Anion-Mediated Fragmentation Reactions. Mechanistic and Synthetic Aspects of the Fragmentation and Rearrangement Reactions of Pyrimidinedione–Alkyne Photoadducts

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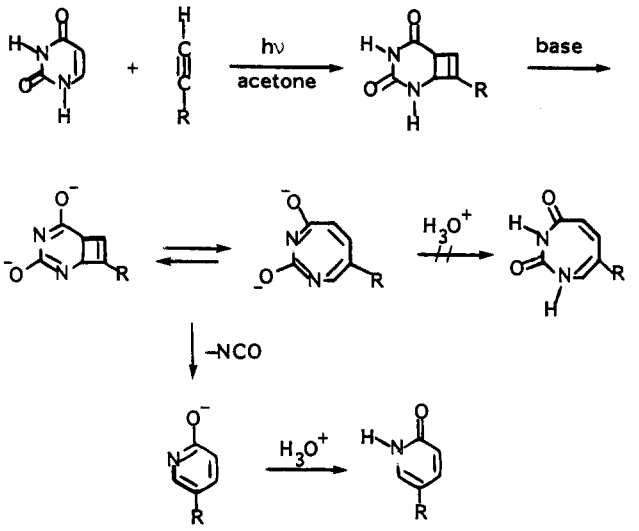
The acetone-sensitized photocycloaddition reactions of uracil, thymine, 5-fluorouracil, and 5-(trimethylsilyl)uracil with alkynes afford 2,4-diazabicyclo[4.2.0]oct-7-ene-3,5-diones. It is noteworthy that 5-(trimethylsilyl)uracil gives very high yields in these reactions. High regioselectivity is exhibited for the reaction of uracil, 5-fluorouracil, and 5-(trimethylsilyl)uracil with 1-alkynes, the 8-alkyl-substituted product being formed nearly exclusively. Reaction of the cycloadducts mentioned above with 2 equiv of potassium *tert*-butoxide gives the appropriate pyridones in good yield. Three of these cycloadducts were rearranged to 1,3-diaza-5,7-octadiene-2,4-diones by silylation followed by treatment of the crude silylation product with silica gel. Thus, a sequence of photocycloaddition and base-mediated fragmentation converts uracil-type systems to pyridones while photocycloaddition followed by rearrangement converts uracil systems to two-carbon ring-expanded heterocycles. The mechanism of the above transformation has been examined by using ^{13}C- and ^{15}N-labeled systems. This work together with kinetic studies of the fragmentation of these photoadducts in basic media gives a reasonable mechanistic picture of this chemistry.

The photocycloaddition reactions of uracil and a number of its derivatives with alkenes and alkynes afford a one-step route to the 2,4-diazabicyclo[4.2.0]octyl ring system.[1,2] Often these photocycloadditions with terminal alkenes and alkynes are highly selective,[2,3] forming the 8-substituted ring system regiospecifically. The subsequent chemistry of the 2,4-diazabicyclo[4.2.0]octyl ring system has not been extensively studied.[2b,4] Thus, we have explored some of the chemistry of these systems with the idea of developing routes to both known and unknown heterocyclic ring systems.

One idea was that photocycloaddition of uracils and alkynes followed by dianion formation and ring opening would comprise a two-atom ring expansion of uracils to 1,3-diazacycloocta-5,7-diene-2,4-diones (Scheme I). As we reported in 1979,[4a] instead of isolating ring-expanded uracils from this reaction, a fragmentation reaction ensued, yielding pyridones. We report here a detailed study of the mechanism of this fragmentation reaction and a successful route from uracil–alkyne-type photoadducts to 1,3-diazacycloocta-5,7-diene-2,4-diones.

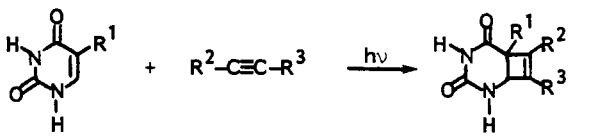
Scheme I. Intended Strategy for Two-Carbon Ring Expansion of Uracils



Photochemical Cycloaddition Studies

The acetone-sensitized photocycloadditions of uracil and its substituted derivatives with alkynes are summarized in Table I. Since full spectroscopic and analytical data for these products are given in the Experimental Section, only the pertinent points concerning the assignment of structure will be noted here. The reactions of uracil with 1-propyne, 1-pentyne, and 1-heptyne all gave one isolable photocycloaddition product in modest yields (Table I, entries, 1–3). The remaining constituents of the reaction mixture were uracil-type dimers. The regiochemistry of the propyne adduct **3a** was established by reduction with deuterium followed by ^1H NMR analysis of the di-

Table I. Photocycloaddition of Pyrimidinediones and Alkynes



1 2 3

entry	compd	R^1	R^2	R^3	yield, %
1	a	H	H	CH_3	43
2	b	H	H	n-C_3H_7	25
3	c	H	H	n-C_5H_{11}	30
4	d	H	CH_3	CH_3	54
5	e	H	C_2H_5	C_2H_5	31
6	f	CH_3	CH_3	H	28
7	g	CH_3	CH_3	CH_3	32
8	h	F	H	CH_3	29
9	i	F	H	n-C_4H_9	33
10	j	F	H	n-C_5H_{11}	29
11	k	$Si(CH_3)_3$	H	n-C_3H_7	95
12	l	$Si(CH_3)_3$	H	n-C_5H_{11}	86

(1) (a) Hyatt, J. A.; Swenton, J. S. *J. Am. Chem. Soc.* **1972**, *94*, 7605. (b) Swenton, J. S.; Hyatt, J. A.; Lisy, J. M.; Clardy, J. *Ibid.* **1974**, *96*, 4885. (c) Wexler, A. J.; Hyatt, J. A.; Raynolds, P. W.; Cottrell, C.; Swenton, J. S. *Ibid.* **1978**, *100*, 512.

(2) (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.

(3) Swenton, J. S.; Grimm, F.; Fritzen, E. L. "Symposium on Photochemistry as a Route to Chemicals" presented before the Division of Petroleum Chemistry, Inc., Joint Meeting of the American Chemical Society and Chemical Society of Japan, Honolulu, April 1–6, 1969, pp 121–129.

(4) For preliminary reports of some of this work, see: (a) Comber, R. N.; Swenton, J. S.; Wexler, A. J. *J. Am. Chem. Soc.* **1979**, *101*, 5411. (b) Kaminski, V. V.; Swenton, J. S. *Tetrahedron Lett.* **1982**, *23*, 4207–4210.

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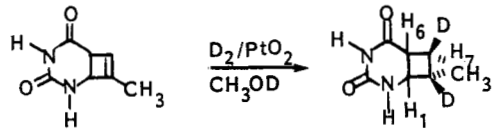
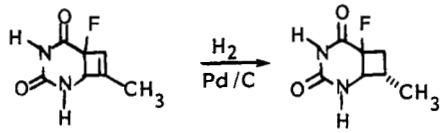


3a 4

deuterated product [^{1}H NMR (pyridine) δ 1.01 (CH_3, s, 3 H), 1.81 (H_7, broadened d, J = 6 Hz, 1 H), 3.28 (H_6, d of d, J = 8.7, 6 Hz, 1 H), 4.07 (H_1, d of d, J = 8.7, ~3 Hz which collapses to a d, J = 8.7 Hz, upon shaking with D_2O, 1 H)]. If the alternative regiochemistry had been the case for **3a**, the deuteration product analogous to **4** would have shown H_6 as a simple doublet, and H_1 would have appeared as a doublet of doublets. The purity of the photocycloaddition products of uracil with 1-pentyne and 1-heptyne was established by ^{13}C NMR spectroscopy, and the assigned regiochemistry was inferred by analogy with **3a**. While the high regioselectivity of the uracil photocycloadditions to 1-alkyne was surprising, the poor mass balance in the reaction does not exclude the possibility of some head-to-head isomer formation.

In a similar manner, the orientation of the photocycloaddition products of 5-fluorouracil with propyne, 1-pentyne, and 1-hexyne was assigned as the head-to-tail isomers **3h–j**, respectively. Thus, hydrogenation of **3h** gave the known **5**.[2b] The regiochemistry of **3i** and **3j** was inferred



3h 5

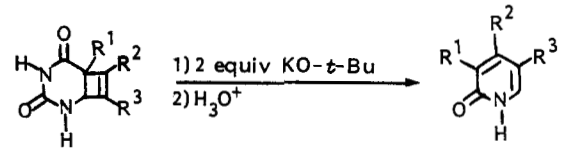
from the established structure for **3h** together with the similarity of the ^{19}F coupling constant of the C_7 vinylic carbon in the ^{13}C NMR spectrum. The head-to-head regiochemistry of the thymine-propyne photocycloadduct **3f** was confirmed by its subsequent chemistry (vide infra). The regioselectivity observed with other uracil reactions is not a general characteristic of thymine reactions. For example, the photocycloaddition of thymine to 1-heptyne gave a 38% yield of a 1.2:1 mixture of regioisomers as determined by ^{13}C NMR spectroscopy.

The photocycloaddition chemistry[5] of 5-(trimethylsilyl)uracil with alkynes is especially noteworthy. First, not only is the reaction highly regioselective, as noted earlier,[5] but also the yields of isolated photoadduct are very high (entries 11 and 12). One reason for the higher yield of cycloadducts with 5-(trimethylsilyl)uracil relative to the other nitrogen bases may be a slower rate of photochemical dimerization of 5-(trimethylsilyl)uracil. For examination of this possibility, solutions of 0.01 M uracil and 5-(trimethylsilyl)uracil were irradiated at 300 nm under identical conditions. The concentration of uracil as assayed by UV analysis decreased to 65% of its initial concentration in a time period in which no change was detected in the concentration of 5-(trimethylsilyl)uracil. Thus, a major factor in the increased yields of 5-(trimethylsilyl)uracil photocycloaddition reactions is its greater photochemical stability.

Fragmentation Studies

While the pK_a's for the cycloadducts were unknown, the pK_1 for dihydrouracil in water had been reported as 11.5.[6]

Table II. Fragmentation Reactions of Uracil-Alkyne-Type Photoadducts



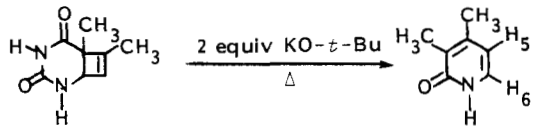
3 6

entry	compd	R^1	R^2	R^3	yield, %
1	a	H	H	CH_3	61
2	b	H	H	n-C_3H_7	55
3	c	H	H	n-C_5H_{11}	70
4	d	H	CH_3	CH_3	62
5	e	H	C_2H_5	C_2H_5	67
6	f	CH_3	CH_3	H	69
7	g	CH_3	CH_3	CH_3	66
8	h	F	H	CH_3	47
9	j	F	H	n-C_5H_{11}	70
10	k	$Si(CH_3)_3$	H	n-C_3H_7	66

Potassium *tert*-butoxide in *tert*-butyl alcohol would certainly completely deprotonate the cycloadducts at N_3, and it seemed reasonable that the dianion arising from deprotonation at N_1 also could be present in a finite concentration at equilibrium. Thus, potassium *tert*-butoxide in *tert*-butyl alcohol appeared as a reasonable medium for examining the ring-expansion chemistry outlined in Scheme I.

When the adduct **3a** was reacted with 2 equiv of potassium *tert*-butoxide in refluxing *tert*-butyl alcohol followed by quenching of the reaction mixture with aqueous acid, a new product was isolated in 61% yield by column chromatography. The new compound had the formula C_6H_7NO by high-resolution mass spectrometry, indicating the loss of HNCO from **3a**. This new compound exhibited physical and spectroscopic properties nearly identical with those reported for 5-methylpyridone[7] (**6a**): mp 180–181 °C (lit.[7] mp 182–183 °C); UV (H_2O) 302 nm (ϵ 5600), 227 (7400) [lit.[7] UV (CH_3OH) 302 nm (ϵ 5700), 227 (8100)]; ^{1}H NMR, identical with the published spectrum. This reaction then corresponds to the loss of potassium cyanate from the anion of the cycloadduct. When the salt formed in the fragmentation reaction was filtered, the IR (KBr) spectrum of this material showed absorptions at 2185, 1306, 1212, 652, and 642 cm^{-1}. The reported[8] absorptions for potassium cyanate are 2170, 1300, 1205, 636, and 626 cm^{-1}. Thus, the overall fragmentation reaction is demonstrated to form pyridone and potassium cyanate.

