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The Norrish Type II reaction in organic synthesis

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The Norrish Type II reaction in organic synthesis

by

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I. INTRODUCTION

The Norrish Type II photocyclization has been known to organic chemists for several decades. However, to our knowledge the reaction has not been exploited for the synthesis of naturally-occurring compounds. We have studied the use of the Norrish Type II reaction toward the synthesis of aflatoxins, alkaloids, and sugar derivatives. Ultraviolet irradiation of certain aromatic and aliphatic oxygen- and nitrogen-containing carbonyl compounds results in hydrogen atom abstraction by the carbonyl and cyclization of the resulting biradical. We have used this reaction to synthesize an advanced intermediate towards aflatoxin M_2 and sugar derivatives, including derivatives of two rare sugars: penta-O-acetyl-D-gulopyranose and penta-O-acetyl-D-idopyranose.

This thesis will deal with our studies of the use of the Norrish Type II photocyclization toward the synthesis of naturally-occurring compounds.

II. BACKGROUND

A. Excited State Model

Photochemical excitation of a carbonyl compound involves the promotion of an electron from a lower energy orbital into a higher energy orbital. The electron undergoing excitation originates from the non-bonding n-orbital and ends up in the antibonding π^*-orbital; hence the process is called an n,π^* transition. The electrons which were spin-paired in the ground state can adopt either an antiparallel spin, a singlet state, or a parallel spin, a triplet state. Upon direct irradiation, the population of the triplet state depends on the intersystem crossing efficiency (isc) which is unity for aryl ketones, but varies for alkyl ketones (isc(acetone) = 0.9-1.0; isc(2-hexanone) = 0.27; isc(5-methyl-2-hexanone) = 0.11).[1] Substituent effects dictate the n,π^* absorption maximum for alkyl ketones and aldehydes (λmax(acetone) = 278.5 nm; λmax(3-methyl-2-butanone) = 284.5 nm).[2] For aryl ketones the maxima lie at longer wavelengths. Benzophenone has its n,π^* absorption maximum at 348 nm.[2]

An examination of a simple model of the n,π^* state explains its reactivity. The spatial distribution of electrons around the carbonyl group is changed upon electronic excitation. It can be seen below that the excitation produces a half-filled electrophilic n-orbital in the plane of the molecule and a nucleophilic π^*-orbital perpendicular to the plane of the molecule. Because of this, there is a stereoelectronic factor inherent in the n,π^* state of this functional group. The remarkable feature of this transformation is the unpaired electron in a p-type

orbital on oxygen. Therefore, it can be expected that many of the reactions of a carbonyl in the n,π^* state resemble reactions of alkoxy radicals. The nucleophilic π^* orbital created makes

nucleophilic attack at the carbon of the carbonyl unlikely. This model provides a fair representation of all the processes that happen from the carbonyl n,π^* state such as photo-addition, photofragmentation, and inter- and intramolecular hydrogen atom abstraction.

B. Intermolecular Hydrogen Atom Abstraction

The irradiation of a carbonyl compound in a solvent can initiate hydrogen atom abstraction from the solvent, which produces free radicals which can undergo disproportion-ation or coupling. For example, the irradiation of acetone in *n*-hexane yields 2-propanol.[3] The formation of product is quenched by added diene; therefore, the reduction arises from the triplet state (isc(acetone) =~ 1.0). Other alkyl ketones and cyclic ketones having lower intersystem crossing efficiencies are reduced from the triplet state, but less efficiently than acetone.

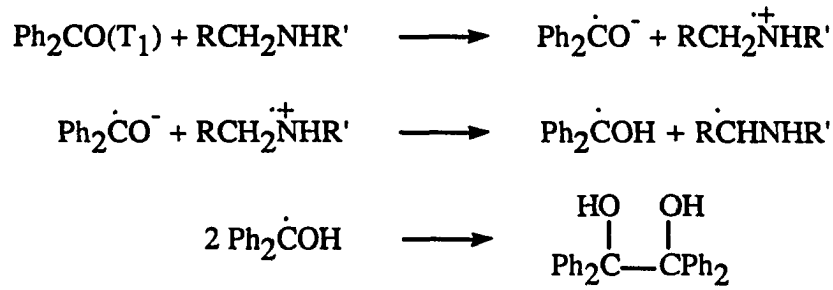
Aryl ketones also undergo reduction. Irradiation of benzophenone in a hydrocarbon solvent efficiently affords the pinacol with a quantum yield of 0.39.

$$Ph_2CO \xrightarrow{h\nu} Ph_2CO(S_1) \longrightarrow Ph_2CO(T_1)$$

$$Ph_2CO(T_1) \xrightarrow{RH} Ph_2\dot{C}OH + R\cdot$$

$$2\,Ph_2\dot{C}OH \longrightarrow \begin{matrix} HO & OH \\ | & | \\ Ph_2C & -CPh_2 \end{matrix}$$

The involvement of electron transfer in the presence of amines has been shown to be important in photoreduction.[4] An example is pinacol formation from benzophenone upon irradiation in the presence of secondary amines. The reduction of the ketone cannot be quenched by triplet quenchers because of the intervention of an electron transfer step, even though the reduction does involve the triplet state of the carbonyl.

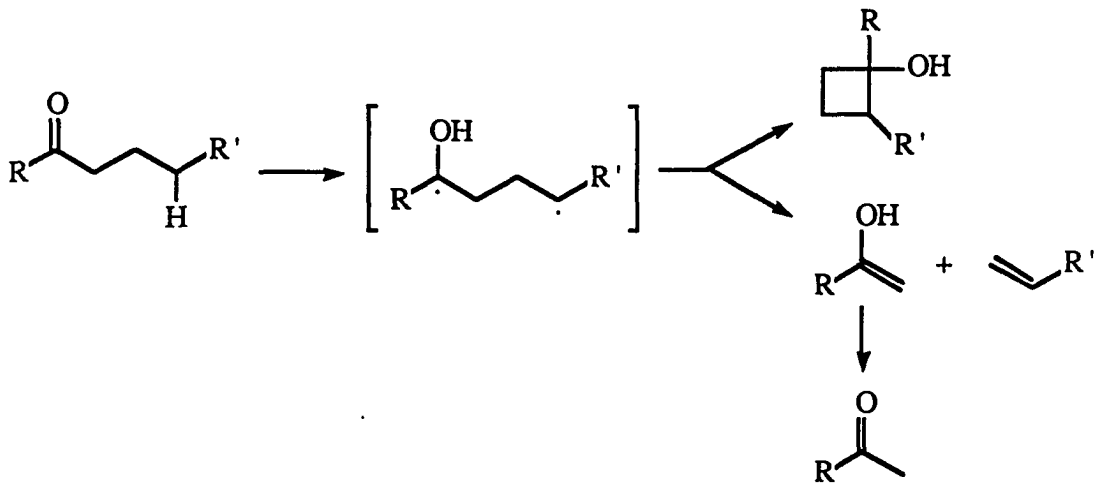


Many ketones fail to photoreduce in alcoholic media. The substitution pattern on diaryl ketones greatly affects their ability to abstract hydrogen atoms from a substrate. Substitution on the molecule can change the lowest triplet state from n,π^* to π,π^*. In the n,π^* state the excitation energy is centered on the carbonyl group, while in the π,π^* state the energy is associated with the whole system of the aromatic molecule and so tends to increase the electron density on oxygen, thus lessening its electrophilicity.[5] Therefore, compounds which have their π,π^* state lower in energy than their n,π^* state would fail to photoreduce. Examples are p-methoxy- and ortho-methylacetophenone derivatives and p-hydroxy- and p-aminobenzophenones.

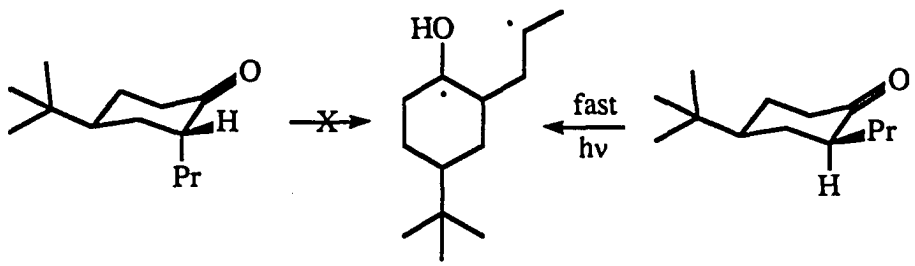
C. Intramolecular Hydrogen Atom Abstraction

1. γ-Hydrogen atom abstraction

Upon excitation, a carbonyl compound with a γ-hydrogen will undergo a 1,5-hydrogen atom transfer to yield a biradical. This biradical can back hydrogen transfer to give starting material or fragment or cyclize. The latter two reactions are indicative of a process known as the Norrish Type II reaction.[6] From the discussed excited state model, it is evident that hydrogen abstraction will occur via the half-filled n-orbital of the oxygen atom. It is also clear that the hydrogen to be transferred must be able to get close to the half-filled orbital. Wagner[7] has studied this problem for both cyclic and acyclic systems and has established that intramolecular reactivity in acyclic triplet ketones is controlled by normal conformational



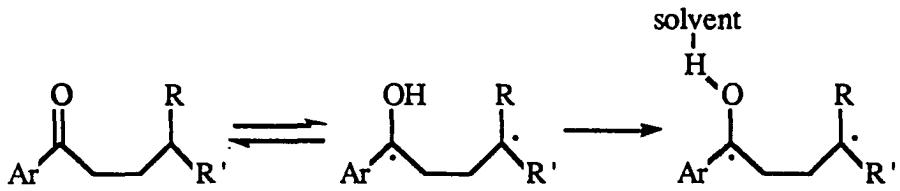
factors. He found that for conventional, open-chain systems the 1,5-hydrogen transfer involving an excited triplet state γ-hydrogen abstraction is the most rapid. In fact, such a transfer is 20 times faster than a 1,5-transfer in cyclic systems. One could imagine the flexible, open-chain molecule adopting the most strain-free transition state available, the six-membered system, of all the possible conformations. In a cyclic system there are only a few conformations available to the molecule in which hydrogen abstraction can take place. The 2-*n*-propyl-4-*t*-butylcyclo- hexanone case is illustrated below. Only the equatorially disposed *n*-propyl group can get near enough to the carbonyl for abstraction to take place.[8]



