Pearlman, B. A. *J. Am. Chem. Soc.* **1979**, *101*, 6398.
(5) For intramolecular example, see: Eaton, P. E.; Cole, T. W. *J. Am. Chem. Soc.* **1964**, *86*, 3157.
(6) (a) Ishihara, H.; Wang, S. Y. *Nature (London)* **1966**, *210*, 1222; (b) *Biochemistry* **1966**, *5*, 2302. (c) Langmuir, M. E.; Hayon, J. *J. Chem. Phys.* **1969**, 4893.
(7) Acetone-sensitized photocycloaddition of isobutylene with 5-chlorouracil gave a complex mixture of products.
(8) For a study of the photohydration of 5-fluorouracil, see; Fikus, M.; Wierzchowski, K. L.; Shugar, D. *Photochem. Photobiol.* **1965**, *4*, 521.
(9) The formation of trans-fused cycloadducts in uracil cycloadditions is very uncommon,[10] and all the compounds reported herein are assigned the cis ring fusion.
(10) Swenton, J. S.; Hyatt, J. A.; Lisy, J. M.; Clardy, J. *J. Am. Chem. Soc.* **1974**, *96*, 4885.
(11) Williamson, K. L.; Li, Y.-K.; Hall, F. H.; Swager, S. *J. Am. Chem. Soc.* **1966**, *88*, 5678.
(12) Abraham, R. J.; Cavalli, L. *Molecular Physics* **1965**, *9*, 67.

Table I. Photocycloaddition Products from 1,3-Dimethyl-5-fluorouracil (4) and 5-Fluorouracil (7)



entry	reaction	R^2	R^3	R^4	R^5	yield, %	^{19}F[e]	J_{H_1F}[f]	J_{H_2F}[f]	J_{H_4F}[f]
1	4 and isopropenyl acetate[a]	H	OAc	H	CH_3	32	−144.9	23	19	9
		H	CH_3	H	OAc	16	−146.9	20	15	5
2	7 and isopropenyl acetate[a]	H	OAc	H	CH_3	39	−150.1	23	17	11
		H	CH_3	H	OAc	17	−152.6			
3	7 and cyclohexenyl acetate		$-(CH_2)_4-$	H	OAc	85	−170.4	25		5
		H	OAc		$-(CH_2)_4-$	14	−144.4	23	25	
4	7 and cyclopentenyl acetate		$-(CH_2)_3-$	H	OAc	64	−170.3	20		5
5	7 and tetramethylene[c]	CH_3	CH_3	CH_3	CH_3	79	−158.1	23		
6	7 and 1-methylcyclopentene[b]		$-(CH_2)_3-$	H	CH_3	68	−164.5	22		5
		H	CH_3		$-(CH_2)_3-$	14[d]	−144.4	22	23	
7	7 and 2-methyl-2-butene	CH_3	CH_3	H	CH_3	65[d]	−166.8	24		7
		H	CH_3	CH_3	CH_3	20[d]	−142.1	23	23	
		CH_3	CH_3	CH_3	H	10[d]	158.2	23		
		CH_3	H	CH_3	CH_3	5[d]	−161.0	22		
8	7 and propene	H		H			−145.7			
			$(CH_3)(H)$		$(H)(CH_3)$	57[d]				
		H		H			−145.7			
			H				−160.7			
		$(CH_3)(H)$		$(CH_3)(H)$		18[d]				
			H		H		−181.7			
		R^2	R^4	R^3	R^5					
9	4 and isobutylene	H	H	CH_3	CH_3	75	−140.4	23	17	9
10	7 and isobutylene	H	H	CH_3	CH_3	90	−145.6	23	17	9
11	7 and methylenecyclopentane	H	H	$-(CH_2)_4-$		76				
12	7 and methylenecyclohexane	H	H	$-(CH_2)_5-$		72	−145.4	23	20	6
13	7 and methylene cycloheptane	H	H	$-(CH_2)_6-$		78				

[a] Some additional coupling resulting in line broadening. [b] The ^{19}F NMR spectrum of the reaction mixture showed three minor peaks ~11% of the major adduct to which structures have not been assigned. [c] A coupling of 3Hz to the CH_3 group was also present. [d] Product not isolated pure. [e] Shifts are reported upfield from CCl_3F. [f] Coupling constants are given in hertz.

with a large coupling constant (J = 20–25 Hz) with H-1 (θ = 0°) and a smaller coupling constant (J = 5 Hz) with H-7 endo (θ = 120°). For the minor endo adduct with cyclohexenyl acetate, the ^{19}F NMR signal appeared as a pseudotriplet with the center signal slightly split since the dihedral angles with H-1 and H-7 exo are about 0° and thus the coupling constants have similar magnitudes (entries 3–5 in Table I). Thus the photocycloadditions of 5-fluorouracil and enol acetates afford head-to-head cycloadducts in good yield with high regioselectivity.