Reaction of the other photocycloadducts listed in Table II likewise gave the pyridones in good isolated yield. The assigned structures of the pyridones are supported by combustion analysis and/or exact mass, ^{13}C NMR, ^{1}H NMR measurements as detailed in the Experimental Section. For the thymine/propyne cycloadduct, **3f**, the



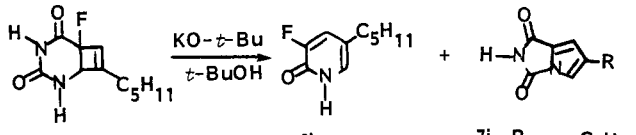
3f 6f

structure of the pyridone was used to establish the structure of the adduct. Thus, the pyridone **6f** showed in

(5) Chih, C.; Fritzen, E. L.; Swenton, J. S. *J. Org. Chem.* **1980**, *45*, 4462.
(6) Levene, P. A.; Bass, L. W.; Simms, H. S. *J. Biol. Chem.* **1926**, *70*, 229.
(7) Abramovitch, R. A., Ed. "Pyridine and Its Derivatives, Supplement Part III"; Wiley: New York, 1974; p 8661.
(8) Waddington, T. C. *J. Chem. Soc.* **1959**, 2499.

its ^1H NMR spectrum the olefinic hydrogens H_5 and H_6 as a clean AX pattern with signals at δ 6.08 (J = 7 Hz) and 7.18 (J = 7 Hz). This substitution pattern in the pyridone **6f** is consistent only with the head-to-head orientation of the photocycloadduct **3f**.

While no other significant products were isolated in the fragmentation reaction of uracil, thymine, or 5-(trimethylsilyl)uracil, a highly fluorescent minor product was noted in the fragmentation reactions of 5-fluorouracil cycloadducts **3h** and **3j**. The new product **7j** had the mo-



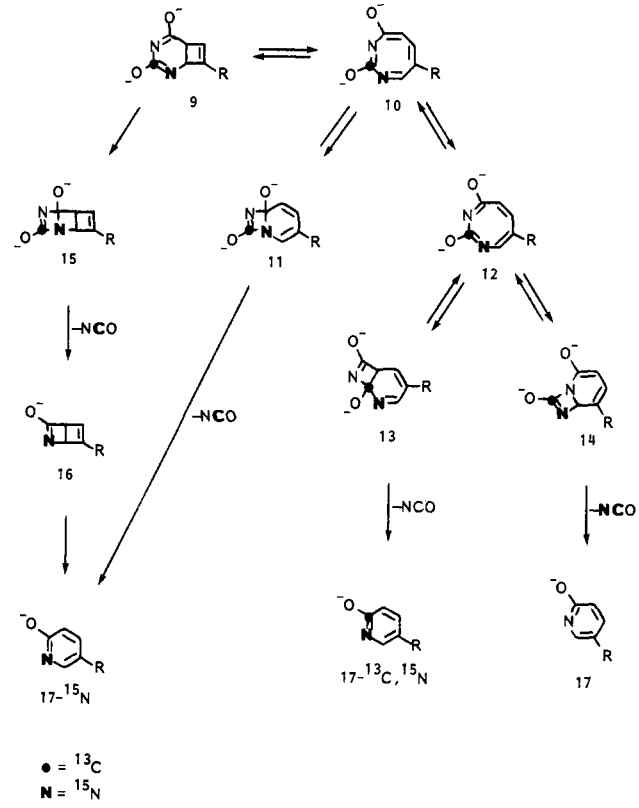
lecular formula $C_{11}H_{14}N_2O_2$ by combustion analysis and exact mass measurement, corresponding to loss of hydrogen fluoride from **3j**. The ^1H NMR spectrum (Me_2SO-d_6) [δ 0.09 (distorted t, $J \simeq 6$ Hz, 3 H), 1.35 (m, 6 H), 2.49 (obscured by Me_2SO), 6.7 (s, 1 H), 7.24 (s, 2 H), 11.3 (br s, 1 H)] showed in addition to the absorptions of the aliphatic side chains two vinyl hydrogens and one N–H resonance. The reported[9] ^1H NMR spectrum (Me_2SO-d_6) for pyrrole-1,2-dicarboximide (**8**) gave vinyl absorptions at δ 6.6, 6.9, and 7.5 and an N–H absorption at δ 11.2. The ^{13}C NMR spectrum showed 11 lines. The absorptions at 158.9 and 148.2 ppm are assigned as carbonyl carbons; the 134.9- and 126.1-ppm signals are assigned as quaternary sp^2 carbons with the two remaining hydrogen-bearing sp^2 carbons at 116.3 and 114.6 ppm. Finally, the IR ($CHCl_3$) absorptions reported[9] for **8** were at 3440, 1795, and 1745 cm^{-1}, while **7j** exhibited IR ($CHCl_3$) absorptions at 3425, 1797, and 1748 cm^{-1}. Thus, the spectroscopic data strongly support the structural assignment of **7j**.

Structural Aspects of the Rearrangement

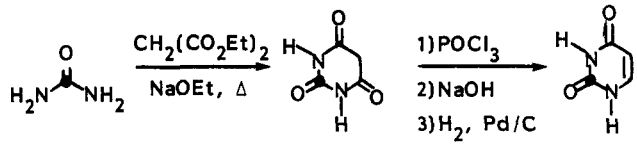
Although the ring-expansion pathway outlined in Scheme I did not occur under the basic fragmentation conditions, a diazacyclooctatetraene-type structure was still a plausible intermediate in the formation of the pyridone. However, attempts to detect intermediate products in the **3** → **6** fragmentation by quenching the reaction at incomplete conversion of **3** led only to isolation of a mixture of **3** and **6**. Since the direct observation of an intermediate in this fragmentation was unsuccessful, a method which would demonstrate the intervention of a diazacyclooctatetraene-type species was developed. If such an intermediate were present in the reaction, the known chemistry of cyclooctatetraene suggested that under the reaction conditions an equilibrium could exist between different bicyclic dianions and the bond-shift isomer **12** (Scheme II).[10] Three of these bicyclic isomers, **11**, **13**, and **14**, could undergo [2 + 2] cycloreversion to give the observed pyridone. In addition, the sequence **9** → **15** → **16** → **17** could afford pyridone without involving an eight-membered-ring intermediate.

Appropriate ^{13}C- and ^{15}N-labeling experiments as outlined in Scheme II would furnish evidence on the course of the **3** → **6** fragmentation. If ring-expanded intermediates **10** or **12** are involved in the reaction, then the ^{13}C and ^{15}N labeling shown in Scheme II would establish whether fragmentation occurs exclusively from **11**, **13**, or

Scheme II. Mechanistic Possibilities for Pyridone Formation from Uracil-Alkyne Photoadduct

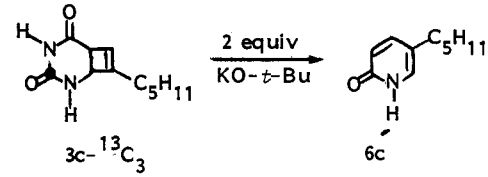


Scheme III. Synthesis of Uracil-$^{13}C_2$



14 since a differently labeled pyridone would result. Likewise, if pyridone formation is occurring from **11**, **13**, and **14**, some ratio of **17**-^{15}N, **17**-^{13}C,^{15}N, and **17** would result. Unfortunately, the above labeling does not distinguish between the pathways **9** → **15** → **16** → **17**-^{15}N and **9** → **10** → **11** → **17**-^{15}N.

Rather than employ a doubly labeled uracil, two singly labeled systems were prepared. The ^{13}C-labeled uracil was prepared from urea-^{13}C (90 atom % ^{13}C) as outlined in Scheme III. For the photocycloaddition to 1-heptyne, it was diluted with uracil to afford **3c** (10 atom % ^{13}C). Fragmentation of **3c**-$^{13}C_3$ gave pyridone **6c** which showed

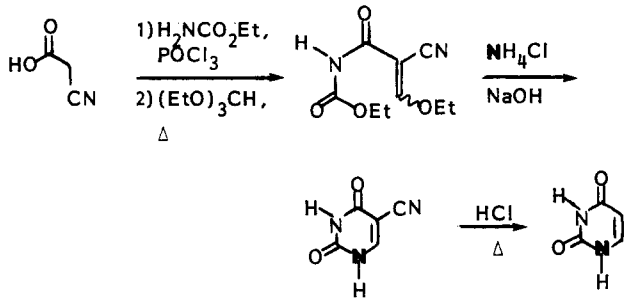


no enhancement of any peak in its ^{13}C NMR spectrum relative to a standard pyridone sample. This complete loss of the ^{13}C label rigorously excludes **13** in the pathway for pyridone formation.

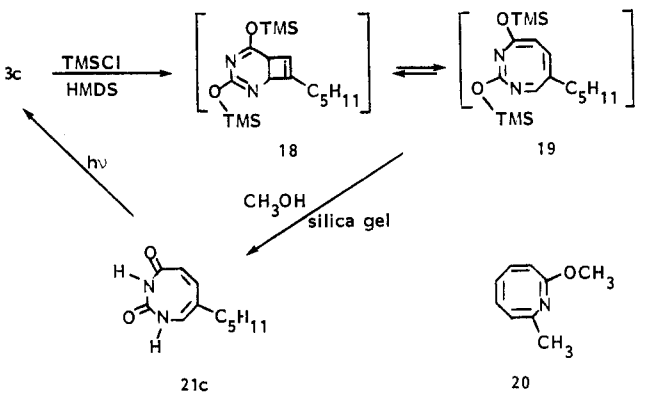
The ^{15}N-labeled uracil was prepared as shown in Scheme IV by employing ammonium chloride (95 atom % ^{15}N). The uracil-$^{15}N_1$ so obtained was diluted with uracil to give uracil-$^{15}N_1$ (28 atom % ^{15}N) which was used in the photocycloaddition. Fragmentation of **3c**-$^{15}N_2$ gave pyridone-^{15}N which had retained >95% of the original ^{15}N.

(9) Papadopoulos, E. P. *J. Org. Chem.* **1972**, *37*, 351.
(10) For a review, see: Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855.

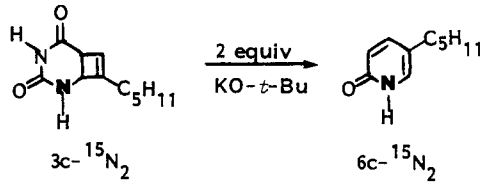
Scheme IV. Synthesis of Uracil-^{15}N



Scheme V. Preparation of 21c



Thus, intermediate **14** is rigorously excluded as an intermediate leading to pyridone.

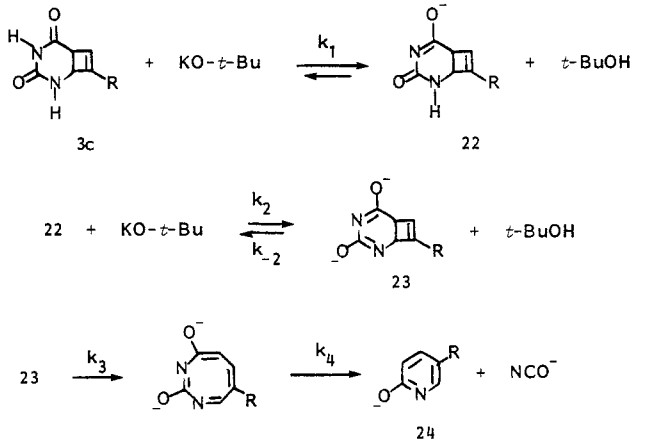


The labeling results noted above afford no evidence for a diazacyclooctatetraene-type intermediate since a pathway of **9** → **15** → **16** → **17** would also accommodate the labeling studies. What was required was an alternative strategy for preparation of the diazacyclooctatetrane-type intermediate. Surmising that anionic repulsion might constitute some of the driving force for the [2 + 2] cycloreversion in a species such as **11**, we examined silylation of **3c**. For the disilylated compound **19**, such a driving force would be absent, and perhaps the ring-expanded system could be detected.