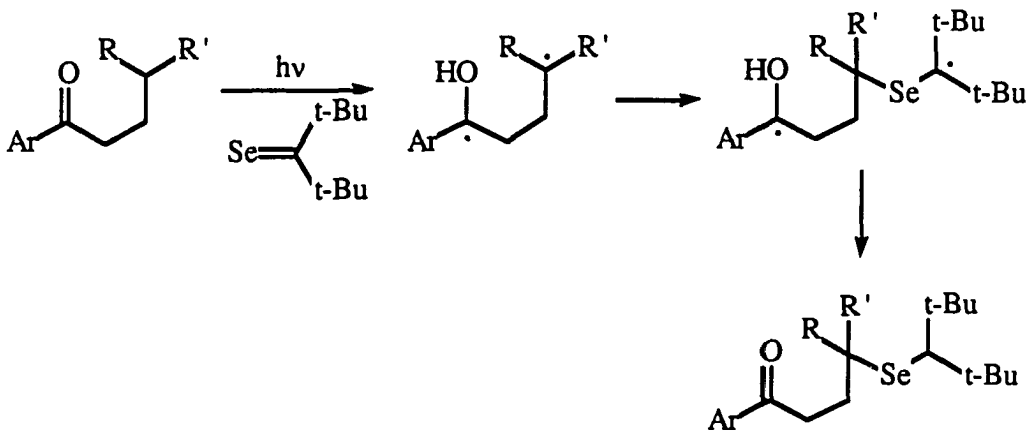
The Norrish Type II reaction for aliphatic ketones is only partially quenched by known triplet state quenchers. This shows that hydrogen abstraction in aliphatic ketones occurs from

both the singlet and triplet states. The percentage of reaction arising from the singlet biradical depends upon the strength of the γ-hydrogen bond. The weaker the γ-hydrogen bond strength, the greater the percentage of reaction from the singlet state. Some examples are: 5-methyl-2-hexanone with a γ-H bond strength of 380 kJ/mol reacts mostly from the singlet state; 2-hexanone with a bond strength of 395 kJ/mol reacts from the singlet and triplet states equally; 2-pentanone with a γ-H bond strength of 410 kJ/mol reacts mostly from the triplet state.[9] Aryl ketones always react from the triplet state because of their unit intersystem crossing efficiency. The rate at which γ-abstraction occurs depends on substitution in the molecule. In a study of a series of cyclic ketones, it was shown that tertiary γ-hydrogens are 165 times more reactive than primary γ-hydrogens. The hydrogen abstraction rate also depends on the nature of the γ-substituent. The abstraction is faster when the γ-substituent is better able to stabilize a free radical.

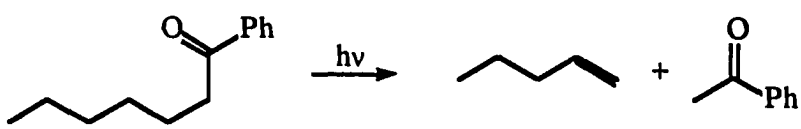
The abstraction of the γ-hydrogen yields a biradical. The lifetime of the biradical is influenced by several factors. Because of conservation of spin, a singlet carbonyl group will produce a singlet biradical and a triplet carbonyl group will give rise to a triplet biradical. The disappearance of a singlet biradical will surely be faster than that of a triplet because of the need for spin inversion in the triplet case. Both substituents and reaction solvent affect the lifetime of a triplet biradical. According to Scaiano,[10] the lifetime of a triplet biradical is increased in polar solvents. The solvent apparently affects populations of the biradical conformations, but it was Wagner[11] who was first to observe that alcohol solvents could be used to increase fragmentation in phenyl ketones and to stop back hydrogen transfer and racemization. As is illustrated below, these latter two effects can be rationalized as a result of hydrogen-bonding by solvent. With intersystem crossing, the hydrogen-bonded biradical is unable to back hydrogen transfer so fragmentation can occur more readily.

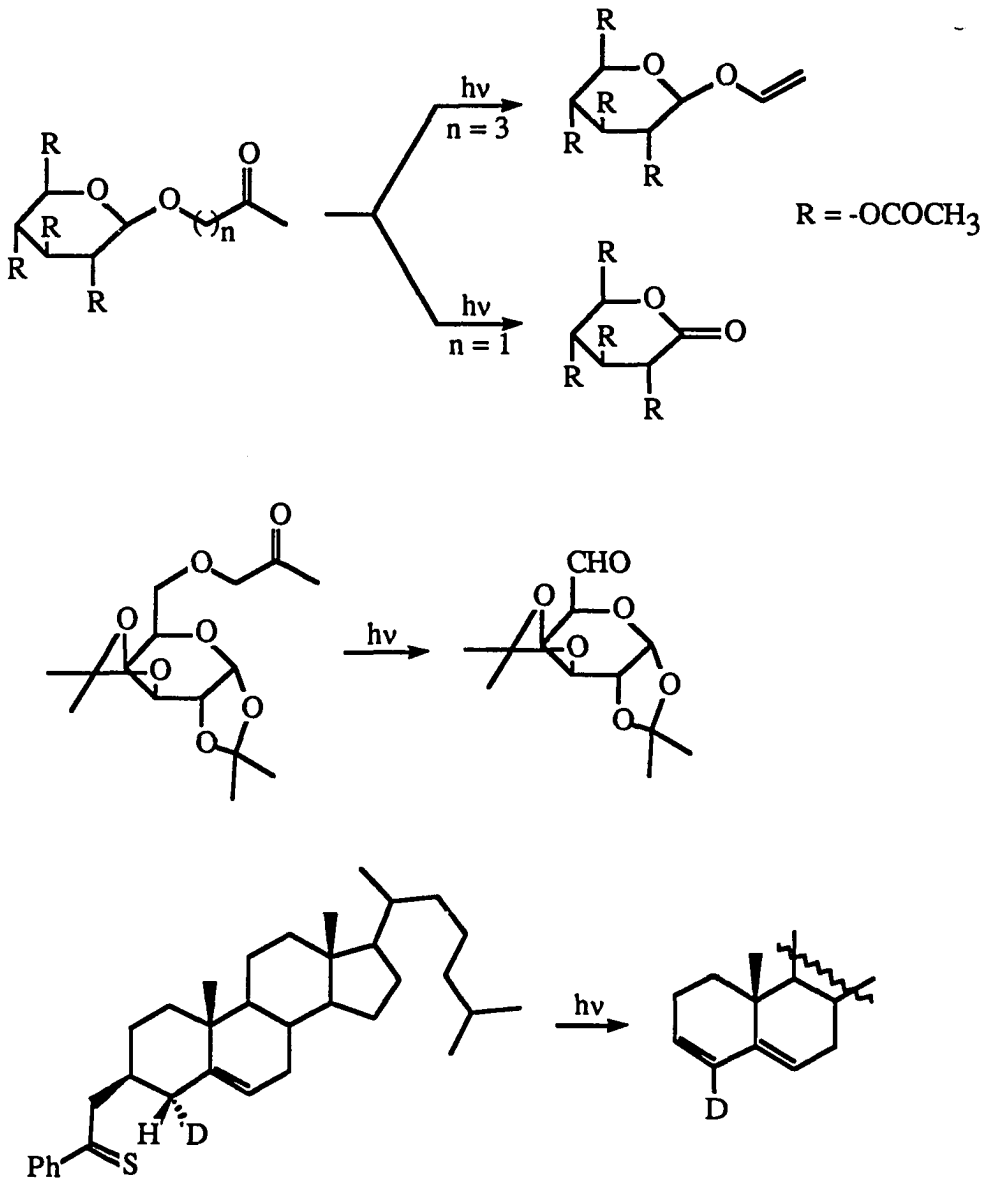


The existence of biradical intermediates in such processes has been proven by spectroscopic techniques and by trapping of intermediate biradicals by such reagents as oxygen, alkenes, and di-*t*-butylselenoketone.



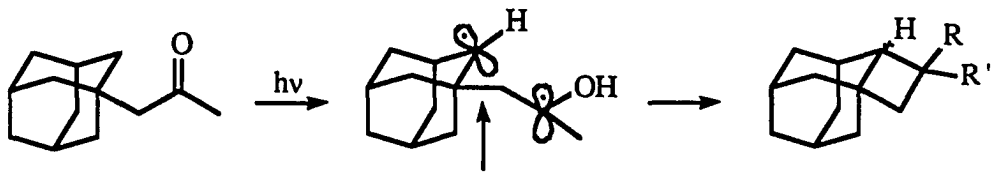
The fragmentation reaction that can arise from a γ-hydrogen abstraction has been shown to have considerable synthetic utility. As is shown below, photofragmentation has been used for side chain manipulations and protecting group removal in carbohydrate systems,[12-15] for the high yield preparation of isomerically pure alkenes,[12] and for synthesis of a steroid derivative using selective syn elimination of a thiobenzoate.[16]





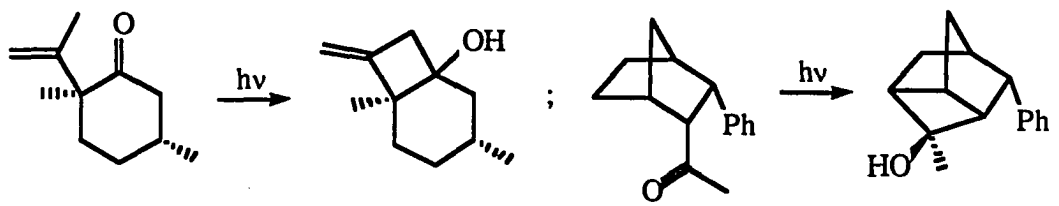
Another possible reaction of a 1,4-biradical resulting from a γ-hydrogen abstraction is cyclization. An important determinant of the path a biradical reaction will take is stereoelectronic factors.[17] These factors manifest themselves in the stereoelectronic requirements necessary for good orbital overlap and thus for bond formation or fragmentation to occur. For example, it can be seen below that hydrogen atom abstraction in the adamantyl ketone gives a

biradical which has its β-bond, the bond which usually fragments, perpendicular to one of the half-filled orbitals. Therefore, cyclization happens in preference to bond fission and the cyclobutanols are the result.



a. R = Me; R'= OH
b. R = OH; R'= Me

There are many examples of cyclobutanol synthesis by this method. Many of the efforts have concerned making strained molecules that would be difficult or tedious to make by any ground state paths.