Photocycloaddition Reactions of 5-Fluorouracil (7) and Simple Olefins

The absence of complications from carbon–halogen bond cleavage in the photochemistry of 5-fluorouracil (7) prompted an examination of its photocycloaddition reactions with simple olefins. The reaction of 7 with isobutylene was performed first (entry 10, Table I). Surprisingly, one photocycloaddition product was obtained from this reaction in high yield. The ^{19}F NMR spectrum of the crude reaction mixture indicated some formation of 5-fluorouracil photodimers, but no evidence of a regioisomeric product could be found. Similarly, one major product was formed in high yield from 7 and methylene cyclopentane, cyclohexane, and cycloheptane (entries 11–13, Table I). The orientation was established as the 8,8-disubstituted compound from the appearance of H-1 as a doublet (J = 22–23 Hz) in the ^1H NMR spectrum of the products as well as by additional analytical and spectroscopic data (as detailed in the Experimental Section).

Photocycloadditions of 1,1-disubstituted olefins to cycloalkenones[13] and uracils[3,14] show reasonable regioselectivity (2–3:1), favoring the head-to-tail isomer. However, olefins mono-, 1,2-di-, and trisubstituted with simple alkyl substituents show lower regioselectivity as illustrated by the nearly 1:1 ratio of regioisomers formed from propene and cyclopentenone.[14,15] Thus, 1-methylcyclopentene, 2-methyl-2-butene, and propene were selected to probe the degree of regioselectivity with 5-fluorouracil in photocycloaddition reactions. An additional complication in the photocycloadditions of 7 and these olefins is the formation of endo and exo products in addition to regioisomers. Isomeric photoproducts from uracil photocycloaddition are especially difficult to separate chromatographically; thus, in these reactions, only the major products were isolated in a pure form. However, with a knowledge of ^{19}F chemical shifts and hydrogen–fluorine coupling constants from the earlier reaction products, a good estimate could be made of the regioselectivity and product ratios by careful analysis of the ^{19}F NMR spectrum of the crude reaction mixtures.

The structures of the products given in Table I (entries 6–8) were assigned on the basis of the coupling constants in the ^{19}F NMR spectra as detailed above. In addition, the pronounced shielding of the ^{19}F resonance (20–30 ppm) by a syn alkyl group (compare isomers in entries 3, 4, 6, and 8, Table I) was a check on the regiochemistry and

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(14) Shih, C.; Fritzen, E. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 4462.
(15) Eaton, P. E. *Acc. Chem. Res.* **1967**, *1*, 50.

stereochemistry assigned from the coupling constants. While the structure assignments for the minor products which were not isolated pure must be considered tentative, we are reasonably confident of the assignments.

The above studies show that the regioselectivity of head-to-head vs. head-to-tail photoproducts are 89:11 for 1-methylcyclopentene, 85:15 for 2-methyl-2-butene, and 76:24 for propene. While it is unfortunate that the nearly exclusive head-to-tail regioselectivity observed for 1,1-disubstituted ethylenes did not carry over to the above systems, this is a substantial improvement over photocycloadditions with uracil itself, which afford with similar olefins difficultly separable and unanalyzable mixtures of regioisomers.

Summary

The photochemical cycloaddition reactions of 5-fluorouracil (7) with enol acetates give head-to-tail regioisomers in good yield. In contrast to simple uracil derivatives, the photochemical cycloaddition reactions of 7 with simple olefins give primarily head-to-tail regioisomers, the degree of regioselectivity depending on the structure of the olefin. This chemistry makes the derivatives of the 2,4-diazabicyclo[4.2.0]octane ring system available regioselectively in one step from commercially available compounds. The following paper presents the use of these products in a mild, high-yield synthesis of 5-substituted uracils. A discussion of the origin of the fluorine effect of regioselectivity is deferred until mechanistic work in progress is complete.[16] However, we feel at this time that a high ratio of closure vs. cleavage of the 1,4-biradical leading to the head-to-tail product is a major factor in the regioselectivity of 5-fluorouracil photocycloadditions noted here.[16]

Experimental Section[17]

General Procedure for Irradiations. All irradiations were performed in a standard immersion apparatus with Corex-filtered light from a 450-W Hanovia medium-pressure source. For reactions of −70 °C, the quartz immersion well was insulated from the reaction vessel with a Dewar flask; when gaseous olefins were used, a dry ice condenser was placed on top of the immersion well. The progress of the reaction was followed by TLC on silica gel using 1–10% $CH_3OH/CHCl_3$ as eluant depending on the system. After completion of the reaction, the solvent was removed in vacuo, and the product was directly crystallized or chromatographed on silica gel. Note that the isomeric photocycloaddition products are often quite difficult to separate by chromatography; thus, overlap fractions were often obtained. The photochemical results for the reactions are reported as follows: g (mmol) of uracil derivative, mL of solvent for irradiation, approximate volume or weight of olefin, irradiation time; purification method (where chromatography was employed the compounds are given in order of elution from the column), spectroscopic and analytical data.