Reaction of **3c** with trimethylsilyl chloride, hexamethyldisilazane, and trimethylamine (Scheme V) gave a new compound with an R_f on TLC slightly greater than that of **3c**. Workup of the reaction mixture followed by chromatography on silica gel gave a new product assigned as **21c** in 71% yield. The ^{1}H NMR spectrum [200 MHz; two N–H absorptions at δ 7.63 (s, 1 H) and 6.80 (s, 1 H), an AB pattern at 6.15 (AB q, J_{AB} = 12 Hz, $\Delta\nu_{AB}$ = 31.4 Hz), a singlet at 5.91 (1 H), and the pentyl side chain at high field], the ^{13}C NMR spectrum, and exact mass analysis strongly supported **21c** as the structure of this new product. Confirming evidence was obtained by the quantitative conversion of **21c** to **3c** upon irradiation. This ring-expansion reaction of photoadducts **3** to the two-carbon ring-expanded compound **21** was also performed with **3i** and **3k** to give **21i** and **21k**, respectively.

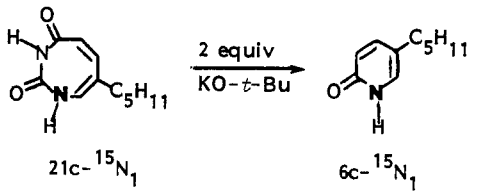
Attempts were made to isolate and study the dynamics of valence isomerizations of the disilylation product of **3c**; however, this compound was extremely labile, decomposing to **3c** and **21c** with any trace of moisture. The crude ^{13}C

Scheme VI. Kinetic Scheme for Fragmentation of 3c



NMR spectrum of the disilylation product was very similar to **21c** with the exception of two additional signals due to the two trimethylsilyl groups. The IR spectrum ($CHCl_3$) showed strong absorptions at 1685, 1660, and 1258 cm^{-1} [11] and the absence of any N–H stretch. The azocine **20** has reported IR (film) absorptions at 1685, 1640, and 1280 cm^{-1}. The ^{1}H NMR spectrum of the disilylation product was nearly identical with that of the vinyl region [δ 6.17 (AB q, J_{AB} = 12 Hz, $\Delta\nu$ = 31 Hz, 2 H) and 5.92 (br s, 1 H)] of **21c**. While recognizing that these spectroscopic data were obtained on the crude silylation product, it appears to us that the major component obtained from silylation of **3c** is the O-silylated compound **19** or its bond-shift isomer.

With the eight-membered-ring system available, its chemical reactivity under the conditions of the fragmentation reaction could be examined. When **21c** was treated with 2 equiv of potassium *tert*-butoxide in *tert*-butyl alcohol, it was converted to the pyridone **6c** in 84% yield. Interestingly, the **21c** → **6c** conversion required 5 min, while the conversion **3c** → **6c** under the same reaction conditions took 4 h. For completeness, the ^{15}N-labeled **21c**



was fragmented, yielding pyridone with >95% retention of the ^{15}N label. Evidence has now been presented for the plausible intermediacy of the dianion of **21** in the **3** → **6** fragmentation reaction.

Kinetic Studies

Kinetic measurements were made on the **3c** → **6c** conversion to obtain more detailed information on the steps in the fragmentation reaction. First, the relative acidity of the N–H protons in **3c** was determined by potentiometric titration of **3c** in *tert*-butyl alcohol with potassium *tert*-butoxide in *tert*-butyl alcohol. One end point in the titration was observed at an apparent pK_a [12,13] of ~14.3. Thus, the monoanion **22** would be nearly completely formed under the reaction conditions. Since a second end

(11) Paquette, L. A.; Hansen, J. F.; Phillips, J. C. *J. Am. Chem. Soc.* **1971**, *93*, 152.

(12) No thermodynamic significance should be attached to the pK_a values obtained in *tert*-butyl alcohol; however, they are valid as measures of relative acidity.

(13) The potentiometric measurements were made as described by: Simms, H. S. *J. Am. Chem. Soc.* **1926**, *48*, 1239.

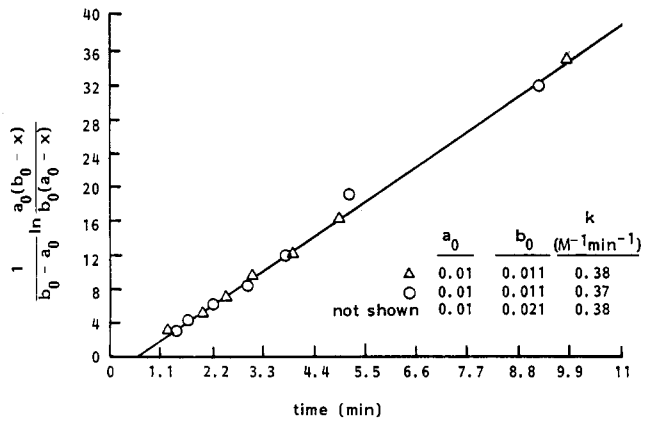


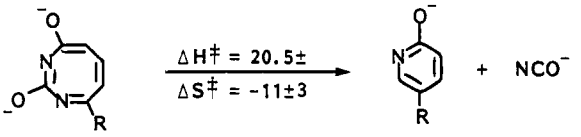
Figure 1. Plot of kinetic expression for **3c** fragmentation: a_0 = initial concentration of **3c**; b_0 = effective base concentration ([KO-*t*-Bu] - a_0); x = concentration of pyridone **6c**.

point was not observed, the dianion **23** can be present only in equilibrium with **22** and potassium *tert*-butoxide (Scheme VI). The rapid conversion **21c** → **6c** suggests that k_4 is not rate determining; thus, the rate of pyridone formation is given by k_3[**23**]. On the assumption of a steady-state concentration of **23**, the rate expression becomes

$$\frac{d[24]}{dt} = k_3\left(\frac{k_2[22][KO\text{-}t\text{-}Bu]}{k_3 + k_{-2}[t\text{-}BuOH]}\right)$$

In the presence of excess potassium *tert*-butoxide, the initial concentration of **22** is equal to the initial concentration of **3c**, $[3c]_0$. One equivalent of base is now needed to convert **3c** to **22**; thus, the effective base concentration is equal to the initial base concentration less $[3c]_0$. On the assumption that $k_3 \ll k_{-2}[t\text{-BuOH}]$, the rate expression becomes $d[24]/dt = k_{obsd}[3c][KO\text{-}t\text{-Bu}]_{eff}$, where $k_{obsd} = k_3K_{eq}/[t\text{-BuOH}]$, $K_{eq} = k_2/k_{-2}$, and $[KO\text{-}t\text{-Bu}]_{eff} = [KO\text{-}t\text{-Bu}]_0 - [3c]_0$. Thus, the rate of pyridone formation should be first order in [**3c**] and $[KO\text{-}t\text{-Bu}]_{eff}$ as demonstrated by Figure 1 and the accompanying data.

The isolation of **21c** also allowed the kinetics of the fragmentation of the ring-expanded uracil to be examined (see Figure 2) without the complications introduced by the acid–base equilibria of Scheme VI. Titration of **21c** in *tert*-butyl alcohol with potassium *tert*-butoxide showed two end points corresponding to apparent pK_a's of 12.8 and 17.3, indicating that in the reaction medium the major form present is the dianion of **25c**. Kinetic measurements showed that the fragmentation of **21c** was first order through 3 half-lives with $\Delta H^{\ddagger} = 20.5 \pm 1$ and $\Delta S^{\ddagger} = -11 \pm 3$ with the maximum errors indicated.



25c

Conclusions and Summary

The labeling and accompanying mechanistic studies provide strong support for the intermediacy of a diazacyclooctatetraene-type intermediate in the potassium *tert*-butoxide induced fragmentation reaction of pyrimidinedione–alkyne photocycloaddition products to pyridones. The favored reaction sequence involves two allowed electrocyclic processes (**9** → **10** and **10** → **11**) followed by a dianion mediated [2 + 2] cycloreversion; however, the pathway **9** → **15** → **16** → **17** cannot rigorously be excluded.

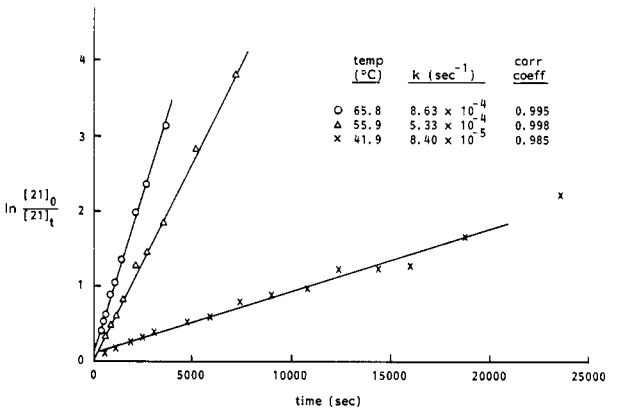
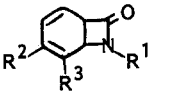


Figure 2. Plot of kinetic expression for **21c** fragmentation.

The results suggest that anion repulsion is an important factor in the cycloreversion. Compounds **25a–c** were re-



25a, $R^1 = CH_3$, $R^2 = Cl$, $R^3 = Cl$
b, $R^1 = CH_3$, $R^2 = H$, $R^3 = Cl$
c, $R^1 = H$, $R^2 = Cl$, $R^3 = H$

ported to undergo cycloreversion at 180, 180, and 120 °C, respectively.[14] We had hoped to compare the rate of fragmentation of **21c** in its dianion form with that of its silylated analogue **19**; however, the lability of the silylated compound discouraged such studies. Thus, there is no model on which to estimate the degree of enhancement of the fragmentation for an anionic form of a reactant vs. its neutral form.

The high specificity of the fragmentation established from the labeling studies was unexpected. There are several ways to account for this specificity (see Scheme II): (1) no bond isomerization of **10** → **12** occurs; thus, bicyclic forms **13** and **14** are never formed; (2) ring-expanded dianion **12** is formed, but the establishment of the **12** ⇄ **13** and **12** ⇄ **14** equilibria is slow relative to formation of **11**; (3) all three bicyclic forms are present, but only **11** undergoes facile [2 + 2] cycloreversion. It is difficult to rule out case 1 since no data are available on the activation energy of the bond-shift isomerization in diazacyclooctatetraenes. For cyclooctatetraenes themselves, the activation enthalpy for the bond-shift isomerization is usually considerably less than 20 kcal/mol.[15,16] Since the fragmentation of **25c** has $\Delta H^{\ddagger} = 20.5$ kcal/mol, if the bond isomerization for the dianion of **25c** is in this range, then the **10** ⇄ **12** process would be occurring under the reaction conditions. However, azocines (i.e., **20**) appear to have a much higher activation enthalpy for bond isomerization, and if azocines were employed as models, then the **10** ⇄ **12** isomerization would not be occurring under the reaction conditions.[17] We do not favor case 1 as accounting for the

(14) Somekawa, K.; Imai, R.; Furukido, R.; Kumamoto, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1112.

(15) The bond shift process for a range of cyclooctatetraenes[16] are: $\Delta H^{\ddagger} = 12.8\text{–}15.5$; $\Delta S^{\ddagger} = -(6.3\text{–}23.6)$.

(16) Anet, F. A. L. *J. Am. Chem. Soc.* **1962**, *84*, 671. Anet, F. A. L.; Bourn, A. J. R.; Lin, Y. S. *Ibid.* **1965**, *86*, 3576. Oth, J. F. M. *Pure Appl. Chem.* **1971**, *25*, 573. Gwynne, D. E.; Whitesides, G. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 2862. Lyttle, M. H.; Streitwieser, A.; Klutz, R. *Ibid.* **1981**, *103*, 3232.