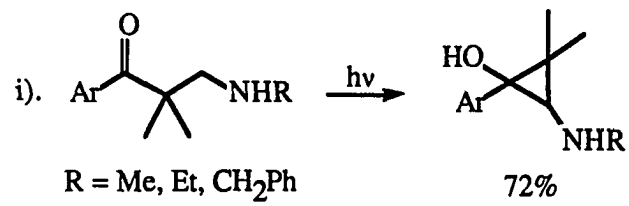


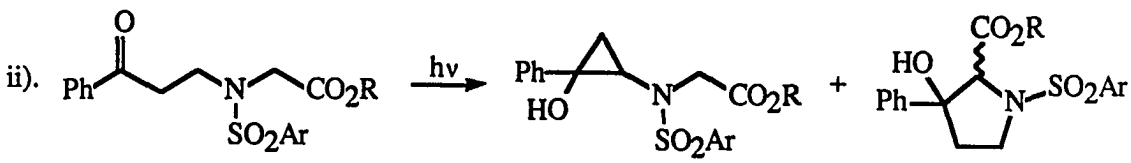
The Norrish Type II reaction normally involves a six-membered transition state, but other reaction pathways are possible and are fairly common. In the case where there are no hydrogens on the γ-carbon or a γ-heteroatom is present, either a larger- or smaller-sized transition state can lead to biradicals that cannot fragment. The following sections will concern these alternative pathways and their use in the synthesis of cyclic compounds.

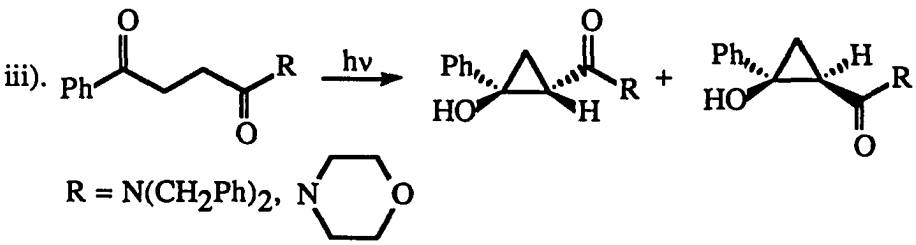
2. β-Hydrogen atom abstraction

Upon excitation of an appropriately substituted molecule, a carbonyl group abstracts a β-hydrogen affording a biradical which can close to give a cyclopropanol. In the examples

shown below, the yields vary. The first reaction produces high yields.[18] In the second example the yield of cyclopropanol is lowered because of competition between reaction paths.[19] The products reflect competing β- and δ-hydrogen abstraction which lead to the 3- and 5-membered rings, respectively. Some nitrogenous ketones may actually be forming their biradicals through an electron transfer process, rather than straightforward hydrogen atom abstraction. This electron transfer process will be discussed in more detail later. The last example produces isomeric cyclopropanols in a 3:1 ratio.[20]



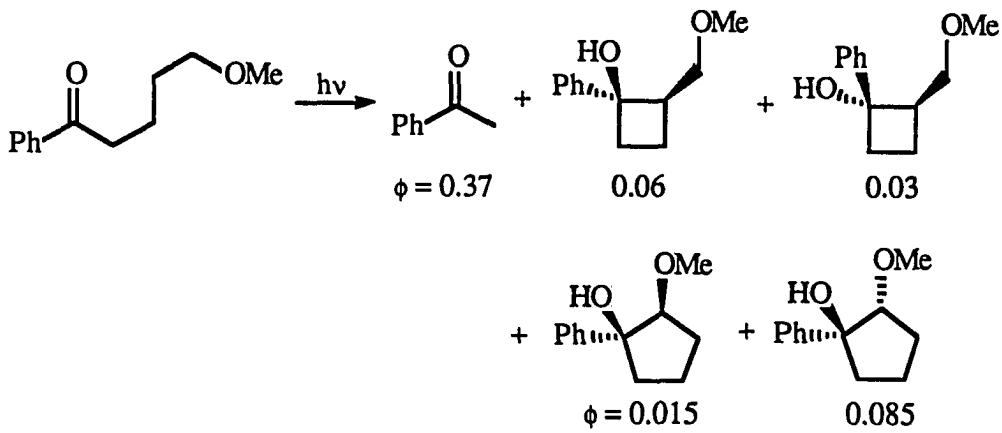




3. δ-Hydrogen atom abstraction

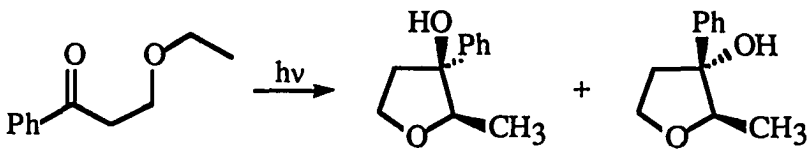
In situations where γ-hydrogens are not available, δ-hydrogen abstraction arises. Excitation of the carbonyl group results in hydrogen abstraction, and cyclization occurs to give 5-membered rings.

There were only a few reports of photoinduced cyclopentanol formation before 1972. These reports involved primarily ketones that have very reactive δ-CH bonds and no γ-hydrogens.[21-25] Even with this evidence, it was still widely believed that photoinduced hydrogen atom abstraction occurred only at the γ-carbon of straight-chain alkanones. This presumed regiospecificity was based in terms of a well-known preference for 1,5-hydrogen atom transfers in radical chemistry.[26] Wagner showed that cyclopentanol formation competes with Type II reactions in δ-alkoxy ketones.[27] The results showed a 20:1 γ:δ preference for abstraction from unactivated methylenes.[28] It was also indicated that the efficiency of cyclization of the 1,5-biradicals is often very low; therefore, the overall quantum efficiency of cyclopentanol formation from straight-chain alkanones is low even if δ-hydrogen abstraction is a competitive reaction. An example is 4-methoxybutyl phenyl ketone for which the quantum efficiency of cyclopentanol formation is only 10%, even though over 50% of the triplet state carbonyls form a 1,5-biradical.[27] Therefore, it is important to learn which 1,5-biradical reactions compete well with cyclization.



In cyclopentanol synthesis by photolysis of β-ethoxypropiophenone, the Z:E ratio depends strongly on solvent polarity. There is little selectivity in Lewis base solvents, but the isomer with the methyl trans to the phenyl is strongly favored in benzene. Use of alcohol

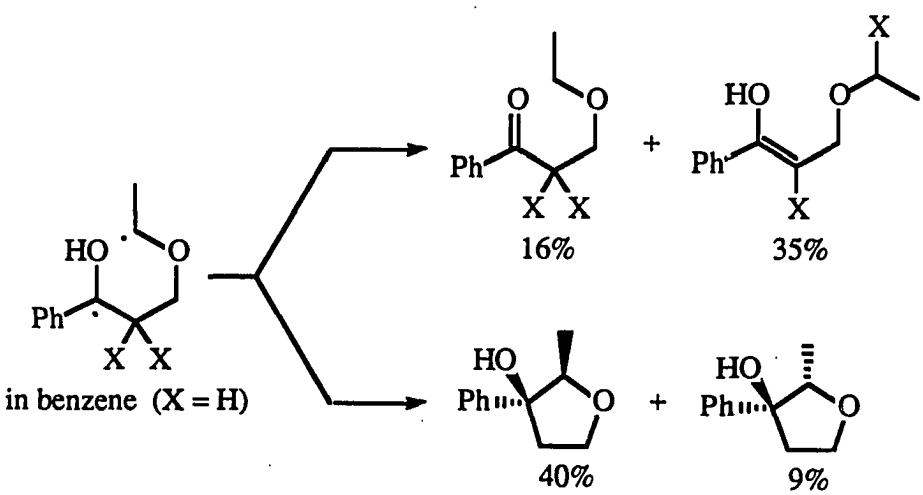
solvents or basic solvents increases the effective bulk of the OH group through hydrogen bonding. This lowers the diastereoselectivity in cyclization.[28,29]



+ enantiomer favored in benzene

+ enantiomer

Studies done on isotope effects on quantum yields and the H-D exchange between the α- and δ-positions in the starting material indicate that competing disproportionation at the α-carbon to form the enol of the starting ketone contributes to the lower-than-100% quantum yield of cyclized product. This method of biradical disproportionation is responsible for 70% of the total reversion in undeuterated β-ethoxypropiophenone.