6-Chloro-2,4,7,7,8,8-hexamethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione and 1,3-dimethyl-5-(1,1,2-trimethyl-2-propenyl)-2,4(1*H*,3*H*)-pyrimidinedione: **1a** (2 g, 11 mmol), acetone (460 mL), tetramethylethylene (25 mL), 54 h at −70 °C; chromatography (2.3 × 60 cm column) using 10% Et_2O/PE as eluant. Compound **2a** was recrystallized (Et_2O/H) to give 0.72 g (33%) of white needles: mp 111–113 °C; IR 1678 (s, br); ^1H NMR ($CDCl_3$) δ 3.73 (s, 1 H), 3.25 (s, 3 H), 3.03 (s, 3 H), 1.32, 1.17, 1.08, 0.86 (4 s, 12 H). Anal. Calcd for $C_{12}H_{19}N_2O_2Cl$: C, 55.8; 7.4; N, 10.8. Found: C, 55.8; H, 7.4; N, 10.7.

Continued elution (20% Et_2O/PE) gave 0.65 g (35%) of **3a**: mp 85–87 °C; IR 1704 (s), 1645 (s, br); ^1H NMR ($CDCl_3$) δ 7.04 (s, 1 H), 4.86 (m, 2 H), 3.42 (s, 3 H), 3.33 (s, 3 H), 1.70 (m, 3 H), 1.38 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 162.3, 151.8, 150.5, 138.6, 120.2, 110.1, 41.1, 37.1, 29.7, 27.8, 26.7, 20.2. Anal. Calcd for $C_{12}H_{18}N_2O_2$: C, 64.9; H, 8.1; N, 12.6. Found: C, 64.9; H, 8.2; N, 12.6.

Continued elution with Et_2O gave 0.54 g of **1a**.

6-Chloro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione and 5-(1,1,2-trimethyl-2-propenyl)-2,4-(1*H*,3*H*)-pyrimidinedione: **1b** (0.35 g, 2.4 mmol), acetone (500 mL), tetramethylethylene (10 mL), 8 h at −78 °C. Chromatography (4 × 37 cm column) with 1–4% $CH_3OH/CHCl_3$ as eluant gave 0.166 g (30%) of **2b**, which was recrystallized (EtOAc/H): mp 270 °C; IR 1715 (s, br); ^1H NMR δ 10.4 (br s, 1 H), 8.0 (br d, J = 5.5 Hz, 1 H), 3.81 (d, J = 5.5 Hz, 1 H), 1.23 (s, 3 H), 1.01 (br s, 6 H), 0.87 (s, 3 H). Anal. Calcd for $C_{10}H_{15}ClN_2O_2$: C, 52.1; H, 6.6; N, 12.1. Found: C, 52.1; H, 6.6; N, 12.1.

Continued elution with 5–6% $CH_3OH/CHCl_3$ gave 0.074 g of a 3:7 mixture of **2b** and **3b**; 6–7% $CH_3OH/CHCl_3$ gave 0.031 g (7%) of **3b** identical with known material; 7–10% $CHCl_3/CH_3OH$ gave 0.20 g of a 1:10 mixture of **3b** and **1b**. Corrected for recovered **1b**, the yields of **2b** and **3b** were 59% and 41%, respectively.

8-(Acetyloxy)-6-fluoro-2,4,8-trimethyl-(1α,6α,8α)-2,4-diazabicyclo[4.2.0]octane-3,5-dione and its 1α,6α,8β isomer: **4** (1 g, 6.3 mmol), acetone (20 mL)/CH_3CN (115 mL), isopropenyl acetate (15 mL), 1.5 h. VPC (13 ft × 18 in. column, 5% SE-30 on 120–140 Chromosorb W at 180 °C) showed two products in a 2:1 ratio. Chromatography (2.3 × 45 cm column) using 60% Et_2O/PE as eluant gave 0.43 g (26%) of **5**: mp 93–95 °C; IR (KBr) 1739 (s), 1721 (s), 1669 (s, br); ^1H NMR ($CDCl_3$) δ 4.13 (d, J = 22 Hz, 1 H), 3.23 (br s, 3 H), 3.12 (s, 3 H), 2.9–2.6 (m, 2 H), 2.03 (s, 3 H), 1.31 (s, 3 H). Anal. Calcd for $C_{11}H_{15}N_2O_4F$: C, 51.1; H, 5.81; N, 10.9. Found: C, 51.1; H, 5.9; N, 10.89.