(17) While this point does not appear to have been specifically noted, it is implicit in the studies of Paquette and co-workers (personal communication from L. Paquette). For leading references, see: Paquette, L. A.; Kakihana, T.; Hansen, J. F.; Philips, J. C. *J. Am. Chem. Soc.* **1971**, *93*, 152.

specificity since the dianion generated from deprotonation of **21c** would be expected to be **12** and not **11**. In fact, the rate of pyridone formation from **21c** is considerably faster than from **3c**.

There is no rigorous distinction between possibilities 2 and 3 noted above. The activation entropy ($\Delta S^{\ddagger} = -11$ eu) associated with the **21c** fragmentation is suggestive that closure to the bicyclic form may be rate determining; $\Delta S^{\ddagger}$ values for this process in 1-phenylcyclooctatetraene[18] and cyclooctatetraene[18] are -5 and -1 eu, respectively. Furthermore, if the rate-determining step was the [2 + 2] cycloreversion, a substantial positive $\Delta S^{\ddagger}$ would have been expected; the $\Delta S^{\ddagger}$ for the cyclobutane to olefin cleavage is ~9.[19] While possibility 2 best accounts for the specificity of the fragmentation, all arguments based on enthalpies and entropies of activation are fragile since the importance of solvation effects have not been considered in our system.

Experimental Section[20]

General Procedure for Photochemical Cycloaddition of Alkynes to Uracils. The uracil derivative was dissolved in hot acetone/water and placed in a standard Hanovia-type immersion well. For reactions involving the more volatile alkynes, the immersion well was fitted with a dry ice condenser. The alkyne was then added, and the solution was irradiated with Corex-filtered light from a 450-W Hanovia medium-pressure source. The progress of the irradiation was monitored by observing the disappearance of the uracil absorption at ca. 260 nm as follows. A 0.05-mL aliquot from the reaction mixture was concentrated in vacuo, and the residue was dissolved in ca. 7 mL of methanol for UV analysis. After the initial pyrimidine absorption had decreased to ca. 5% of its initial value, the reaction mixture was concentrated in vacuo and chromatographed on silica gel.

Uracil–Propyne Photoadduct (3a). A solution of 500 mg (4.46 mmol) of uracil and 5.0 g (125 mmol) of 1-propyne in 200 mL of acetone/water (4:1) was irradiated. The solvent was removed in vacuo, and the residue was chromatographed on a silica gel (17.0 × 3.3 cm) column. Elution proceeded as follows: 100 mL of $CHCl_3$, nil; 200 mL of 1% $CH_3OH/CHCl_3$, 100 mL of 2% $CH_3OH/CHCl_3$, and 200 mL of 3% $CH_3OH/CHCl_3$, 0.154 g of yellow oil, a byproduct of the uracil photoadditions; 250 mL of 3% $CH_3OH/CHCl_3$, 0.339 g of white solid. Crystallization from ethanol afforded 0.291 g (43.0%) of product **3a**: mp 241–242 °C ^1H NMR (Me_2SO-d_6) 1.69 (s, 3 H), 3.54 (br s, 1 H), 4.08 (distorted t, 1 H), 5.96 (br s, 1 H), 7.82 (br s, 1 H), 9.90 (br s, 1 H); IR (KBr) 3220 (m, br), 3070 (m, br), 1709 (s, br), 1482 (m, br), 1366 (m), 1249 (m); ^{13}C NMR (Me_2SO-d_6) 171.5, 152.6, 152.3, 129.6, 51.1, 41.8, 13.3; exact mass calcd for $C_7H_8N_2O_2$ m/e 152.058 57, obsd m/e 152.058 93.

Uracil–1-Pentyne Photoadduct (3b). A solution of 0.5 g (4.46 mmol) of uracil and 4.55 g (67.0 mmol) of 1-pentyne was irradiated as above for 1.75 h, and the concentrated reaction mixture was chromatographed on silica gel (16.0 × 3.3 cm column). Elution proceeded as follows: 100 mL of $CHCl_3$, nil; 100 mL of 1% $CH_3OH/CHCl_3$, nil; 100 mL of 2% $CH_3OH/CHCl_3$, 100 mL of 3% $CH_3OH/CHCl_3$, and 60 mL of 4% $CH_3OH/CHCl_3$, 233 mg of a white solid. Crystallization from 80:20 ethanol/ethyl acetate afforded 200 mg (25%) of product **3b**: mp 240–241 °C; ^1H NMR (Me_2SO-d_6) 0.86 (t, J = 6 Hz, 3 H), 1.43 (septet, $J \simeq 6$ Hz, 2 H), 2.0 (distorted t, 2 H), 3.53 (m, 1 H), 4.10 (t, $J \simeq 4$ Hz, 1 H), 5.93 (br s, 1 H), 7.80 (br s, 1 H), 9.87 (br s, 1 H); IR (KBr) 3230 (m, br), 3075 (m, br), 2935 (m, br), 1720 (s, br), 1487 (m, br), 1370 (m), 1275 (m, br); ^{13}C NMR (Me_2SO-d_6) 171.6, 156.7, 152.3, 128.8, 50.3, 41.8, 29.7, 18.9, 13.6. Anal. Calcd for $C_8H_{12}N_2O_2$: C, 59.98; H, 6.71. Found: C, 59.75; H, 6.85.

Uracil–1-Heptyne Photoadduct (3c). A solution of 0.50 g (4.46 mmol) of uracil and 6.42 g (67.0 mmol) of 1-heptyne was irradiated as above for 1.5 h, and the concentrated reaction mixture was chromatographed on silica gel (17.5 × 3.3 cm column). Elution proceeded as follows: 100 mL of $CHCl_3$, nil; 200 mL of 1% $CH_3OH/CHCl_3$, nil; 200 mL of 2% $CH_3OH/CHCl_3$ and 100 mL of 3% $CH_3OH/CHCl_3$, 0.375 g of a yellow oil; 300 mL of 3% $CH_3OH/CHCl_3$, 0.492 g of a white solid. Crystallization of the compound from ethanol afforded 0.280 g (30%) of product **3c**: mp 223–224 °C dec; ^1H NMR (Me_2SO-d_6) 0.85 (distorted t, 3 H), 1.28 (m, 6 H), 1.99 (m, 3 H), 3.51 (m, 1 H), 4.10 (t, $J \simeq 4$ Hz, 1 H), 5.93 (br s, 1 H), 7.81 (br s, 1 H), 9.86 (br s, 1 H); IR (KBr) 3220 (m, br), 3060 (m, br), 2925 (m), 1690 (s, br), 1480 (m, br), 1363 (m), 1273 (m); ^{13}C NMR (Me_2SO-d_6) 171.6, 156.9, 152.3, 128.6, 50.3, 41.7, 30.9, 27.6, 25.2, 21.7, 13.8. Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.46; H, 7.69. Found: C, 63.57; H, 7.80.

Uracil–2-Butyne Photoadduct (3d). A solution of 0.50 g of uracil (4.46 mmol) and 3.62 g (67.0 mmol) of 2-butyne was irradiated as above for 1 h, and the concentrated reaction mixture was chromatographed on silica gel (18.0 × 3.3 cm column). Elution proceeded as follows: 100 mL of $CHCl_3$, 100 mL of 1% $CH_3OH/CHCl_3$, and 100 mL of 2% $CH_3OH/CHCl_3$, 0.027 g of yellow oil; 150 mL of 3% $CH_3OH/CHCl_3$, 0.058 g of same yellow oil; 250 mL of 3% $CH_3OH/CHCl_3$, 0.465 g of a white solid. Crystallization from ethanol afforded 0.397 g (53.6%) of product **3d**: mp 260–261 °C dec; ^1H NMR (Me_2SO-d_6) 1.58 (s, 6 H), 3.37 (br s, obscured by water resonance, 1 H), 3.93 (br s, 1 H), 7.73 (br s, 1 H), 9.8 (br s, 1 H); IR (KBr) 3225 (m, br), 3070 (m, br), 2915 (m, br), 1712 (s, br), 1483 (m), 1437 (m), 1365 (m), 1270 (m); ^{13}C NMR (Me_2SO-d_6) 170.8, 152.3, 143.3, 138.7, 49.1, 44.5, 11.7, 10.6. Anal. Calcd for $C_8H_{10}N_2O_2$: C, 57.83; H, 6.02. Found: C, 57.53; H, 6.01.

Uracil–3-Hexyne Photoadduct (3e). A solution of 0.50 g of uracil (4.46 mmol) and 5.48 g (67.0 mmol) of 3-hexyne was irradiated as above for 1.5 h, and the concentrated reaction mixture was chromatographed on silica gel (15.5 × 3.5 cm column). Elution proceeded as follows: 100 mL of 3% $CH_3OH/CHCl_3$, 197 mg of yellow oil; 120 mL of 3% $CH_3OH/CHCl_3$, 413 mg of sticky white solid. Crystallization from 80:20 ethanol/ethyl acetate afforded 266 mg (30.7%) of product **3e**: mp 249.5–250.5 °C; ^1H NMR (Me_2SO-d_6) 1.0 (t, J = 7 Hz, 6 H), 2.07 (4-line m, 4 H), 3.43 (m, 1 H), 3.97 (m, 1 H), 7.73 (br s, 1 H), 9.77 (br s, 1 H); IR (KBr) 3240 (m, br), 3090 (m, br), 2975 (m, br), 1714 (s, br), 1485 (m, br), 1372 (m), 1278 (m); ^{13}C NMR (Me_2SO-d_6) 171.2, 152.3, 147.4, 142.7, 47.3, 42.6, 19.9, 18.9, 11.6, 11.2; exact mass calcd for $C_{10}H_{14}N_2O_2$ m/e 194.105 52, obsd m/e 194.106 13.

Thymine–1-Propyne Photoadduct (3f). A solution of 1.5 g (11.9 mmol) of thymine and 10 g (250 mmol) of propyne was irradiated for 1.75 h, and the concentrated reaction mixture was chromatographed on silica gel (20.0 × 3.3 cm column). Elution proceeded as follows: 700 mL of $CHCl_3$, 700 mL of 1% $CH_3OH/CHCl_3$, and 700 mL of 1.5% $CH_3OH/CHCl_3$, nil; 1150 mL of 2% $CH_3OH/CHCl_3$, 0.630 g of a white solid. Crystallization from ethanol/hexane afforded 555 mg (28%) of product **3f**: mp 244–245 °C; ^1H NMR (Me_2SO-d_6) 1.32 (br s, 3 H), 1.64 (br s, 3 H), 3.73 (br s, 1 H), 5.91 (br s, 1 H), 7.66 (br s, 1 H), 9.85 (br s, 1 H); IR (KBr) 3220, 3082 (m, br), 1697, 1701 (br s, poorly resolved d), 1485, 1365, 1377, 1291, 1190 (m); exact mass calcd for $C_8H_{10}N_2O_2$ m/e 166.074 72, obsd m/e 166.074 55.

Thymine–2-Butyne Photoadduct (3g). A solution of 0.60 g of thymine (4.762 mmol) and 3.90 g (72.2 mmol) of 2-butyne was irradiated for 1.5 h, and the concentrated reaction mixture was chromatographed on silica gel (28.0 × 3.3 cm column). Elution proceeded as follows: 200 mL of $CHCl_3$ and 100 mL of $CH_3OH/CHCl_3$, 0.236 g of oil; 50 mL of 2% $CH_3OH/CHCl_3$, 0.026 g of oil and product; 200 mL of 2% $CH_3OH/CHCl_3$, 0.479 g of

(18) Huisgen, R.; Mietzsch, F.; Boche, G.,; Seidl, H. *Spec. Publ.—Chem. Soc.* **1965**, *No. 19*, 3.

(19) Wellman, R. E.; Walters, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 1542. Genaux, C. T.; Kern, F.; Walters, W. D. *Ibid.* **1953**, *75*, 6196.