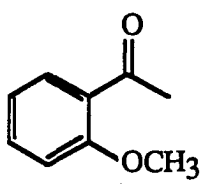
Disproportionation of 1,4-biradicals to the enol of the starting ketone is not known. Such a disproportionation would involve a 1,3-hydrogen transfer which would not be expected to compete with 1,5-transfer. A 1,3-transfer in a 1,4-biradical would be subject to more strain

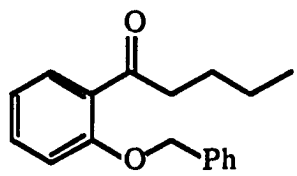
than a 1,4-transfer in a 1,5-biradical. What is interesting is that 1,4-transfer is faster than 1,6-transfer at OH, which is the reverse of the process in which the biradical was formed.

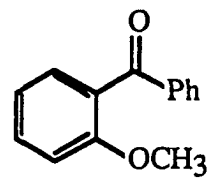
It is assumed that the low quantum yields of cyclopentanol formation seen for other examples of δ-hydrogen abstraction in phenyl alkyl ketones[28] are also due to substantial enol formation via 1,5-biradical disproportionation. Fortunately, only the quantum yield is lowered by this and not the chemical yield.

Ortho-alkoxyphenyl ketones

The most important general findings in an investigation of the kinetics of photocyclization of several ortho-alkoxybenzophenones are that acetophenones are much less reactive and give more by-products than benzophenones,[30] and even the benzophenone triplets have small δ-hydrogen abstraction rate constants. It was found that ortho-methoxyacetophenone does not photocyclize, ortho-(benzyloxy)valerophenone only engages in Norrish Type II photofragmentation, and ortho-methoxybenzophenone undergoes photocyclization, as well as photoreduction in hexane and in methanol.

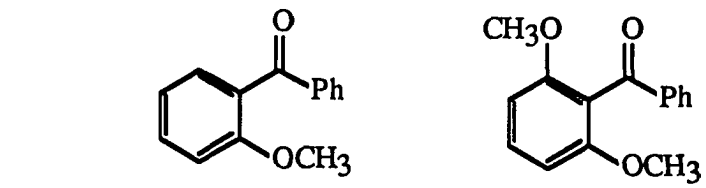




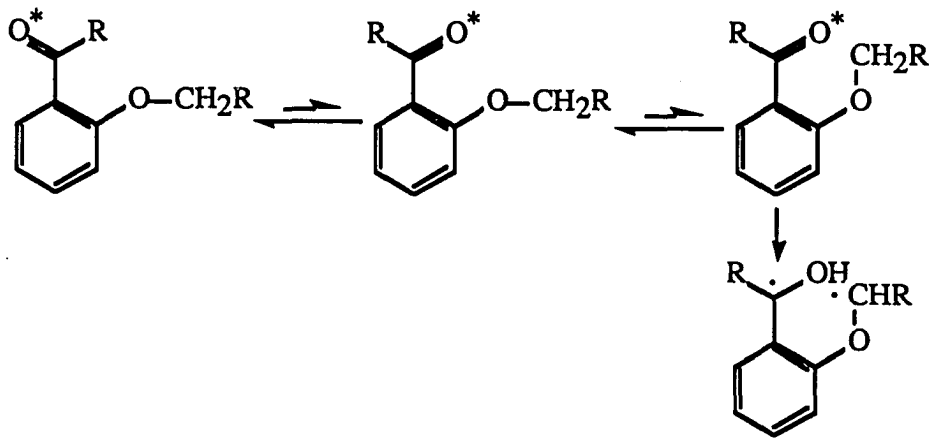


It is certain that conformational factors are responsible for the low rate constants for δ-hydrogen abstraction in these ketones, more specifically a low equilibrium population of the conformation in which the alkyl moiety of the ortho-alkyl group is syn to the carbonyl. It was found that ortho-benzyloxy ketones are much more reactive than ortho-methoxyketones, which is to be expected from their relative bond strengths. This indicates that the reactions are not limited by rates of bond rotation, but instead involve rotational equilibria before the rate-

determining hydrogen abstraction.[7,31] The comparable reactivities of 2-alkoxy and 2,6-dialkoxy ketones[30] reveal that the triplets reach rotational equilibrium about the aromatic-carbonyl bond before reaction, which is anticipated[32] for these unreactive triplets, and that this equilibrium favors the reactive rotamer.



$k_{\delta\text{-H}}(s^{-1})$ 5×10^5 2×10^5

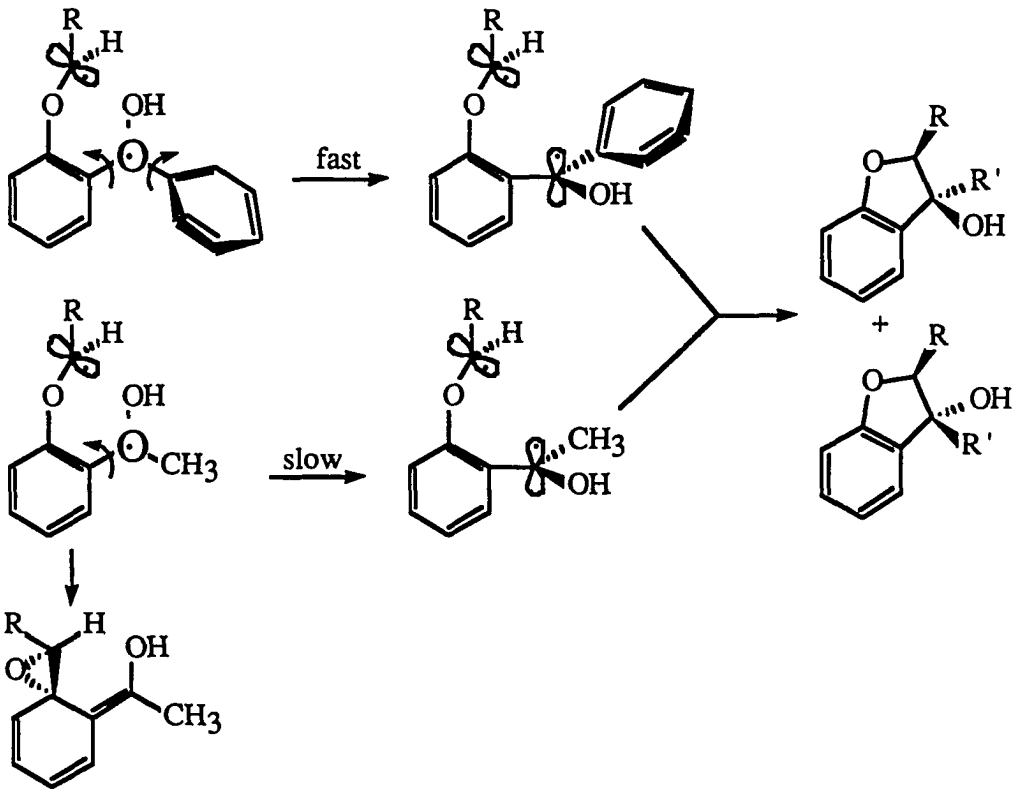


Placing a ring between the carbonyl and the hydrogen being abstracted often causes a tenfold increase in the abstraction rate constants, because of the decreased loss of rotational entropy in the transition state.[33] An example involving γ-hydrogen abstraction is ortho-methylacetophenone ($k = 3 \times 10^9\ s^{-1}$)[32] vs. γ-phenylbutyrophenone ($k = 4 \times 10^8\ s^{-1}$).[34] The corresponding rate comparison for δ-hydrogen atom abstraction is ortho-methoxybenzophenone ($k < 10^6\ s^{-1}$) vs. β-ethoxypropiophenone ($k = 2 \times 10^7\ s^{-1}$).[35] As we can see, the ring in these ortho-alkoxy ketones relative to the acyclic case *decreases* reactivity tenfold. This is another indication of the unfavorable rotational equilibrium mentioned before.

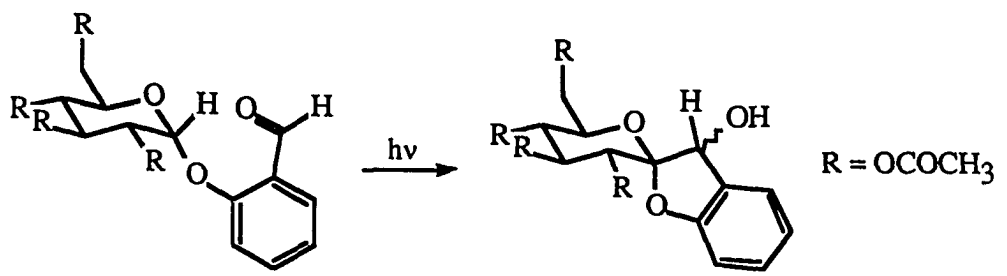
All of the benzophenones studied have n,π* lowest triplets. The ortho-alkoxyacetophenones studied have π,π* lowest triplets which are indicated by significantly lower $k_{\delta\text{-H}}$ values observed for them.[36]