Continued elution (60% Et_2O/PE) gave 0.27 g of **5** and **6** and 0.24 g (15%) of **6** as a colorless oil: IR (neat) 1757 (s), 1727 (s), 1692 (s, br); ^1H NMR δ ($CDCl_3$) 3.90 (d, J = 19 Hz, 1 H), 3.28 (br s, 3 H), 3.2–2.4 (m, with s at 3.08, 5 H), 1.92 (s, 3 H), 1.78 (s, 3 H).

8-(Acetyloxy)-6-fluoro-8-methyl-(1α,6α,8α)-2,4-diazabicyclo[4.2.0]octane-3,5-dione and its 1α,6α,8β isomer: **7** (1 g, 7.7 mmol), 70% acetone water (120 mL), isopropenyl acetate (25 mL), 2.5 h. Rapid chromatography using Et_2O as eluant afforded 1.02 g (57%) of a mixture of the photoproducts in a 7:3 ratio by ^{19}F NMR spectroscopy. Preparative TLC (10% $CH_3OH/CHCl_3$ as eluant) furnished pure samples of the photoadducts. The major product (endo methyl) eluted first and showed: mp 252–254 °C; IR 1739–1660 (structured, s); ^1H NMR (Me_2SO-d_6/D_2O) δ 4.33 (d, J = 23 Hz, 1 H), 2.8–2.4 (m partially obscured by Me_2SO, 2 H), 1.97 (s, 3 H), 1.22 (s, 3 H). Anal. Calcd for $C_9H_{11}N_2O_4F$: C, 47.0; H, 4.77; N, 12.2. Found: C, 46.9; H, 4.9; N, 12.0.

The minor product (exo methyl) showed: mp 219–222 °C (EtOH); IR 1740–1694 (structured, br); ^1H NMR (Me_2SO-d_6/D_2O) 4.11 (d, J = 20 Hz, 1 H), 2.76–2.30 (m partially obscured by Me_2SO, 2 H), 1.88 (s, 3 H), 1.56 (s, 3 H); exact mass calcd for m/e $C_9H_{11}N_2O_4F$ 231.078, obsd m/e 231.078.

8a-(Acetyloxy)-4a-fluorooctahydro-(4aα,4bα,8aα,8bα)-benzo[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione and its 4aα,4bβ,8aβ,8bα isomer: **7** (0.39 g, 3 mmol), acetone (150 mL), cyclohexenyl acetate (4.2 g, 30 mmol), 2 h. Concentration followed by removal of the cyclohexenyl acetate (55 °C/1 mm) and treatment of the residue with boiling CH_3OH (the dimers are very insoluble in CH_3OH) gave the crude mixture of cycloadducts. Recrystallization of this material from EtOAc/H gave 0.31 g (38%) of the major product (endo acetate): mp 261–264 °C; IR 1757, 1727, 1718 (s), strong overlapping absorptions; ^1H NMR (100

(16) Savino, T. G.; Chenard, L. K.; Swenton, J. S. *Tetrahedron Lett.* **1983**, *24*, 4055.

(17) Melting points below 180 °C were taken with a Thomas-Hoover capillary melting-point apparatus and melting points over 180 °C were taken with a hot-stage apparatus. Both sets of melting points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Infracord spectrometer and are reported in cm^{-1}. ^1H NMR spectra were recorded on an Varian A-60A or a JEOLCO 100-MHz instrument in Me_2SO-d_6 unless specified otherwise. Chemical shifts are reported downfield from tetramethylsilane. The ^{13}C NMR spectra were recorded on a Bruker HX-90 at 20 MHz by Dr. Charles Cottrell and Mr. Carl Engelman. The ^{19}F NMR spectra were determined at 86.4 MHz in Me_2SO-d_6 on a Bruker HX-90, and the chemical shifts are reported upfield from CCl_3F. Mass spectra and exact mass measurements were determined on a Consolidated Electronics MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Microanalytical Laboratory, Herlev, Denmark. Silica gel was from E. Merck Co. The following abbreviations were used throughout the Experimental Section: CH_3OH (methanol), $CHCl_3$ (chloroform), Me_2SO (dimethyl sulfoxide), Et_2O (diethyl ether), EtOH (ethanol), EtOAc (ethyl acetate), H (hexane), PE (low-boiling petroleum ether).