(20) All melting points below 200 °C were taken with a Thomas-Hoover capillary melting-point apparatus, and melting points >200 °C were taken on a hot-stage apparatus. Infrared spectra were recorded on a Perkin-Elmer Model 283B grating spectrometer and are reported in reciprocal centimeters. ^1H NMR spectra are reported in δ units unless noted otherwise. Multiplicities reported are apparent multiplicities. ^{13}C NMR spectra (Me_4Si reference) were recorded on a Bruker HX-90 instrument at 20 MHz in $CDCl_3$ by Mr. Carl Engelman. Mass spectra and exact mass measurements were obtained by Mr. C. R. Weisenberger on a Consolidated Electronic MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Microanalytical Laboratory. Aluminum oxide and silica gel were from E. Merck Co.

(21) (a) "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. II, p 60. (b) Baddeley, J.; Tapham, A. *J. Chem. Soc.* **1944**, 678. (c) Bredereck, H.; Bräuninger, A.; Hayer, D.; Wollmann, H. *Chem. Ber.* **1959**, *92*, 2937. (d) Cresswell, R. M.; Wood, H. C. S. *J. Chem. Soc.* **1960**, 4768.

white solid. Crystallization from ethanol afforded 279 g (32%) of product **3g**: mp 290–295 °C; ^{1}H NMR (Me_2SO-d_6) 1.27 (s, 3 H), 1.55 (s, 6 H), 3.59 (br s, 1 H), 7.63 (br s, 1 H), 9.72 (br s, 1 H); IR (KBr) 3230 (m, br), 3105 (m, br), 1701 (s, br), 1482 (m), 1367 (m), 1273 (m), 1188 (m); ^{13}C NMR (Me_2SO-d_6) 173.5, 152.3, 142.4, 139.6, 56.1, 48.2, 16.9, 10.3, 9.3; exact mass calcd for $C_9H_{12}N_2O_2$ m/e 180.089 87, obsd m/e 180.090 37.

5-Fluorouracil–1-Propyne Photoadduct (3h). A solution of 0.50 g (3.8 mmol) of 5-fluorouracil and 5.0 g (125 mmol) of 1-propyne was irradiated for 1 h, and the concentrated reaction mixture was chromatographed on silica gel (31 × 2.5 cm column). Elution proceeded as follows: 400 mL of $CHCl_3$, nil; 400 mL of 1% $CH_3OH/CHCl_3$, nil; 200 mL of 2% $CH_3OH/CHCl_3$, 0.03 g of yellow oil; 175 mL of 3% $CH_3OH/CHCl_3$, 85 mg of white solid; 700 mL of 3% $CH_3OH/CHCl_3$, 250 mg of the same white solid. Recrystallization from ethanol/hexane afforded 190 mg (29%) of product **3h**, mp 273–275 °C (with decomposition); ^{1}H NMR (Me_2SO-d_6) 1.82 (d of unresolved t, $J_{CH_3,F}$ = 5.5 Hz, 3 H), 4.26 (d, J_{HF} = 5.6 Hz, 1 H), 6.20 (poorly resolved t, 1 H), 8.17 (br s, 1 H), 10.48 (br s, 1 H); IR (KBr) 3220 (m, br), 3075 (m, br), 2960 (m, br), 1720 (s, br), 1487 (m), 1305 (m), 1210 (m); ^{13}C NMR (Me_2SO-d_6) 167.5 (J_{CF} = 29.3 Hz), 154.8 (J_{CF} = 21.5 Hz), 151.6, 129.5 (J_{CF} = 25.4 Hz), 85.3 (J_{CF} = 229.5 Hz), 57.3 (J_{CF} = 18.5 Hz), 13.0 (J_{CF} = 2.9 Hz); exact mass calcd for $C_7H_7N_2O_2F$ m/e 170.049 15, obsd m/e 170.047 56.

5-Fluorouracil–1-Heptyne Photoadduct (3i). A solution of 0.50 g (3.85 mmol) of 5-fluorouracil and 5.54 g (58 mmol) of 1-heptyne was irradiated for 1.25 h, and the concentrated reaction mixture was chromatographed on silica gel (18 × 3.3 cm column). Elution proceeded as follows: 100 mL of $CHCl_3$, 100 mL of 1% $CH_3OH/CHCl_3$, 100 mL of 2% $CH_3OH/CHCl_3$, and 100 mL of 3% $CH_3OH/CHCl_3$, 0.368 g of unidentified yellow oil; 300 mL of 3% $CH_3OH/CHCl_3$, 0.437 g of a white solid still partly contaminated with the yellow oil. Crystallization from ethanol gave 0.252 g (29%) of product **3i**: mp 229–230 °C; ^{1}H NMR (Me_2SO-d_6) 0.87 (t, J = 6 Hz, 3 H), 1.33 (m, 6 H), 2.10 (m, 2 H), 4.5 (center of d of d, J = 6.0, 2.7 Hz, 1 H), 6.22 (br s, 1 H), 8.15 (br s, 1 H), 10.45 (br s, 1 H); IR (KBr) 3220 (m, br), 3080 (m, br), 2930 (m, br), 1735 (s, br), 1711 (sh), 1675 (m, br), 1631 (m), 1379 (m), 1295 (m); ^{13}C NMR (Me_2SO-d_6) 167.5 (J_{CF} = 29.3 Hz), 158.6 (J_{CF} = 20.5 Hz), 151.6, 128.5 (J_{CF} = 25.4 Hz), 85.3 (J_{CF} = 231.4 Hz), 56.9 (J_{CF} = 18.5 Hz), 30.8, 27.1 (J_{CF} = 2 Hz), 24.9, 21.7, 13.7. Anal. Calcd for $C_{11}H_{15}N_2O_2F$: C, 58.41; H, 6.64. Found: C, 58.61; H, 6.74.

5-Fluorouracil–1-Hexyne Photoadduct (3j). A solution of 0.50 g (3.85 mmol) of 5-fluorouracil and 8.0 g (97.5 mmol) of 1-hexyne was irradiated in 200 mL of acetone for 2.5 h, and the concentrated reaction mixture was chromatographed on silica gel (15.0 × 2.2 cm column). Elution proceeded as follows: 100 mL of CH_2Cl_2, nil; 100 mL of 0.5% CH_3OH/CH_2Cl_2, nil; 100 mL of 1.0% CH_3OH/CH_2Cl_2, nil; 100 mL of 1.5% CH_3OH/CH_2Cl_2, nil; 30 mL of 1.5% CH_3OH/CH_2Cl_2, 0.03 g of a yellow oil; 30 mL of 1.5% CH_3OH/CH_2Cl_2, 0.045 g of yellow oil and **3i**; 40 mL of 2.5% CH_3OH/CH_2Cl_2 and 150 mL of 2.0% CH_3OH/CH_2Cl_2, 0.295 g of a white solid. Recrystallization from ethanol afforded 272 mg (33%) of **3j**: decomposition point 232 °C; ^{1}H NMR (Me_2SO-d_6) 0.86 (distorted t, 3 H), 1.2–1.8 (m, 4 H), 1.9–2.4 (m, 2 H), 4.27 (d of d, J = 2, 2.6 Hz, 1 H), 6.22 (s, 1 H), 8.19 (br s, 1 H), 10.42 (br s, 1 H); IR (KBr) 3220 (m, br), 3080 (m, br), 2960 (m), 2925 (m, br), 1735 (s), 1712 (sh), 1680 (m, br, sh), 1385 (m, br); ^{13}C NMR (Me_2SO-d_6) 167.4 (J_{CF} = 28.6 Hz), 158.5 (J_{CF} = 19.8 Hz), 151.5, 128.3 (J_{CF} = 26.4 Hz), 85.2 (J_{CF} = 230.9 Hz), 56.4 (J_{CF} = 18.7 Hz), 27.2, 26.7 (J_{CF} = 2.2 Hz), 21.6, 13.4; exact mass calcd for $C_{10}H_{13}N_2O_2F$ m/e 212.0961, obsd m/e 212.0968.

5-(Trimethylsilyl)uracil–1-Pentyne Photoadduct (3k). A solution of 0.502 g (2.35 mmol) of 5-(trimethylsilyl)uracil and 13.0 g (191 mmol) of 1-pentyne in 450 mL of acetone was irradiated for 2 h, and the colorless solution was distilled to dryness to yield a white solid residue. Recrystallization of the residue from ethyl acetate/petroleum ether gave 611 mg (92%) of **3k**. An analytical sample was recrystallized from ethanol to give a white solid: mp 222–223 °C dec; ^{1}H NMR (Me_2SO-d_6) 0.08 (s, 9 H), 0.86 (t, J = 7 Hz, 3 H), 1.1–1.55 (m, 2 H), 2.0 (t, J = 7 Hz, 2 H), 3.90 (d, J = 4 Hz, 1 H), 5.93 (s, 1 H), 7.70 (br s, 1 H), 9.68 (br s, 1 H); IR (KBr) 3250 (m, br), 3105 (m, br), 2998 (m), 1729 (s, br), 1700 (sh), 1679 (m), 1375 (m), 1262 (m), 843 (m, br); ^{13}C NMR (Me_2SO-d_6) 173.2, 154.5, 152.3, 131.7, 52.3, 44.5, 29.5, 19.2, 13.4, –3.52; exact mass calcd for $C_{12}H_{20}N_2O_2Si$ m/e 252.12939, obsd m/e 252.13019.

5-(Trimethylsilyl)uracil–1-Heptyne Photoadduct (3l). A solution of 0.415 g (2.26 mmol) of 5-(trimethylsilyl)uracil and 12.0 g (125 mmol) of 1-heptyne in 450 mL of acetone was irradiated for 2.5 h, and the solution was distilled to dryness to yield a slightly yellow oily solid residue. The residue was triturated with 10 mL of petroleum ether and then recrystallized from ethanol/water to give 542 mg (86%) of a white solid: mp 214.5–216 °C dec; ^{1}H NMR (Me_2SO-d_6) 0.06 (s, 9 H), 0.65–1.03 (br m, 3 H), 1.03–1.70 (br m, 6 H), 1.80–2.25 (br m, 2 H), 3.91 (d, J = 3 Hz, 1 H), 5.93 (s, 1 H), 7.74 (br s, 1 H), 9.67 (br s, 1 H); IR (KBr) 3215 (m, br), 3070 (m, br), 3955 (m, br), 1708 (s), 1687 (sh), 1360 (m), 1250 (m), 842 (m); ^{13}C NMR (Me_2SO-d_6) 173.2, 154.7, 152.4, 131.5, 52.3, 44.5, 30.8, 27.4, 25.5, 21.7, 13.7, –3.5; exact mass calcd for $C_{13}H_{24}N_2O_2Si$ m/e 266.11399, obsd m/e 266.11235.

Hydrogenation of 3a. A mixture of 100 mg (0.66 mmol) of **3a**, 25 mL of methanol-d, and 10 mL of platinum oxide was stirred at room temperature under ~1 atm of deuterium. Filtration of the crude product through Celite, concentration, and recrystallization from methanol gave 86 mg (84%) of **4**: mp 207–211 °C; ^{1}H NMR (pyridine) 1.01 (s, 3 H), 1.81 (d, J = 6.0 Hz, 1 H), 3.28 (d of d, with appearance of t, J = 8.7, 6.0 Hz, 1 H), 4.07 (center of d of d, J = 8.7, 3.0 Hz, 1 H; appear as a doublet after addition of D_2O, J = 8.7 Hz); IR (KBr) 3219 and 3059 (m, br), 2945 (m), 2200 (weak C–D stretch), 1706 and 1689 (poorly resolved d, s, br), 1482, 1381, 1369, 1292, 1265 (m).

Hydrogenation of 3h. A mixture of 100 mg (0.59 mmol) of **3h**, 50 mL of methanol, and 30 mg of 10% palladium on carbon was stirred for 3 h under an atmosphere of hydrogen. The workup followed by crystallization of the crude product from ethyl acetate/cyclohexane gave 86 mg (86%) of **5**: mp 216–218 °C; ^{1}H NMR (Me_2SO-d_6) 0.92 (d, J = 6 Hz, 3 H), 1.7–2.8 (br, struc m, 3 H), 4.23 (dd, J = 20, 7 Hz with added D_2O, 1 H), 7.94 (br s, 1 H), 10.62 (br s, 1 H); IR (KBr) 3225 (m, br), 3078 (m, br), 1735 and 1720 (s, br), 1485 (m), 1379 (m), 1301 (m), 1193 (m); exact mass calcd for $C_7H_7N_2O_2F$ m/e 172.0648, obsd m/e 172.0052.