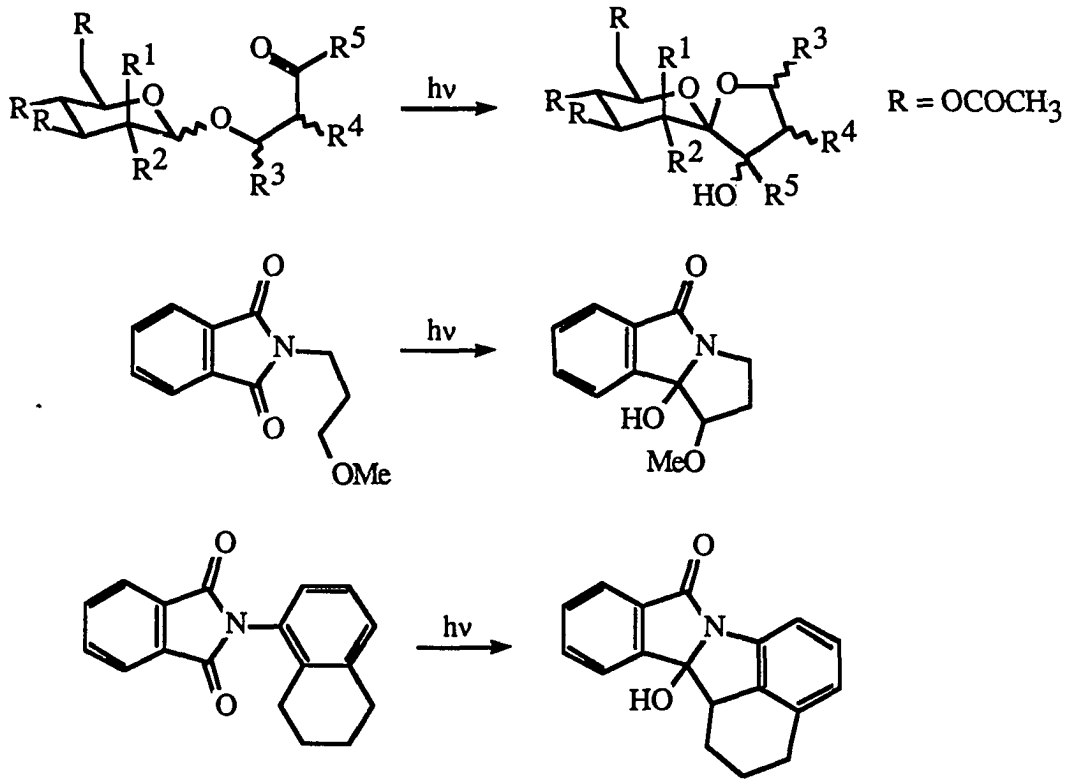
Product yields and product distribution for ortho-alkoxyphenyl ketones strongly depend on solvent and differ greatly for acetophenones and benzophenones. Cyclization of ortho-(benzyloxy)benzophenone occurs with almost 100% efficiency in benzene and with less efficiency in the presence of pyridine or other Lewis bases.[37] Here the *unsolvated* biradical undergoes almost no back hydrogen transfer, which is just opposite of what is seen for all other 1,4- and 1,5-hydroxy biradicals. The solvated biradical, established by the characteristic drop in Z:E cyclization ratio, apparently engages in some other reaction which competes with cyclization to a benzodihydrofuranol. The original examiners of this reaction noticed the same phenomenon in the discovery of phenols as by-products in alcohol solvents.[23] Polar solvents also cause reduced cyclization quantum yields for (ortho-alkoxyphenyl)glyoxalate esters.[22]

In the presence of pyridine, cyclization efficiency of ortho-(benzyloxy)acetophenone in benzene increases tenfold, but at the expense of stereoselectivity. This behavior is normally expected for hydroxyl biradicals.[38] Most of the lower quantum efficiency is due to the low rate of δ-hydrogen abstraction, after which only 10% of the unsolvated 1,5-biradicals cyclize. The large difference in this regard between the benzophenone and the acetophenone has no analogy in other hydrogen atom abstraction reactions and has been attributed to *spirocyclization.* The degree of competition between spirocyclization and benzodihydrofuranol formation depends upon the ease of rotation about the benzene-hydroxybenzyl radical bond in the biradical, which is fast in the benzophenone-derived biradical, but is slow in the acetophenone-derived biradical.[37] This competition represents another unique example of conformational restrictions on a reactive intermediate. Phenols and diketones which are found as by-products probably arise from air oxidation of the presumed spiroenol intermediates.



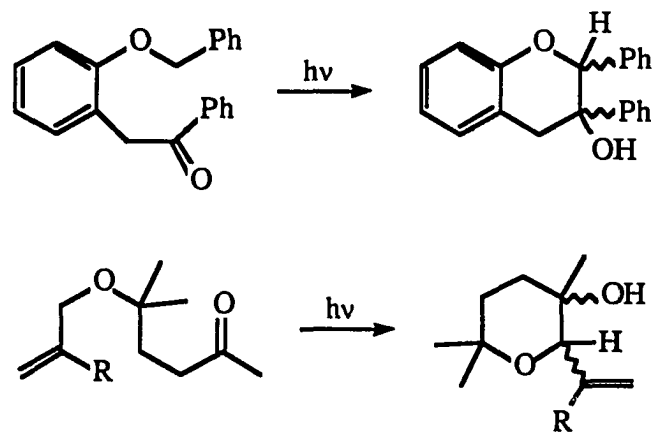
Additional examples of δ-hydrogen abstraction /cyclization reactions include photolysis of carbohydrate derivatives[39,40] and of phthalimide derivatives. Most of the phthalimide photochemistry involves a heteroatom exerting a regiochemical influence in the H-abstraction. Electron transfer could be involved.[41]





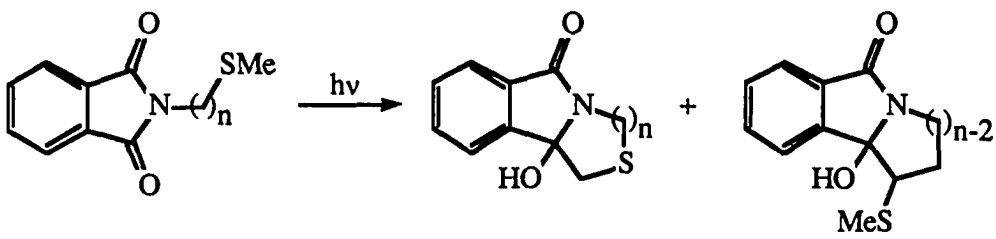
4. Distant site hydrogen atom abstraction

Hydrogen abstractions from sites farther than a δ-position are not as well known. Two examples of ε-abstractions are shown below, where a dihydropyran is formed by photolysis

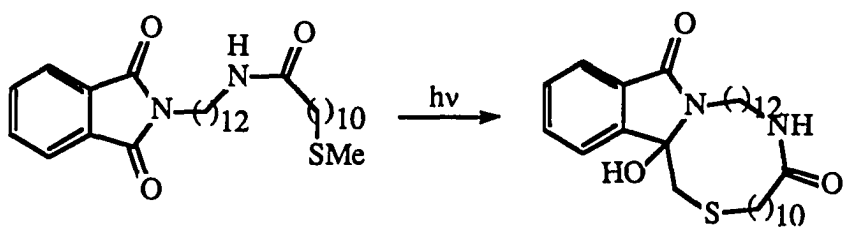


of an aryl ketone, and a tetrahydropyran arises from cyclization of an alkyl ketone with its γ- and δ-positions blocked. As was presented earlier in the phthalimide system, the oxygen atom directs the site of attack. In addition, the resultant radical is allylic which is preferred over the radical that might have been formed at the β-position.

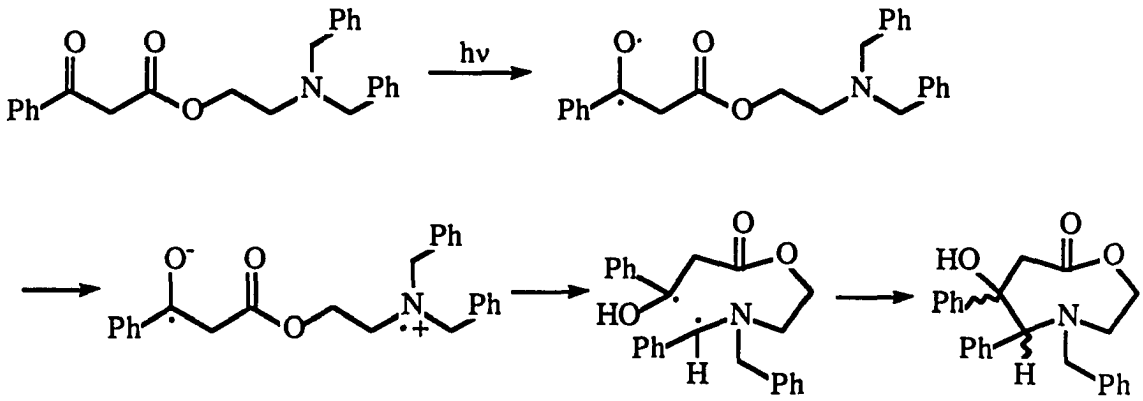
There are examples of hydrogen atom abstraction from sites even more distant. The principal area in which this has been studied is in the study of phthalimide derivatives. The irradiation of substituted phthalimides can create medium to large ring systems. The yields of the large ring diaza compounds are variable, but in some cases it is possible to attain high yields.[41]



n = 5 to 12 25 - 78% 0 - 10%



Hasegawa and co-workers[42] present an example where (dibenzylamino)ethyl benzoate undergoes intramolecular hydrogen abstraction via charge transfer through a ten-membered cyclic transition state to provide eight-membered azalactones.