MHz) δ 10.9 (s, 1 H), 8.02 (d, J = 4 Hz, 1 H), 4.28 (q, J = 4, 25 Hz, 1 H), 2.2–1.0 (with s at 2.04, 11 H). Anal. Calcd for $C_{12}H_{15}N_2O_4F$: C, 53.5; H, 5.6; N, 10.4. Found: C, 53.3; H, 5.5; N, 10.1.

The two major products could be separated by careful chromatography using 1:1 Et_2O/PE through Et_2O and then 10% $CH_3OH/CHCl_3$ as eluant. This afforded 89% of the major product [R_f (6% $CH_3OH/CHCl_3$) 0.67] and 14% of the minor adduct [exo acetate, R_f (6% $CH_3OH/CHCl_3$) 0.70]: mp 188–190 °C; IR 1715 (s, br); ^1H NMR (100 MHz) δ 10.7 (s, 1 H), 8.0 (d, J = 4 Hz, 1 H), 4.4 (q, J = 4, 23 Hz, 1 H), 2.2–1.0 (with s at 2.04, 11 H).

7a-(Acetyloxy)-4a-fluorohexahydro-(4aα,4bβ,7aα,7bα)-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione and its 4aα,4bβ,7aβ,7bα isomer: 7 (0.39 g, 3 mmol), acetone (150 mL), cyclopentenyl acetate (3.78 g), 2 h. Concentration and heating at 70 °C (0.4 mm) gave a residue which was dissolved in hot CH_3OH, and the dimeric product was filtered. The concentrated filtrate was recrystallized from EtOAc/cyclohexane to afford 0.49 g (64%) of the major adduct (endo acetate): mp 224–226 °C; IR 1735 (br, s), 1710 (br, s); ^1H NMR (100 MHz) δ 10.7 (s, 1 H), 7.84 (d, J = 4 Hz, 1 H), 4.10 (q, J = 4, 20 Hz, 1 H), 2.92 (br s, 1 H), 1.97 (s, 3 H), 1.84 (br s, 6H).

6-Fluoro-2,4,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]-octane-3,5-dione: 4 (0.95 g, 6 mmol), acetone (210 mL), isobutylene (10 mL), 2 h. Workup and recrystallization gave 0.97 g (75%): mp 63–65 °C; IR 1711 (s), 1694 (s), 1677 (s, br); ^1H NMR δ 3.67 (d, J = 23 Hz, 1 H), 3.19 (d, J = 1 Hz, 3 H), 2.97 (s, 3 H), 2.6–1.8 (strong m, 2 H), 1.35 (s, 3 H), 0.92 (s, 3 H); exact mass calcd for m/e $C_{10}H_{15}N_2O_2F$ 214.1117, obsd m/e 214.1122.

6-Fluoro-8,8-dimethyl-*cis*-2,4-diazabicyclo[4.2.0]octane-3,5-dione: 7 (0.39 g, 3 mmol), acetone (150 mL), isobutylene (10 mL), 2 h. Recrystallization (EtOH/H_2O) gave 0.5 g (90%) of photocycloadduct: mp 244–245 °C; IR 1730 (s), 1710 (s); ^1H NMR δ 10.5 (s, 1 H), 7.94 (br s, 1 H), 3.79 (q, J = 4, 23 Hz, 1 H), 2.0–2.5 (m, 2 H partially obscured by Me_2SO), 1.18 (s, 3 H), 0.90 (s, 3 H). Anal. Calcd for $C_8H_{11}N_2O_2F$: C, 51.6; H, 6.0; N, 15.1. Found: C, 51.6; H, 6.0; N, 14.9.

6′-Fluoro-*cis*-spiro[cyclopentane-1,8′-[2,4]diazabicyclo-[4.2.0]octane]-3′,5′-dione: 7 (0.39 g, 3 mmol), acetone (150 mL), methylenecyclopentane (4 mL), 2 h. Recrystallization from EtOAc gave 0.47 g (76%) of photocycloadduct: mp 265–266 °C (sealed capillary); IR 1700 (s, br); ^1H NMR δ 10.44 (br s, 1 H), 8.02 (s, 1 H), 3.95 (d, J = 21 Hz, 1 H), 2.6–2.0 (m, partially obscured by Me_2SO), 1.9–1.0 (br m, 8 H). Anal. Calcd for $C_{10}H_{13}N_2O_2F$: C, 56.6; H, 6.2; N, 13.2. Found: C, 56.7; H, 6.2; N, 13.2.