General Procedure for Transformation of Cycloadducts to Pyridones. Potassium *tert*-butoxide was prepared by heating to reflux dry *tert*-butyl alcohol containing the required amount of potassium. After the potassium had dissolved, the indicated amount of the 2,4-diazabicyclo[4.2.0]oct-7-ene-3,5-dione derivative (hereafter referred to as the cycloadduct) was added, and the yellow solution was heated to reflux for the indicated time. The reactions were conveniently monitored by acidifying an aliquot of the reaction mixture to pH ~5 and observing the increase in the ca. 310 nm (CH_3OH) absorption by UV spectroscopy. A specific procedure is described for preparation of the 5-pentyl-2-pyridone. For the remaining systems, data are reported as follows: milligrams (equivalents) of potassium; milliliters of *tert*-butyl alcohol; milligrams (equivalents) of cycloadduct; reflux time; purification.

5-Pentyl-2-pyridone (6c). A solution of potassium *tert*-butoxide was prepared by reacting 1.32 g (33.8 mmol) of potassium with 200 mL of dry *tert*-butyl alcohol under nitrogen. To this solution was added 2.05 g (9.66 mmol) of the uracil–1-heptyne photoadduct, and the solution was heated at reflux for 4 h. After neutralization to pH 5 with concentrated hydrochloric acid, the solvent was removed in vacuo. Chloroform (~80 mL) was added, the mixture was filtered, and the filtrate was concentrated. Chromatography of the residue on silica gel (22.0 × 3.3 cm column) proceeded as follows: 150 mL of $CHCl_3$, nil; 150 mL of 1.5% $CH_3OH/CHCl_3$, nil; 175 mL of 2.5% $CH_3OH/CHCl_3$, nil; 75 mL of 3.5% $CH_3OH/CHCl_3$, 1.20 g of white solid, mp 55–60 °C. The white solid was taken up in ether and precipitated as the hydrochloride by bubbling in hydrogen chloride gas. The crystalline hydrochloride was filtered and washed with ether (1.46 g, mp 86–88 °C). The pyridone was obtained from its salt by addition of saturated bicarbonate to a slurry of the salt in ether. Concentration of the ether layer followed by low-temperature recrystallization from ether gave 1.14 g (72%) of 5-pentyl-2-pyridone: mp 64–65 °C; ^{1}H NMR ($CDCl_3$) 0.87 (t, J = 6 Hz, 3 H), 1.3 (m, 6 H), 2.37 (t, J = 6 Hz, 2 H), 6.52 (d, $J_{3,4}$ = 9 Hz, 1 H), 7.15 (m, 1 H), 7.32 (d of d, $J_{3,4}$ = 9 Hz, $J_{4,6}$ = 2.5 Hz, 1 H); IR (KBr) 3200–2440 (s, br), 1691 (m, sh), 1659 and 1619 (s, br), 1547 (m), 1469 (m), 1430 (m); ^{13}C NMR ($CDCl_3$) 164.9, 143.4, 132.1, 121.0,

119.9, 31.5, 31.1, 30.1, 22.5, 13.9. Anal. Calcd for $C_{10}H_{15}NO$: C, 72.72; H, 9.09. Found: C, 72.68; H, 9.17.

5-Methyl-2-pyridone (6a) was prepared by reacting 108 mg (2.76 mmol) of potassium, 20 mL of *tert*-butyl alcohol, and 200 mg (1.31 mmol) of cycloadduct for 5 h. Purification of the crude product was by silica gel chromatography (18.0 × 2.0 cm column). Elution proceeded as follows: 75 mL of $CHCl_3$, 100 mL of 1% $CH_3OH/CHCl_3$, and 160 mL of 2% $CH_3OH/CHCl_3$, 13 mg of a combination of starting material, product, and an unidentified compound at R_f considerably above that of starting material; 240 mL of 2% $CH_3OH/CHCl_3$, 87 mg (61%) of product **6a** which was pure by proton NMR: mp 181–183 °C; ^1H NMR 2.07 (s, 3 H), 6.51 (d, $J_{3,4}$ = 9.2 Hz, 1 H), 7.14 (br m, 1 H), 7.33 (partially obscured d of d, $J_{3,4}$ = 9.2 Hz, $J_{4,6}$ = 2.4 Hz, 1 H); IR (KBr) 3200–3540 (s, br), 1654 and 1616 (s, br), 1548 (m), 1463 (m), 1430 (m), 772 (m); exact mass calcd for C_6H_7NO m/e 109.052 76, obsd m/e 109.053 03.

5-*n*-Propyl-2-pyridone (6b) was obtained by reacting 130 mg (3.3 mmol) of potassium, 25 mL of *tert*-butyl alcohol, and 200 mg (1.1 mmol) of cycloadduct for 4 h. Column chromatography on silica gel (18.0 × 2.0 cm column) proceeded as follows: 100 mL of $CHCl_3$, nil; 100 mL of 1% $CH_3OH/CHCl_3$, nil; 50 mL of 2% $CH_3OH/CHCl_3$, nil; 50 mL of 2% $CH_3OH/CHCl_3$ and 125 mL of 3% $CH_3OH/CHCl_3$, 128 mg of a low-melting white solid. Sublimation (60 °C/0.1 mmHg) of the solid afforded 83 mg (54.5%) of product **6b**. The product was recrystallized from ether at −70 °C: mp 68–69 °C; ^1H NMR ($CDCl_3$) 0.91 (t, J = 7 Hz, 3 H), 1.53 (6-line m, 2 H), 2.37 (t, J = 7 Hz, 2 H), 6.54 (d, $J_{3,4}$ = 9.2 Hz, 1 H), 7.17 (br s, 1 H), 7.34 (center of d of d, $J_{3,4}$ = 9.2 Hz, $J_{4,6}$ = 2.6 Hz, 1 H); IR (KBr) 3200–2500 (s, br), 1665 (s, br), 1625 (s, br), 1545 (m), 1460 (m), 1425 (m); ^{13}C NMR ($CDCl_3$) 164.9, 143.5, 132.2, 120.7, 120.0, 33.6, 23.6, 13.4; exact mass calcd for $C_8H_{11}NO$ m/e 137.084 06, obsd m/e 137.084 44.

4,5-Dimethyl-2-pyridone (6d) was obtained by reacting 141 mg (3.6 mmol) of potassium, 25 mL of *tert*-butyl alcohol, and 200 mg (1.2 mmol) of cycloadduct for 4 h. Column chromatography on silica gel (21.5 × 2.0 cm column) proceeded as follows: 100 mL of 1% $CH_3OH/CHCl_3$, nil; 75 mL of 2% $CH_3OH/CHCl_3$, nil; 325 mL of 3% $CH_3OH/CHCl_3$, 96 mg of a white solid. Crystallization from benzene afforded 92 mg (62%) of product **6d**: mp 213–214 °C; ^1H NMR ($CDCl_3$) 2.0 (s, 3 H), 2.17 (s, 3 H), 6.33 (s, 1 H), 7.04 (s, 1 H); IR (KBr) 3200–2500 (s, br), 1665 (s, br), 1632 (s), 1605 (m), 1535 (m), 1438 (m), 1158 (m); ^{13}C NMR ($CDCl_3$) 165.0, 153.6, 131.8, 118.8, 116.3, 20.1, 15.4. Anal. Calcd for C_7H_9NO: C, 68.29; H, 7.31. Found: C, 68.19; H, 7.34.

4,5-Diethyl-2-pyridone (6e) was obtained by reacting 61 mg (1.54 mmol) of potassium, 20 mL of *tert*-butyl alcohol, and 150 mg (0.77 mmol) of cycloadduct for 25 h. Column chromatography on silica gel (18.0 × 2.0 cm column) proceeded as follows: 100 mL of 1% $CH_3OH/CHCl_3$, nil; 50 mL of $CH_3OH/CHCl_3$, 0.016 g of starting material; 25 mL of 1% $CH_3OH/CHCl_3$, 0.005 g mixture of starting material and product; 200 mL of 1% $CH_3OH/CHCl_3$, 0.1091 g of a white solid. Crystallization of the solid from benzene/hexane afforded 70 mg (67%) of product **6e**: mp 106.5–107.5 °C; ^1H NMR ($CDCl_3$) 1.5 (t, $J \simeq$ 7 Hz, 3 H), 1.6 (t, $J \simeq$ 7 Hz, 3 H), 2.2–2.6 (4-line m, 4 H), 6.44 (s, 1 H), 7.13 (s, 1 H), 13.6 (br s, 1 H); IR (KBr) 3200–2600 (s, br), 1660 (s), 1622 (s), 1522 (m), 1440 (m); ^{13}C NMR ($CDCl_3$) 165.2, 158.4, 131.0, 121.6, 116.9, 25.2, 21.7, 13.8, 13.0; exact mass calcd for $C_9H_{13}NO$ m/e 151.099 80, obsd m/e 100 07.

3,4-Dimethyl-2-pyridone (6f) was obtained by reacting 104 mg (2.6 mmol) of potassium, 25 mL of *tert*-butyl alcohol, and 200 mg (1.2 mmol) of cycloadduct for 6 h. Column chromatography on silica gel (17.0 × 2.0 cm column) proceeded as follows: 100 mL of $CHCl_3$, 100 mL of 1.0% $CH_3OH/CHCl_3$, and 50 mL of 2% $CH_3OH/CHCl_3$, nil; 100 mL of 2% $CH_3OH/CHCl_3$, 0.02 g of starting material; 25 mL of 2% $CH_3OH/CHCl_3$, 4 mg of a mixture of starting material and product; 200 mL of 2% $CH_3OH/CHCl_3$, 0.092 g (69%) of a white solid which was pure by ^1H NMR spectroscopy. Crystallization from benzene afforded product **6f**: mp 180–182 °C; ^1H NMR ($CDCl_3$) 2.10 (s, 3 H), 2.19 (s, 1 H), 6.10 (d, J = 6.2 Hz, 1 H), 7.18 (d, $J \simeq$ 6.2 Hz, 1 H); IR (KBr) 3200–2500 (s, br), 1656 (s, sh), 1632 (s, br), 1620 (s, sh), 1473 (m); ^{13}C NMR ($CDCl_3$) 165.3, 148.4, 130.3, 125.9, 110.1, 19.9, 12.0; exact mass calcd for C_7H_9NO m/e 123.068 40, obsd m/e 123.068 67.

3,4,5-Trimethyl-2-pyridone (6g) was obtained by reacting 66 mg (1.69 mmol) of potassium, 20 mL of *tert*-butyl alcohol, 150 mg (0.83 mmol) of cycloadduct for 22 h. Column chromatography (17.0 × 2.0 cm column) on silica gel proceeded as follows: 75 mL of 1% $CH_3OH/CHCl_3$, nil; 25 mL of 1% $CH_3OH/CHCl_3$, 0.008 g of product contaminated with unwanted oil; 125 mL of 1% $CH_3OH/CHCl_3$, 0.095 g (83%) of a white solid. Crystallization from benzene afforded 75 mg (65.8%) of product **6g**: mp 229–230 °C; ^1H NMR ($CDCl_3$) 2.02 (s, 3 H), 2.13 (br s, 6 H), 7.05 (s, 1 H); IR (KBr) 3200–2500 (s, br), 1647 (s), 1626 (s), 1539 (m), 1476 (m, sh), 1469 (m), 1370 (m), 870 (m), 784 (m); ^{13}C NMR ($CDCl_3$) 164.4, 148.4, 128.5, 125.5, 116.0, 16.4 (2 carbons), 12.4. Anal. Calcd for $C_8H_{11}NO$: C, 70.07; H, 8.03; N, 10.22. Found: C, 69.91; H, 8.01; N, 10.55.