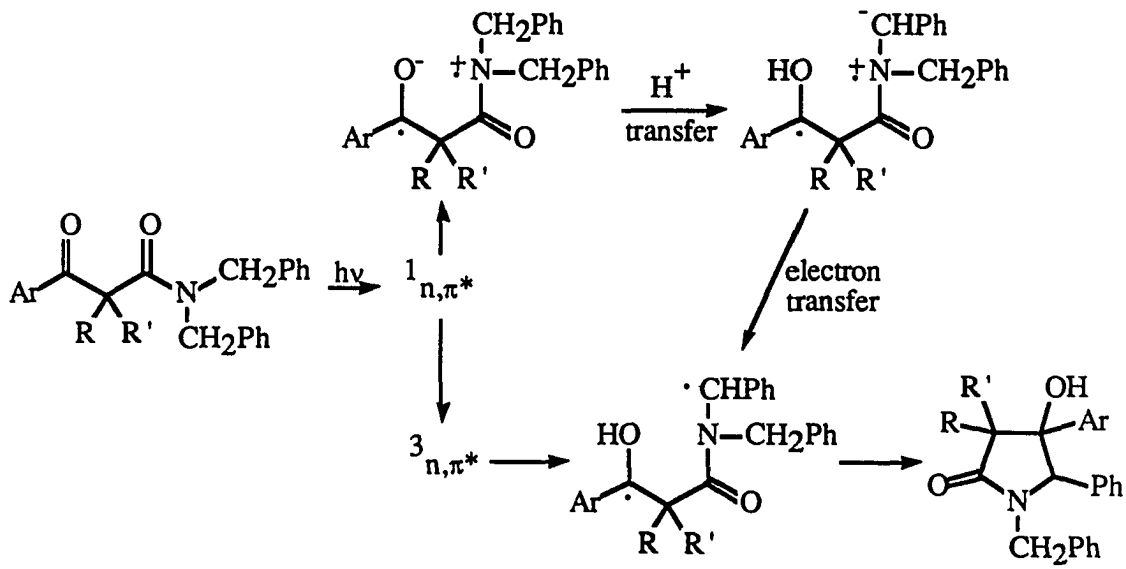


5. β-Oxoamide photochemistry

Aromatic ketones generally undergo a Norrish Type II reaction from their n,π^* triplet states. Aminoketones react similarly, although the mechanism of hydrogen atom abstraction by the carbonyl is different. The excited carbonyl engages in electron transfer with the nitrogen to create a zwitterion, after which a proton shift occurs, thus creating a biradical. This charge transfer interaction becomes less efficient upon substitution of an electron-withdrawing group on the nitrogen atom,[43] but it is found[44] that charge transfer interaction between the amide nitrogen and the excited carbonyl still plays an important role in cyclization. Little attention had been paid to the photochemistry of β-oxoamides before the work of Hasegawa in 1976,[45] in which substituted N-alkyl-4-hydroxy-2-pyrrolidinones were made photochemically from β-oxoamides in yields up to 90%.

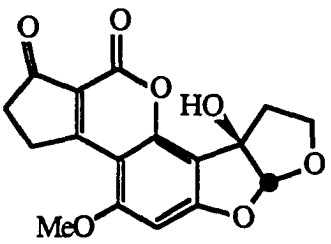
Quenching studies were done on the photolyses of N,N-dibenzyl benzoylacetamides in benzene and in methanol.[44] Quenching by known triplet quenchers was not observed in benzene and the reaction in methanol was only partially quenched. The failure to completely quench the reactions and the observed solvent effects suggest intervention of a zwitterionic intermediate. The smaller contribution of the charge transfer process in methanol can be explained in terms of solvation. Solvation of the ketone and amide groups by methanol should hinder close approach of the ketone to the lone pair on the amide nitrogen and therefore

make the electron transfer interaction inefficient. The β-oxoamide, upon excitation to the n,π* singlet, undergoes electron transfer with the amide nitrogen to create a zwitterion. Proton transfer occurs between the ketyl radical and the position α to the nitrogen, followed by another electron transfer, to produce the same 1,5-biradical that would be obtained from direct hydrogen atom abstraction via the n,π* triplet. Cyclization gives an N-substituted-4-hydroxy-2-pyrrolidinone. Yields for the N,N-dibenzyl benzoylacetamides are reported to be near 90%.[44]



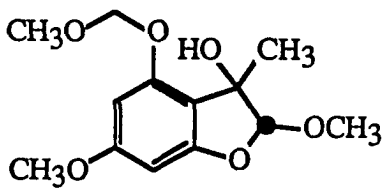
III. RESULTS AND DISCUSSION

We have been pursuing a direct approach to aflatoxin M_2[46] via Norrish Type II chemistry. Many of the aflatoxins are readily available; however, aflatoxin M_2 is relatively rare and there is considerable interest in metabolites of aflatoxin M_2.

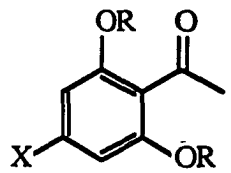


Aflatoxin M_2

Our approach involves synthesis of a model system such as **1** which would be made via photocyclization of ketone **2**. Studies by Wagner and coworkers showed that electron-donating groups dramatically decreased the quantum yields for hydrogen atom abstraction due to low equilibrium levels of the n,π^* state.[36,47] However, examination of molecular models



1



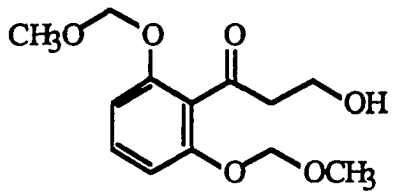
2a: X = OCH_3, R = CH_2OCH_3

2b: X = H, R = CH_2OCH_3

2c: X = H, R = CH_3

2d: X = H, R = $CH_2CH{=}CH_2$

revealed that the carbonyl in **2a-2d** would likely exist in a conformation almost orthogonal to the aromatic ring; therefore, compounds **2a-2d** might react more like aliphatic ketones, with the influence of the alkoxy groups greatly lessened. Supporting this hypothesis is the ultraviolet spectrum of **3** which exhibits an absorption maximum at 232 nm, compared to 260 nm calculated by the method of Scott.[48] The results of our photolyses of compounds **2a-2d** have been reported in the literature.[49] These successful photocyclizations were the basis for our further research toward the synthesis of aflatoxin M_2.

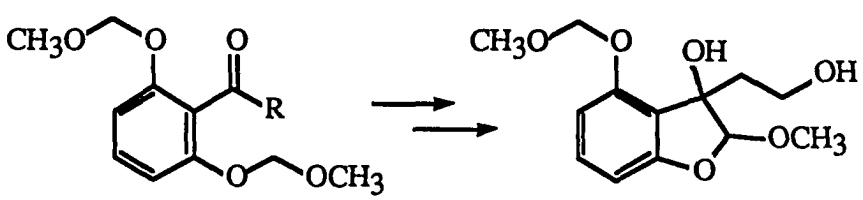


3

I will first discuss our studies toward aflatoxin M_2, followed by a discussion of our work toward the securinine alkaloids and other alkaloids, and finally I will present our results on the synthesis of sugar derivatives, including derivatives of two rare sugars: D-gulose and D-idose.

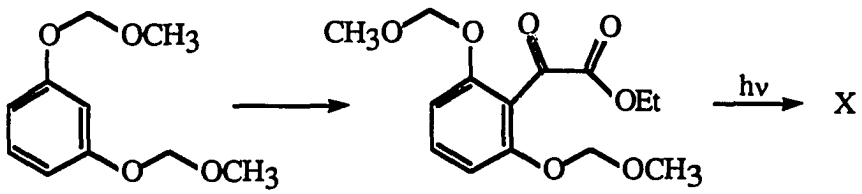
A. Aflatoxin M_2 Study

Work was undertaken to synthesize ketone **4** in which R is a functionalized one- or two-carbon unit, so that after photocyclization compound **5** could be obtained in a minimum



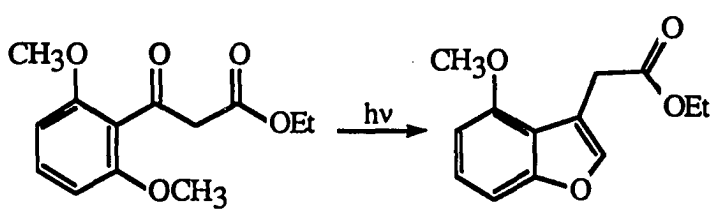
4 **5**

number of steps. Compound **7** was chosen for initial study. Benzene **6** was metallated[50] with *n*-butyllithium in boiling ether and quenched with ethyl oxalyl chloride at -78 °C to give **7** in 50% yield. All ultraviolet irradiations of **7** or the methyl ester (**7** /*t*-BuOK / CH_3OH) with a variety of solvents and glass filters (benzene, quartz; benzene, Pyrex; benzene, Pyrex, $NaHCO_{3(s)}$; CH_3CN, quartz, 0 °C) gave unrecognizable decomposition products.



6 **7**

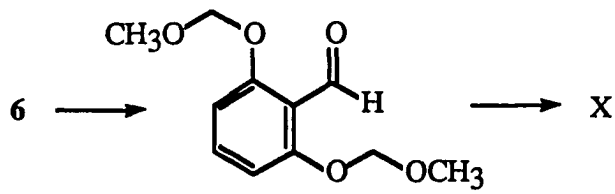
We decided to pursue the photolysis of a β-ketoester, based on our unreported successes in the Norrish Type II cyclizations of aliphatic δ-alkoxy-β-ketoesters. We expected that this route would lead directly to compound **5** after photocyclization and reduction. 2,6-Dimethoxybenzaldehyde was converted into a β-ketoester using the method of Holmquist and Roskamp.[51] A dichloromethane solution of 2,6-dimethoxybenzaldehyde was added slowly to a solution of tin(II) chloride dihydrate and ethyl diazoacetate. Aqueous workup and purification afforded a 54% yield of β-ketoester **8** which was immediately subjected to irradiation in benzene in a quartz tube for a total of nine hours. Concentration and flash



8 **9**

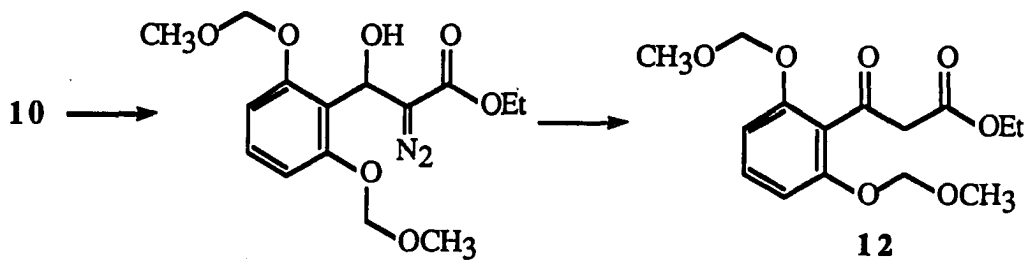
column chromatography of this model system gave a 2.4% yield of the benzofuran **9** with only 13% recovery of starting material. With this promising, albeit low-yielding, result, we went for the actual system, **12**.