6′-Fluoro-*cis*-spiro[cyclohexane-1,8′-[2,4]diazabicyclo-[4.2.0]octane]-3′,5′-dione: 7 (0.39 g, 3 mmol), acetone (150 mL), methylenecyclohexane (4.3 g, 45 mmol), 2 h. Recrystallization from EtOAc gave 0.49 g (72%) of photoadduct: mp 263–265 °C; IR 1730 (s), 1720 (s); ^1H NMR δ 10.5 (s, 1 H), 8.02 (d, J = 4 Hz, 1 H), 3.72 (q, J = 4, 23 Hz, 1 H), 2.4–1.9 (br m, partially obscured by Me_2SO), 1.0–1.8 (br m, 10 H). Anal. Calcd for $C_{11}H_{15}N_2O_2F$: C, 58.4; H, 6.7; N, 12.4. Found: C, 58.2; H, 6.7; N, 12.2.

6′-Fluoro-*cis*-spiro[cycloheptane-1,8′-[2,4]diazabicyclo-[4.2.0]octane]-3′,5′-dione: 7 (0.52 g, 4 mmol), acetone (150 mL), methylenecycloheptane (5.3 g, 49 mmol), 2.3 h. Recrystallization from EtOAc gave 0.75 g (78%) of photoadduct: mp 259–260 °C; IR 1730 (s), 1715 (s); ^1H NMR δ 10.5 (s, 1 H), 8.02 (br s, 1 H), 3.78 (q, J = 4, 23 Hz, 1 H), 2.4–1.8 (m, partially obscured by Me_2SO), 1.8–1.0 (br s, 12 H). Anal. Calcd for $C_{12}H_{17}N_2O_2F$: C, 60.0; H, 7.1; N, 11.7. Found: C, 59.9; H, 7.1; N, 11.7.

6-Fluoro-7,7,8,8-tetramethyl-*cis*-2,4-diazabicyclo[4.2.0]-octane-3,5-dione: 7 (0.52 g, 4 mmol), acetone (150 mL), tetramethylethylene (4 g, 48 mmol), 2.3 h. Recrystallization from EtOAc gave 0.68 g (79%) of photoadduct: mp 267–268 °C; IR 1720 (s, br); ^1H NMR δ 10.4 (s, 1 H), 7.9 (br s, 1 H), 3.82 (q, J = 3.5, 23 Hz, 1 H), 1.13 (d, J = 3 Hz, 3 H), 1.05, 0.93, 0.82 (3 s, 9 H). Anal. Calcd for $C_{10}H_{15}N_2O_2F$: C, 56.06; H, 7.1; N, 13.1. Found: C, 56.2; H, 7.1; N, 13.0.

4a-Fluorohexahydro-7a-methyl-(4aα,4bα,7aα,7bβ)-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione: 7 (0.39 g), acetone (150 mL), 1-methylcyclopentene (3.7 g, 45 mmol), 2 h. The ^{19}F NMR of the reaction mixture (90% yield) showed two absorptions in the ratio 7:34 comprising 91% of the total fluorine. Two recrystallizations from EtOAc gave the major product as white needles: mp 232–234 °C; IR 1710 (s, br); ^1H NMR δ 10.5 (s, 1 H), 7.8 (br s, 1 H), 3.66 (q, J = 4, 23 Hz, 1 H), 2.0–1.4 (br m, 6 H), 1.02 (s, 3 H). Anal. Calcd for $C_{10}H_{13}N_2O_2F$: C, 56.6; H, 6.2; N, 13.1. Found: C, 56.5; H, 6.3; N, 13.1.

The minor adduct was not obtained pure but its structure was inferred from its ^{19}F NMR spectrum (see text).

5-Fluorouracil and 2-methyl-2-butene photoadducts: 7 (0.39 g, 3 mmol), acetone (150 mL), 2-methyl-1-butene (3.2 g, 45 mmol), 2 h. The ^{19}F NMR spectrum showed four compounds in the ratio 20:10:5:65 with signals at δ −142.1 (t), −158.2 (d), −161.0 (d), −166.8 (t). No attempt was made to isolate the pure products.