3-Fluoro-5-methyl-2-pyridone (6h) was obtained by reacting 63 mg (1.61 mmol) of potassium, 20 mL of *tert*-butyl alcohol, and 130 mg (0.76 mmol) of 5-fluorouracil cycloadduct for 5 h. Column chromatography on silica gel (17.5 × 2.0 cm column) proceeded as follows: 125 mL of 0.5% $CH_3OH/CHCl_3$, nil; 100 mL of 1% $CH_3OH/CHCl_3$, 20 mg (17%) of **7h**; 75 mL of 2% $CH_3OH/CHCl_3$, nil; 150 mL of 2% $CH_3OH/CHCl_3$, 48 mg (47%) of a white solid that was pure by ^1H NMR spectroscopy. Crystallization from benzene gave product **6h**: mp 144–146 °C; ^1H NMR ($CDCl_3$) 2.09 (s, 3 H), 7.0 (br s, 1 H), 7.08 (m, 1 H), 13.53 (br s, 1 H); IR (KBr) 3200–2500 (s, br), 1672 (s), 1621 (s, br), 1281 (m), 1244 (m), 1140 (m), 826 (m), 700 (m); exact mass calcd for C_6H_6NOF m/e 127.043 34, obsd m/e 127.043 60.

Product **7h** was isolated as a white solid crystallized from methylene chloride/hexane: mp 231–232 °C; ^1H NMR (10% Me_2SO-d_6/$CDCl_3$) 2.07 (s, 3 H), 6.47 (s, 1 H), 6.88 (s, 1 H), 10.5 (br s, 1 H); IR (KBr) 3232 (m, br), 1792 (s), 1746 (s, sh), 1721 (s, br), 1494 (m), 1422 (m), 1385 (m), 1327 (m); exact mass calcd for $C_7H_6N_2O_2$ m/e 150.042 92, obsd m/e 150.043 36.

3-Fluoro-5-pentyl-2-pyridone (6j) was obtained by reacting 72 mg of potassium, 25 mL of *tert*-butyl alcohol, and 200 mg of 5-fluorouracil cycloadduct. Column chromatography on silica gel (19.0 × 2.0 cm column) proceeded as follows: 150 mL of $CHCl_3$, nil; 25 mL of $CHCl_3$ and 75 mL of 2% $CH_3OH/CHCl_3$, 0.017 g of a white solid, **7j**; 125 mL of 2% $CH_3OH/CHCl_3$, 0.137 g of a clear oil, **6j**. Molecular distillation (0.09 mm/135 °C) afforded 0.113 g (70%) of the major product, 3-fluoro-5-pentyl-2-pyridone (**6j**), which crystallized in the receiver: mp 43–45 °C; ^1H NMR ($CDCl_3$) 0.90 (t, J = 7 Hz, 3 H), 1.36 (m, 6 H), 2.41 (m, 2 H), 7.03 (br s, 1 H), 7.14 (d of d, partially obscured, J = 2 Hz, J_{HF} = 11.5 Hz, 1 H); IR (KBr) 2970 (m, br), 1670 (s, br), 1625 (s, br), 1570 (m), 1465 (m, br), 1260 (m, br), 1130 (m), 967 (m, br); ^{13}C NMR ($CDCl_3$) 157.8 (J_{CF} = 24.4 Hz), 151.9 (J_{CF} = 250 Hz), 127.1 (J_{CF} = 4.9 Hz), 124.4 (J_{CF} = 15.6 Hz), 120.5 (J_{CF} = 3.9 Hz), 31.6, 31.1, 29.9, 22.4, 13.9. Anal. Calcd for $C_{10}H_{14}NOF$: C, 65.57; H, 7.64. Found: C, 65.76; H, 7.77.

7j from 3j by Employing Excess Potassium *tert*-Butoxide. In a manner similar to that employed above, 200 mg (0.88 mmol) of **3j** in potassium *tert*-butoxide/*tert*-butyl alcohol [formed from 104 mg (2.6 mmol) of potassium in 25 mL of dry *tert*-butyl alcohol] was heated to reflux for 4 h. The solvent was removed in vacuo, and approximately 10 mL of water was added. The solution was acidified to pH ~5 by dropwise addition of concentrated hydrochloric acid. The products were extracted with chloroform (2 × 20 mL). TLC of the chloroform extracts showed the presence of three products: two at higher R_f, one possessing an intense light-blue fluorescence and the other a product which was not isolated in sufficient quantities to be identified. The third product was at an R_f corresponding to fluorinated pyridone. Column chromatography on silica gel (18.0 × 2.0 cm column) proceeded as follows: 125 mL of $CHCl_3$, nil; 125 mL of $CHCl_3$, 0.106 g of a white solid, **7j**; 250 mL of $CHCl_3$, nil; 250 mL of $CHCl_3$, 15 mg of a compound which remains unidentified; 425 mL of $CHCl_3$, 54 mg of a clear oil, **6j**. Crystallization of the white solid from hexane/carbon tetrachloride afforded 96 mg (52.7%) of a needlelike solid, **7j**: mp 96–98 °C; ^1H NMR ($CDCl_3$) 0.90 (distorted t, 3 H), 1.42 (m, 6 H), 2.49 (distorted t, 2 H), 6.67 (s, 1 H), 7.03 (s, 1 H), 8.13 (br s, 1 H); IR ($CHCl_3$) 3425 (m, br), 2930 (m, br), 1797 (s, br), 1749 (s, br), 1493 (m, br), 1420 (m, br), 1142 (m); ^{13}C NMR ($CDCl_3$) 158.9 (s), 148.2 (s), 134.9 (s), 126.1 (s), 116.3 (d), 114.6 (d), 31.4 (t), 29.9 (d), 26.9 (t), 22.5 (t), 14.0 (q). Anal. Calcd for $C_{11}H_{14}N_2O_2$: C, 64.08; H, 6.79; N, 13.59. Found: C, 63.97; H, 6.81; N, 13.51.

3-(Trimethylsilyl)-5-*n*-propyl-2-pyridone (6k) was obtained by reacting 96 mg (2.45 mmol) of potassium, 20 mL of *tert*-butyl alcohol, and 200 mg (0.79 mmol) of **3k**. Column chromatography on silica gel (16 × 2.0 cm column) proceeded as follows: 50 mL of CH_2Cl_2, 100 mL of 0.5% CH_3OH/CH_2Cl_2, 50 mL of 1.0% CH_3OH/CH_2Cl_2, 50 mL of 1.5% CH_3OH/CH_2Cl_2, and 65 mL of 2.0% CH_3OH/CH_2Cl_2, nil; 20 mL of 2.0% CH_3OH/CH_2Cl_2, 0.008 g of yellow oil; 100 mL of 2.0% CH_3OH/CH_2Cl_2 and 30 mL of 3.0% CH_3OH/CH_2Cl_2, 110 g (66%) of an oil which solidified upon removal of solvent. Trituration from pyridine/water afforded an analytical sample of **6k** as a white solid: mp 126.5–127.5 °C; ^1H NMR ($CDCl_3$) 0.22 (s, 9 H), 0.85 (t, J = 7 Hz, 3 H), 1.15–1.70 (7-line m, J = 7 Hz, 2 H), 2.28 (t, J = 7 Hz, 2 H), 7.07 (d, J = 2 Hz, 1 H), 7.33 (d, J = 2 Hz, 1 H); IR (KBr) 3260–2370 (m, br), 1640 (s), 1615 (s), 1534 (m), 1465 (m), 1245 (m), 1052 (m), 907 (m), 840 (s); ^{13}C NMR ($CDCl_3$) 167.0, 149.2, 133.0, 131.0, 120.2, 33.7, 23.8, 13.5, −1.7; exact mass calcd for $C_{11}H_{19}NOSi$ m/e 209.123 58, obsd m/e 209.124 17.

7-*n*-Pentyl-1,3-diazacycloocta-5,7-diene-2,4-dione (21c). A solution of 490 mg (2.36 mol) of **3c** and 50 mL of dry tetrahydrofuran was heated under a nitrogen atmosphere to 55 °C. To this stirred solution was added 2.0 mL (14.35 mmol) of triethylamine, 4.0 mL (18.96 mmol) of hexamethyl disilazane, and 5.0 mL (39.4 mmol) of trimethylsilyl chloride via syringe, and the resulting slurry was stirred at 55 °C. The reaction was monitored by removal of TLC aliquots and elution with 1.5% CH_3OH/CH_2Cl_2 (TLC plates must be irradiated with UV light to reveal starting **3c**). After 1.5 h the reaction appeared complete, and the mixture was allowed to cool to <40 °C. The mixture was vigorously stirred, 700 mg of silica gel (silica gel 60 PF-254) was added, and the reaction mixture was stirred for 15 min. To this slurry was added 10 mL of methanol, and the stirring was continued for an additional 5 min. The mixture was then filtered, and the silica gel was washed with methanol (4 × 10 mL). The cloudy filtrate was filtered through sintered glass and concentrated to dryness in vacuo. The resulting residue was taken up in 15 mL of water and 25 mL of methylene chloride, shaken vigorously, and separated. The aqueous layer was extracted with an additional 25 mL of methylene chloride, and the combined organic extracts were dried (calcium sulfate), concentrated on a rotary evaporator, and filtered through a silica gel plug (6 × 2 cm column) with 0.5% CH_3OH/CH_2Cl_2. The product **21c** was isolated in the first 100 mL of elution solvent as a white solid which was recrystallized from carbon tetrachloride/petroleum ether to give 350 mg (71.4%) of **21c**: mp 101.5–103 °C; ^1H NMR ($CDCl_3$, 200 MHz) 7.60 (br s, 1 H), 6.80 (br s, 1 H), 6.15 (AB q, J_{AB} = 12 Hz, $\Delta\nu_{AB}$ = 31 Hz, 2 H), 5.9 (br s, 1 H), 2.1 (t, J = 7 Hz, 2 H), 1.4–1.2 (m, 6 H), 0.86 (t, J = 7 Hz, 3 H); IR (KBr) 3345–2800 (s, br), 1706 (s), 1661 (s), 1457 (m), 1400 (m, br), 1312 (m), 800 (m); ^{13}C NMR ($CDCl_3$) 167.7, 157.2, 138.0, 133.9, 125.4, 121.3, 33.5, 31.1, 27.8, 22.2, 13.9; exact mass calcd for $C_{11}H_{16}N_2O_2$ m/e 208.121 17, obsd m/e 208.121 90.

A solution of 23 mg (0.11 mmol) of **21c** in 2 mL of acetone was irradiated by a Hanovia 450-W mercury arc lamp through a Vycor filter. After 4 h, TLC monitoring (1.5% CH_3OH/CH_2Cl_2) revealed no more starting **21c** and a lower R_f spot which exactly corresponded to authentic **3c**. The solvent was removed in vacuo, and the solid residue was taken up in 25% ether/petroleum ether (6 mL), filtered, and dried in vacuo to yield a quantitative recovery of **3c** (mp 219–221 °C) which was spectroscopically identical with authentic **3c**.

5-Fluoro-7-*n*-butyl-1,3-diazacycloocta-5,7-diene-2,4-dione (21i). In a manner similar to that above, a mixture of 175 mg (0.83 mmol) of **3i**, 1.0 mL (7.18 mmol) of triethylamine, 2.0 mL (9.48 mmol) of hexamethyldisilazane, and 3.0 mL (23.6 mmol) of trimethylsilyl chloride in 40 mL of tetrahydrofuran was heated to reflux for 36 h. The reaction was incomplete at this time. The workup was as above, and chromatography of the crude product on silica gel proceeded as follows: 50 mL of CH_2Cl_2, nil; 50 mL of 0.5% CH_3OH/CH_2Cl_2, nil; 50 mL of CH_3OH/CH_2Cl_2, nil; 50 mL of 0.84% CH_3OH/CH_2Cl_2, nil; 30 mL of 1% CH_3OH/CH_2Cl_2, nil; 20 mL of 1% CH_3OH/CH_2Cl_2, 0.20 g of unidentified yellow oil; 30 mL of 1.2% CH_3OH/CH_2Cl_2, 25 mg (14%) of **21i**. Recrystallization of this product from carbon tetrachloride/petroleum ether gave pure **21i**: mp 165–166.5 °C; ^1H NMR ($CDCl_3$) 7.42 (br s, 1 H), 6.54 (br s, 1 H), 6.04 (d, J_{HF} = 16.6 Hz, 1 H), 5.94 (d, J = 2.0 Hz, 1 H), 2.11 (t, J = 7 Hz, 2 H), 1.42–1.13 (9-line m, 4 H), 0.83 (t, J = 7 Hz, 3 H); IR (KBr) 3320–2850 (m, br), 1715 (s), 1695 (s), 1667 (s), 1435 (m), 1389 (m), 1365 (m); exact mass calcd for $C_{10}H_{13}N_2O_2F$ m/e 212.096 10, obsd m/e 212.069 69.