Metallation of **6**, followed by dropwise addition of N,N-dimethylformamide[50] at room temperature, gave benzaldehyde **10** in 73% yield. Subjecting this aldehyde to Roskamp conditions ($SnCl_2 \cdot 2H_2O$, ethyl diazoacetate, CH_2Cl_2) gave a mixture of unidentifiable products! Another synthetic method was necessary. The work of Pelliciari and coworkers[52]



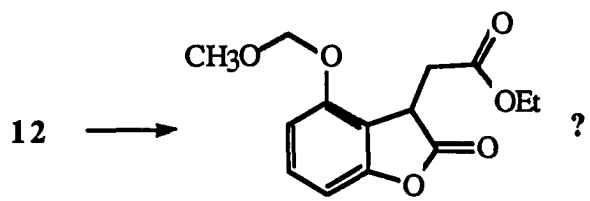
10

provided the answer. A solution of LDA at 0 °C was added dropwise to a -78 °C cooled solution of **10** and ethyl diazoacetate in THF. In situ deprotonation of the diazoester and attack of the aldehyde makes an α-diazo-β-hydroxyester. Quenching at -78 °C with acetic acid and aqueous workup afforded a 90% yield of **11** after Florisil chromatography. Dilution of **11** in dry dimethoxyethane and addition of catalytic rhodium(II) acetate ($Rh_2(OAc)_4$) at room temperature caused a nitrogen extrusion and hydride transfer to give the enolic ester



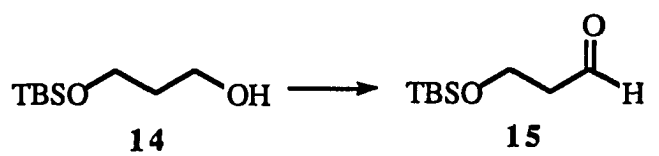
11 **12**

which tautomerized to the desired β-ketoester **12** in 96% yield. A number of photolyses of **12** were performed in benzene using various glass filters (quartz, Pyrex,Vycor). Every trial gave approximately a 20% yield of a compound we suspected was **13**, but we were unable to positively identify it. Reduction with lithium aluminum hydride was done on separate runs with the hope of obtaining a more easily interpretable proton NMR spectrum. The result was a compound which was both unstable to silica gel chromatography and impossible to identify. We decided to pursue another pathway.

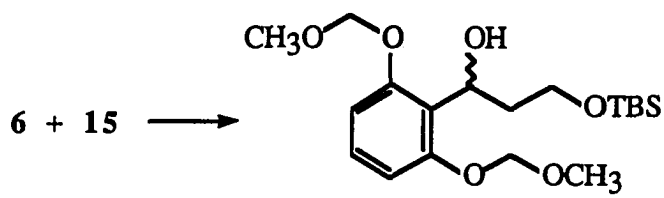


13

The next attempt to make compound **5** was successful. Alkylation of the anion of **6** with aldehyde **15** gave **16** in 69% yield. Aldehyde **15** was made in two steps. Reaction of 1,3-propanediol with one equivalent of NaH and *t*-butyldimethylsilyl chloride in THF[53] gave the monosilylated diol **14** in 91% yield, which was oxidized in 83% yield to aldehyde **15**

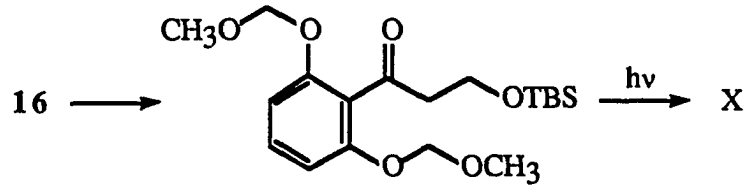


14 **15**



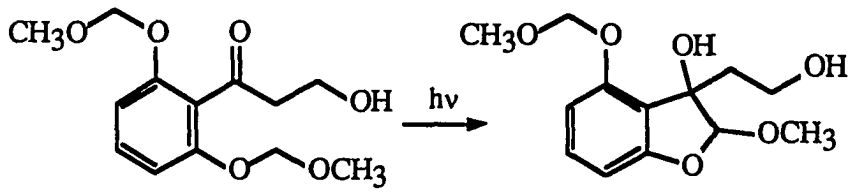
16

using Swern oxidation conditions (oxalyl chloride, DMSO, Et_3N, CH_2Cl_2).[54] Oxidation of the hydroxy compound **16** with activated manganese(IV) oxide[55] in ether gave the ketone **17** in 78% yield. Photolysis of this ketone in benzene (0.005 M) using a quartz filter at ambient temperature for 3.5 hours gave a product which we could not identify. Suspecting that the silyl group could be causing the problem, we deprotected the hydroxyl group with excess



17

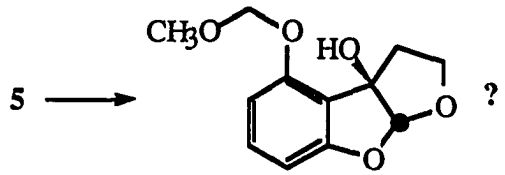
triethylammonium fluoride[56] in THF at 70 °C to give hydroxyketone **3** in 57% yield. Irradiation of this ketone for 40 minutes in benzene (0.01 M solution) using a quartz filter at ambient conditions produced **5** in 30% isolated yield after silica gel chromatography. The diol



3 5

appeared to be one diastereomer. The chromatographic stability of **5** may be due to intramolecular hydrogen bonding or to inductive effects. Acid-catalyzed intramolecular transacetalation to make the tetrahydrobenzofurofuranol **18** was tried using several conditions. Amberlite IR-120 Plus acidic ion-exchange resin[57] in the presence of 4 Å molecular sieves at 70 °C in benzene led only to recovery of starting material. Catalytic p-toluenesulfonic acid and molecular sieves in benzene at room temperature led only to starting material; however,

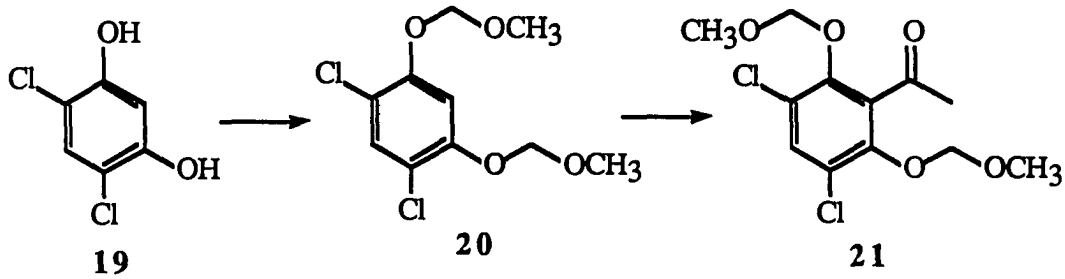
when heated, decomposition occurred. There was also no reaction with catalytic pyridinium p-toluenesulfonate and molecular sieves in dichloromethane at room temperature. Heating to reflux led to decomposition. It is clear that conditions must be found to convert **5** into **18**.



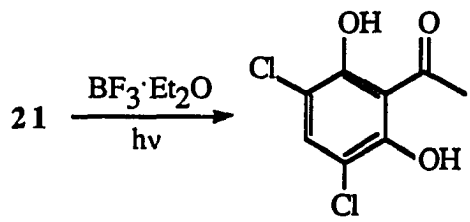
18

We then performed a series of studies to increase the yield of **5**. Changing the concentration of the photolysis solution (0.004 M **3** in benzene) proved fruitless. Work done by Wagner and Siebert[47] suggested that substitution ortho and ortho' to the alkoxy groups might increase both the rate and yield of the cyclization by tilting the abstraction sites out of the plane of the aromatic ring, so that the hydrogen atoms are closer to the oxygen of the carbonyl. We expected this strategy to help maximize the yield of our photocyclization. We needed a functional group that could be easily placed in the 3- and 5-positions and that could be removed easily after cyclization. We decided on ketone **21**.

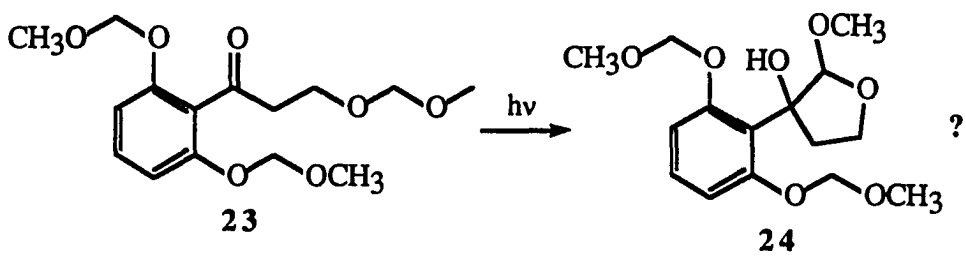
Dichlorination of 1,3-dihydroxybenzene was done with two separate treatments of sulfuryl chloride[58] in boiling ether to give **19** in 100% yield. Treating the disodium dianion of **19** (2.2 equivalents NaH in DMF) with two equivalents of chloromethyl methyl ether[50] at 0 °C afforded **20** in 84% yield. Metallation with *n*-butyllithium in boiling ether and alkylation with acetaldehyde at 0 °C gave the carbinol in 59% yield which was oxidized with activated MnO_2 in ether to provide the desired ketone **21** in 70% yield. All photolyses of **21** using different solvents and glass filters led to decomposition (benzene, quartz; benzene, Pyrex; ether, Pyrex). Perhaps the carbon-chlorine bonds were susceptible to homolytic cleavage with UV irradiation. Lewis acid-assisted photolysis of **21** according to Lewis and Barancyk[59]



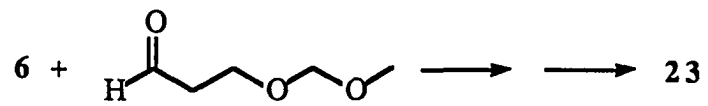
using boron trifluoride etherate and dichloromethane with a Pyrex filter only removed the methoxymethyl groups to afford the dichlorodihydroxyketone in good yield.