6-Fluoro-8-methyl-(1α,6α,8α)-2,4-diazabicyclo[4.2.0]octane-3,5-dione and isomers: 7 (0.39 g, 3 mmol), 150 mL of acetone, propylene (bubbled through −5 °C reaction mixture), 2 h. The crude product was sublimed (150 °C/0.1 mm) to give 0.39 g (75%) of a mixture of photoadducts. Preparative TLC (20% diethylamine/PE as eluant) resolved two bands. The top band was the pure 8-*exo*-methyl compound: mp 239–241 °C (sealed capillary); IR 1730–1710 (s, overlapping); ^1H NMR δ 10.5 (s, 1 H), 8.09 (br s, 1 H), 3.61 (after D_2O wash, q, J = 7, 20 Hz, 3 H), 2.5–1.5 (br m, 3H), 1.1 (d, J = 6 Hz, 3 H); ^{19}F NMR δ −145.83, −145.98, −146.20, −146.35, −146.40. Anal. Calcd for $C_7H_9N_2O_2F$: C, 48.8; H, 5.3; N, 16.3. Found: C, 48.9; H, 5.4; N, 16.3.

The bottom band (0.23 g, 44%) was shown by ^1H, ^{19}F, and ^{13}C NMR spectroscopy to be a two-component mixture. The ^1H NMR spectrum showed two doublets at δ 0.92 (J = 7 Hz) and δ 1.16 (J = 7 Hz) in the ratio 2:1, the δ 0.92 signal being at the same position as the 8-*endo*-methyl photocycloadduct. ^{19}F NMR spectrum showed two multiplets: one centered at δ −145.7 and the other at δ −160.7 in the ratio 2.3:1. ^{13}C NMR spectrum showed a sharp singlet at δ 13.54 and a doublet at δ 14.00 (J = 6.1 Hz) assigned to the methyl groups of the 7-methyl isomer and the 8-*endo*-methyl isomer. Since the crude ^{19}F NMR spectrum showed three multiplets at δ −145.7, −160.7, and 181.7 in the ratio 76:18:8, the signal at −145.7 was assumed to arise from coincident absorptions of the 8-*endo*- and 8-*exo*-methyl isomers. The regiochemistry of the addition was assigned on the basis of these data as 76:24.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

Registry No. **1a**, 31217-00-2; **1b**, 1820-81-1; **2a**, 90295-98-0; **2b**, 90295-99-1; **3a**, 90296-00-7; **3b**, 90296-01-8; **4**, 3013-92-1; **5**, 57767-87-0; **6**, 57794-74-8; **7**, 51-21-8; (1α,6α,8α)-8-(acetyloxy)-6-fluoro-8-methyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 57794-72-6; (1α,6α,8β)-8-(acetyloxy)-6-fluoro-8-methyl-2,4-diazabicyclo-[4.2.0]octane-3,5-dione, 57767-86-9; (4aα,4bα,8aα,8bα)-8a-(acetyloxy)-4a-fluorooctahydrobenzo[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione, 57794-71-5; (4aα,4bβ,8aβ,8bα)-8a-(acetyloxy)-4a-fluorooctahydrobenzo[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione, 57767-85-8; (4aα,4bβ,7aα,7bα)-7a-(acetyloxy)-4a-fluorohexahydro-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]-pyrimidine-2,4(3*H*,4a*H*)-dione, 90365-45-0; (4aα,4bβ,7aβ,7bα)-7a-(acetyloxy)-4a-fluorohexahydro-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione, 57767-84-7; *cis*-6-fluoro-2,4,8,8-tetramethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90296-02-9; *cis*-6-fluoro-8,8-dimethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 59137-86-9; *cis*-6′-fluorospiro[cyclopentane-1,8′-[2,4]diazabicyclo[4.2.0]octane]-3′,5′-dione, 59137-87-0; *cis*-6′-fluorospiro[cyclohexane-1,8′-[2,4]diazabicyclo[4.2.0]octane]-3′,5′-dione, 59137-88-1; *cis*-6′-fluorospiro[cycloheptane-1,8′-[2,4]diazabicyclo[4.2.0]octane]-3′,5′-dione, 59137-89-2; *cis*-6-fluoro-7,7,8,8-tetramethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 59137-90-5; (4aα,4bα,7aα,7bβ)-4a-fluorohexahydro-7a-methyl-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione, 90365-46-1; (1α,6α,8α)-6-fluoro-8-methyl-2,4-diazabicyclo-[4.2.0]octane-3,5-dione, 59137-93-8; (1α,6α,8β)-6-fluoro-8-methyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90365-47-2; 6-fluoro-7-methyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90320-61-9; (4aα,4bβ,7aβ,7bα)-4a-fluorohexahydro-7a-methyl-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione, 90365-48-3; (4aα,4bα,7aα,7bα)-4a-fluorohexahydro-7a-methyl-1*H*-cyclopenta[3,4]cyclobuta[1,2-*d*]pyrimidine-2,4(3*H*,4a*H*)-dione, 59137-92-7; (1α,6α,7α)-6-fluoro-7,8,8-trimethyl-2,4-diazabicyclo-