A solution of 20 mg (0.094 mmol) of **21j** in 2 mL of acetone was irradiated by a Hanovia 450-W mercury arc lamp through a Vycor filter. After 4 h, the solvent was removed in vacuo as a white solid which was washed with petroleum ether and dried in vacuo. TLC analysis showed one compound corresponding exactly to **3i** which was recovered in quantitative yield and was spectroscopically identical with authentic **3i**.

Elution was continued as follows: 20 mL of 1.2% CH_3OH/CH_2Cl_2, nil; 50 mL of 1.4% CH_3OH/CH_2Cl_2, 101 mg (58%) of recovered **6i**.

5-(Trimethylsilyl)-7-*n*-propyl-1,3-diazacycloocta-5,7-diene-2,4-dione (21k). The reaction employed 500 mg (1.78 mmol) of **3k**, 50 mL of tetrahydrofuran, 2.0 mL (14.35 mmol) of triethylamine, 4.0 mL (18.96 mmol) of hexamethyldisilazane, and 5.0 mL (39.4 mmol) of trimethylsilyl chloride and was performed in a manner similar to that of **3c**. Column chromatography (silica gel, 15 × 2.2 cm column) of the yellow residual oil proceeded as follows: 100 mL of CH_2Cl_2 and 80 mL of 0.5% CH_3OH/CH_2Cl_2, nil; 20 mL of 0.5% CH_3OH/CH_2Cl_2 and 20 mL of 1.0% CH_3OH/CH_2Cl_2, 0.04 of yellow oil; 30 mL of 1.0% CH_3OH/CH_2Cl_2, 0.06 g of yellow oil and product **21k**; 50 mL of 1.0% CH_3OH/CH_2Cl_2 and 80 mL of 1.5% CH_3OH/CH_2Cl_2, 0.355 g of an off-white solid. Recrystallization of the solid from ethanol/water afforded 300 mg (66%) of **21k**: mp 160.5–161.5 °C; ^1H NMR ($CDCl_3$) 0.14 (s, 9 H), 0.79 (t, J = 7 Hz, 3 H), 1.06–1.57 (m, 2 H), 2.02 (t, J = 7 Hz, 2 H), 5.72 (br s, 1 H), 6.11 (s, 1 H), 7.37 (br s, 1 H), 7.98 (br s, 1 H); IR (KBr) 3340–2860 (s, br), 1710 (s), 1672 (s), 1661 (sh), 1450 (br, m), 1355 (m), 1258 (s), 877 (m), 841 (s); ^{13}C NMR ($CDCl_3$) 171.7, 157.1, 144.4, 141.3, 137.4, 120.3, 35.1, 21.2, 13.4, −1.6; exact mass calcd for $C_{12}H_{20}NO_2O_2Si$ m/e 252.129 40, obsd m/e 252.128 66.

A solution of 50 mg (0.20 mmol) of **21k** in 6 mL of acetone was irradiated with a Hanovia 450-W mercury arc lamp through a Vycor filter. After 5 h the solvent was removed in vacuo, and the solid residue was taken up in 8 mL of 25% ether/petroleum ether, filtered, and dried in vacuo to give 47 mg (94%) of **3k**, mp 214–218 °C. TLC elution and other spectral data showed **3k** to be identical with an authentic sample of **3k**.

Fragmentation of 21c. Potassium metal (163 mg, 4.2 mmol) was dissolved in 15 mL of dry *tert*-butyl alcohol, and 382 mg (1.84 mmol) of **21c** was added. The reaction mixture turned yellow almost immediately and was heated briefly to a pot temperature of 100 °C with stirring. After 5 min the bath was removed, and the solution was allowed to cool. Concentrated hydrochloric acid was added dropwise (pH ~3), and the solvent and excess acid were removed in vacuo. The UV spectrum of the residue corresponded with that of **6c**. The residue was taken up in ether, and dry hydrogen chloride gas was bubbled through the solution. When the organic solution was cooled in a dry ice/carbon tetrachloride bath, the hydrochloride salt of **6c** precipitated: 321 mg (85%); mp 82–83.5 °C. The pyridone was recovered in the manner previously described to give 260 mg of **6c**.

Uracil-$^{13}C_2$ (8 atom % ^{13}C). By use of known procedures[21a–c] 6-chlorouracil-$^{13}C_2$ (8 atom % ^{13}C) was prepared from one part urea-^{13}C (90 atom % ^{13}C) obtained from MSD isotopes (Merck and Co.) and twelve parts of urea. A solution of 1.02 g (6.96 mmol) of the above compound in 40 mL of 1 N sodium hydroxide was hydrogenated with 0.15 g of 5% palladium on carbon in a Paar hydrogenation apparatus for 1.5 h. Filtration of the catalyst was followed by neutralization of the solution to pH 5 with concentrated hydrochloric acid and concentration with heating. Upon cooling of the hot solution, there was obtained 0.63 g (81%) of the title compound. The ^{13}C enrichment was verified by its ^{13}C NMR spectrum.

Uracil-^{15}N (95 atom % ^{15}N). To a solution of 0.789 g (18.7 mmol) of sodium hydroxide and 1.075 g (19.7 mmol) of ammonium-^{15}N chloride (95 atom % ^{15}N) from MDS isotopes (Merck and Co.) in 100 mL of water was added 3.99 g (18.8 mmol) of α-cyano-β-ethoxy-*N*-(ethoxycarbonyl)acrylamide.[22] The solution

(22) (a) Atkinson, M. R.; Shaw, G.; Warrener, R. N. *J. Chem. Soc.* **1956**, 4118. (b) Shaw, G. *Ibid.* **1955**, 1834.

was heated to reflux for 2.5 h, concentrated by distillation to ca. 20 mL, and then cooled to afford 1.82 g (67% based on ammonium chloride) of 5-cyanouracil-^{15}N (95 atom % ^{15}N). The compound was heated to reflux in 50 mL of 6 N hydrochloric acid for 20 h with a bath temperature of 140 °C, and then concentrated in vacuo. The residue was recrystallized from water to give 1.32 g (60% based on ammonium chloride) of the title compound. The ^{15}N chemical shifts were determined at 30.41 MHz on a Bruker WM-300 with formamide as an internal standard as follows: **1c** (Me_2SO-d_6), N_1 = −22.9 ppm, N_3 = 32.6 ppm; **6c** (Me_2SO-d_6), 57.1 ppm; **21c** ($CDCl_3$), N_1 = 0.97 ppm, N_3 = 35.8 ppm. We thank Dr. Charles Cottrell for these measurements.

General Procedure for Kinetics. For all kinetic runs, the solutions of **6c** and **21c** were prepared in volumetric flasks at room temperature. Base solutions were prepared immediately prior to use by dissolving freshly cut potassium in *tert*-butyl alcohol distilled from sodium. This standard solution was titrated with 1.004 M sulfuric acid by using phenolphthalein as an indicator. The required amount of each solution was transferred via syringe to a stoppered flask and diluted to the desired concentration with the appropriate amount of *tert*-butyl alcohol. Aliquots from this stock solution were then sealed into ampules and placed in a constant temperature bath. The ampules were pulled from the bath at appropriate time intervals so that most points would be recorded within the first 3 half-lives of the reaction. The ampules were labeled and placed in a dry ice/2-propanol bath to quench the reaction. The ampules were then warmed to room temperature in a water bath and analyzed by removing an aliquot (40 μL) and diluting it in 2.5 mL of 0.5 N sulfuric acid. Spectrophotometric analysis at 268 nm gave the concentration of the product pyridone.

The data for all kinetics are summarized in Figures 1 and 2. The correlation coefficients for the slopes in Figure 1 are 0.999, 0.996, and 0.999, respectively. Likewise, the correlation coefficients for the slopes in Figure 2 are 0.995, 0.998, and 0.988, respectively.

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Registry No. **1a**, 66-22-8; **1f**, 65-71-4; **1h**, 51-21-8; **1k**, 59523-07-8; **2a**, 74-99-7; **2b**, 627-19-0; **2c**, 628-71-7; **2d**, 503-17-3; **2e**, 928-49-4; **2i**, 693-02-7; **3a**, 72323-49-0; **3b**, 72323-51-4; **3c**, 72323-52-5; **3d**, 72323-50-3; **3e**, 85995-55-7; **3f**, 85995-56-8; **3g**, 72323-55-8; **3h**, 72323-53-6; **3i**, 85995-59-1; **3j**, 72323-54-7; **3k**, 85995-57-9; **3l**, 85995-58-0; **4**, 85995-62-6; **5**, 86023-36-1; **6a**, 1003-68-5; **6b**, 72323-57-0; **6c**, 72323-58-1; **6d**, 72323-56-9; **6e**, 85995-60-4; **6f**, 36330-90-2; **6g**, 72323-61-6; **6h**, 72323-59-2; **6j**, 72323-60-5; **6k**, 85995-61-5; **7h**, 72323-62-7; **7j**, 72323-63-8; **21c**, 85995-63-7; **21i**, 85995-64-8; **21k**, 85995-65-9; uracil-$^{13}C_2$, 35803-45-3; uracil-^{15}N, 85995-66-0.

Ruthenium Tetroxide Catalyzed Oxidations of Aromatic and Heteroaromatic Rings

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In order to determine the absolute stereochemistry of several aromatic and heterocyclic alcohols, it was necessary to oxidize protected derivatives to mono- and dicarboxylic acids of established configuration. A recently improved procedure utilizing aqueous sodium periodate in the presence of catalytic quantities of ruthenium tetroxide has been used to oxidize a number of compounds to the desired acids in satisfactory yield. The oxidations of (−)-α-(2-thienyl)ethyl acetate, (−)-α-(2-furyl)ethyl acetate, and several substituted α-phenylethyl acetates to (*S*)-*O*-acetyllactic acid have been used to confirm their absolute stereochemistries. However, α-(2-pyridyl)ethyl acetate was inert, and α-(3-phenanthryl)ethyl acetate yielded a complex reaction mixture. Prior conversion of the pyridine derivative to its *N*-oxide and of the substituted phenanthrene to the 9,10-dibromo derivative permitted each compound to be degraded to *O*-acetyllactic acid.

In the course of a series of studies on the use of microbially mediated reductions[2] and hydrolyses[3] to prepare chiral alcohols of a predictable absolute stereochemistry, it was necessary to employ chemical methods to unambiguously establish the configuration of some of the resulting alcohols. In most cases this was done by protecting the alcohol through esterification or conversion to an ether, followed by exhaustive ozonolysis of the aromatic and heteroaromatic groups present. While the approach is simple in principle, we and others[2a,4,5] have encountered a number of experimental problems. The first of these was the need to separate a number of related mono- and dicarboxylic acid derivatives formed during the ozonolysis; e.g., α-acetoxyglutaric and α-acetoxyadipic acids are obtained together in the ozonolysis of α-tetralyl acetate.[2a,4]

Table I. Oxidation of Benzocycloalkenyl Acetates

	reaction conditions		products	
starting materials	$NaIO_4$, equiv	reaction time, h	yields as esters, %	configurations
(±)-**1a**	15	20	62	(±)-**3a**
(*S*)-**1b**	15	18	47	(*S*)-**3b**
(*S*)-**2a**	18	45	51	(*S*)-**3c**
(*S*)-**2b**	18	69	49	(*S*)-**3d**

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