[4.2.0]octane-3,5-dione, 90296-03-0; (1α,6α,7β)-6-fluoro-7,8,8-trimethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90365-49-4; (1α,6α,8α)-6-fluoro-7,7,8-trimethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90296-04-1; (1α,6α,8β)-6-fluoro-7,7,8-trimethyl-2,4-diazabicyclo[4.2.0]octane-3,5-dione, 90365-50-7; isopropenyl acetate, 108-22-5; cyclohexenyl acetate, 1424-22-2; cyclopentenyl acetate, 933-06-2; tetramethylene, 563-79-1; 1-methylcyclopentene, 693-89-0; 2-methyl-2-butene, 513-35-9; propene, 115-07-1; isobutylene, 115-11-7; methylenecyclopentane, 1528-30-9; methylenecyclohexane, 1192-37-6; methylenecycloheptane, 2505-03-5.

A Novel Mechanism for Conversion of 5-Fluorouracil-Olefin Photocycloaddition Products to 5-Substituted Uracils. A Synthon for the Uracil 5-Carbanion

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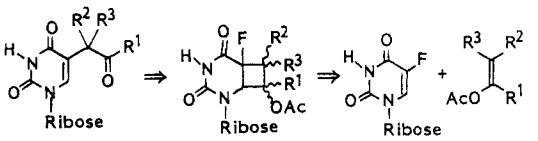
Received October 12, 1983

The photocycloaddition products of 5-fluorouracil and enol acetates undergo fragmentation reactions to afford 5-substituted uracils in good yields. Unexpectedly, certain 5-fluorouracil–olefin photocycloaddition products react with 3 equiv of potassium *tert*-butoxide in *tert*-butyl alcohol to give high yields of 5-substituted uracils. Kinetic, labeling, and product studies of this novel reaction support a reaction mechanism in which the dianion of the cycloadduct rearranges to a spirocyclopropane intermediate which then affords the 5-substituted uracil.

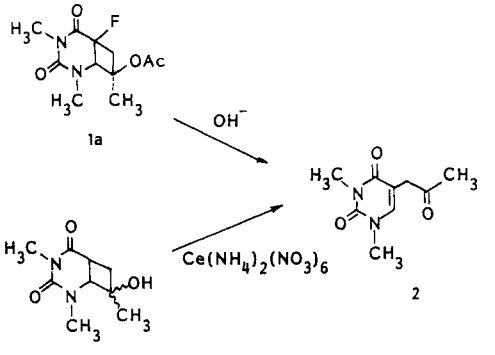
Several years ago we became interested in methods for the direct functionalization of unprotected nucleoside derivatives.[1,2] The intended strategy was to employ 5-fluorouracil as a synthon for the 5-carbanion of uracil by using a sequence of photocycloaddition and fragmentation (Scheme I).[1,3] This route was especially attractive since a variety of nucleosides of 5-fluorouracil have been prepared.[4] Furthermore, the entire reaction sequence would involve only light and base and thus be applicable to systems having a variety of labile functionalities on the carbohydrate portion of the molecule. While this work was never extensively applied to nucleoside functionalization, the model studies for implementing this strategy are of interest. The preceding paper has detailed the preparative aspects of the photocycloaddition chemistry of 5-fluorouracil with olefins.[5] Herein we report details on the fragmentation reactions of 5-fluorouracil–enol acetate and 5-fluorouracil–olefin cycloaddition products to 5-substituted uracils. The mechanism of the unprecedented fragmentations of the latter series of compounds has been extensively studied, and a reasonable interpretation of the reaction pathway is presented.

Scheme I. Strategy for Functionalization of Nucleosides



Fragmentation Reactions of 1,3-Dimethyl-5-fluorouracil–Enol Acetate and 5-Fluorouracil–Enol Acetate Adducts

Reaction of **1a**, the major product from the photocycloaddition of 1,3-dimethyl-5-fluorouracil and isopropenyl acetate, with either aqueous sodium hydroxide or sodium carbonate gave **2** in 66% isolated yield. Gas



chromatographic analysis of the progress of the reaction showed that a transient intermediate was formed, presumably the alcohol, which was converted to **2** as the reaction progressed. Compound **2** was identical with the product obtained from ceric ammonium nitrate oxidation[3] of **3**.

Interestingly, reaction of the minor product from the 1,3-dimethyl-5-fluorouracil–isopropenyl acetate photocycloaddition reaction, **1b**, with base did not afford **2** but rather a new product in 85% yield. The same type of product was obtained from **1c** in 82% yield. Spectroscopic and analytical data for these products, including a detailed ^{1}H NMR,[6] are presented in the supplementary materials section. From a mechanistic viewpoint, we favor structures

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