Still in pursuit of higher yields of our aflatoxin M_2 precursor photolysis product, we decided to test a slightly different approach in our next photocyclization. We wanted to see if we could increase the yield of usable product in our photolyses by giving the aromatic ketone alternative sites from which to abstract a hydrogen atom; that is, prepare a ketone such as **23**. Compound **23** could abstract a hydrogen atom either from the 2,6-alkoxy sites or from the protecting group on the primary alcohol to afford a dihydrobenzofuranol or a compound like **24**. This could be transacetalated to give a tetrahydrobenzofurofuran. Treatment of the

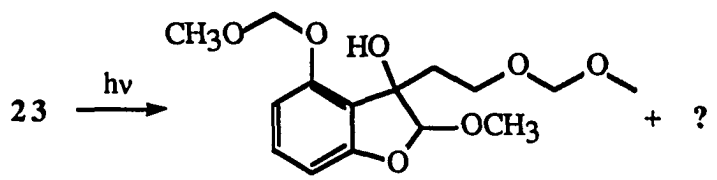


monoanion of 1,3-propanediol (NaH, THF)[53] with one equivalent of chloromethyl methyl ether afforded the monoprotected diol in 51% yield. Oxidation with pyridinium chlorochromate (PCC) adsorbed on Florisil[60] provided the aldehyde **22** in 63% yield. Metallation



22

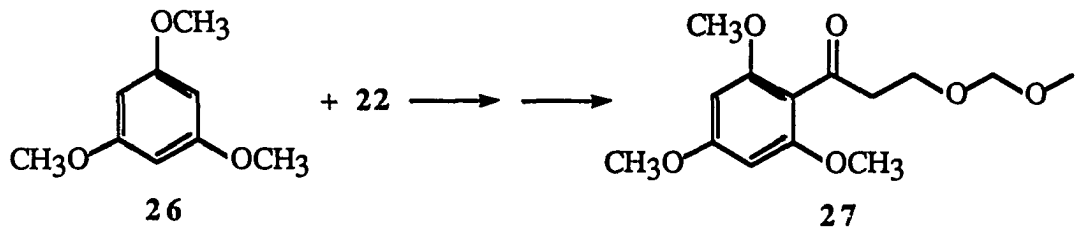
of 1,3-bis[(methoxymethyl)oxy]benzene followed by addition of **22** gave the desired carbinol in 51% yield. Activated MnO_2 oxidation afforded ketone **23** in 47% yield. Irradiation of the ketone as a 0.025 M solution in benzene with a quartz filter for one hour consumed the starting material and produced a 3:2 ratio of **25** and an unidentifiable compound. There was no increase in yield via this route. We hypothesized that perhaps the bulk of the 2,6-(methoxymethyl)oxy groups was hindering close approach to the carbonyl, preventing hydrogen atom abstraction. We decided to study compound **27**. Compound **27** had methoxy groups which might enable the acetal to participate.



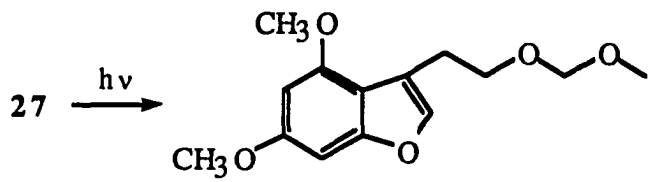
25

Metallation of benzene **26** with *n*-butyllithium in boiling ether followed by addition of **22** at 0 °C gave the desired carbinol in 35% yield. Oxidation with activated MnO_2 afforded a 49% yield of the ketone **27**. The only product of the slow photolysis reaction (benzene, quartz tube, 9 hours) was benzofuran **28** which is probably derived from dehydration during

silica gel chromatography.[49] A conclusion which can be drawn is that in such ketones the photochemically-excited carbonyl prefers to abstract a hydrogen atom from the δ-position of an alkoxy group on the aromatic ring rather than from the δ-position of an alkoxy group on the aliphatic acyl chain probably because of conformational restrictions on the aliphatic acyl chain reflecting steric effects of the groups in the 2- and 6-positions. These latter two results were not foreseen with Wagner's observation[47b] that ortho-(benzyloxy)valerophenone undergoes only Norrish Type II photoelimination to give ortho-(benzyloxy)acetophenone.

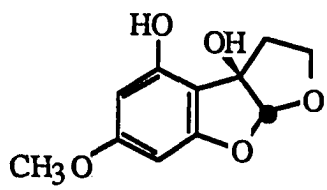


26 27



28

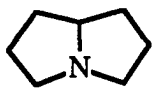
In view of the conversion of **29** into aflatoxin M_2 in one step by Buchi et al.,[61] the synthesis of dihydrobenzofuranol **5** bodes well for a direct photochemical entry into the aflatoxin family.



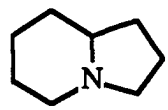
29

B. Alkaloid Synthetic Studies

We studied the use of the Norrish Type II reaction in alkaloid synthesis. We imagined that an irradiated β-amino carbonyl compound would undergo δ-hydrogen atom abstraction to make a five-membered ring which is found in pyrrolizidine and indolizidine alkaloids. Many of the pyrrolizidine and indolizidine alkaloids exhibit interesting biological activity. For

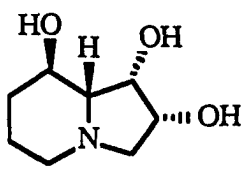


pyrrolizidine skeleton

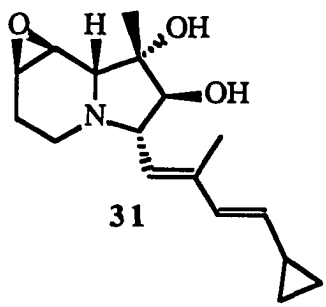


indolizidine skeleton

example, swainsonine **30** is an α-mannosidase inhibitor and is used in cancer research,[62] and cyclizidine **31** shows nonselective immunostimulatory properties.[63] The pharmacological interest in these alkaloids made these seem a prime target for Norrish Type II chemistry. A large number of amino- and amido ketones and aldehydes were made for UV irradiation. Some interesting results were obtained.



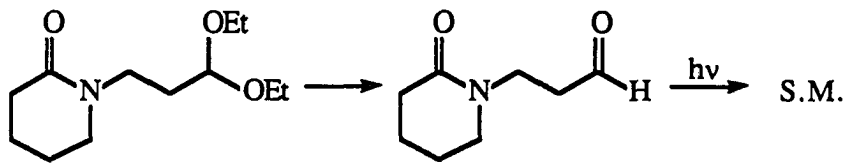
30



31

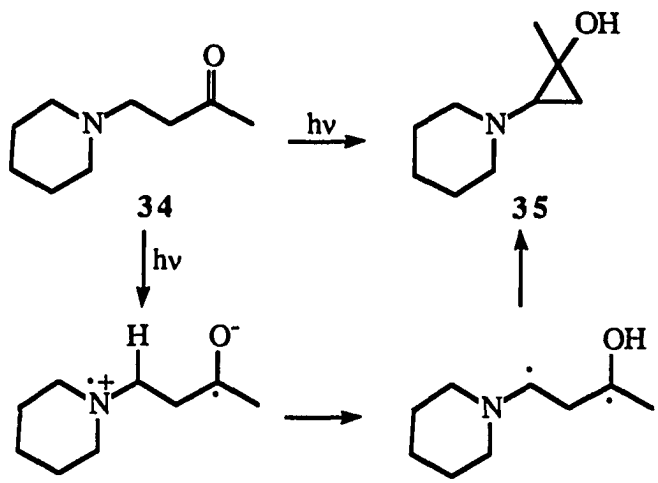
Swainsonine was the first target. Alkylation of δ-valerolactam with 3-chloropropionaldehyde diethyl acetal[64] afforded **32** in 54% yield. Compound **32** was hydrolyzed with

10% H_2SO_4 in acetone and water to give aldehyde **33** in 41% yield. All photolyses of **33** in benzene led to recovery of starting material. Synthesis of the analogous amino aldehyde was impossible.

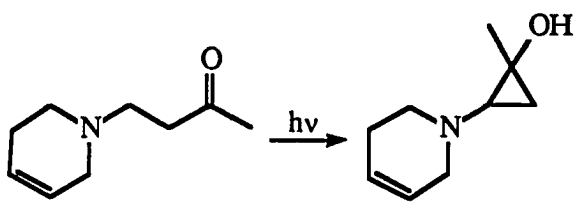


32 **33**

Irradiation of 4-amino-2-butanones was a logical next step. Synthesis of these compounds[65] was accomplished by the reaction of equimolar amounts of secondary amine and methyl vinyl ketone (MVK) at 0 °C with warming to room temperature. Vacuum distillation afforded the 4-amino-2-butanones in 80-85% yields. Irradiation of ketone **34** in benzene with a quartz filter afforded the cyclopropanol **35** in 34% yield. Compound **35** is probably a result of electron transfer rather than β-hydrogen atom abstraction. What is interesting is that after electron transfer, the oxyanion of the zwitterion prefers to deprotonate the β-position creating a 1,3-biradical. It was thought that structural changes to **34** would

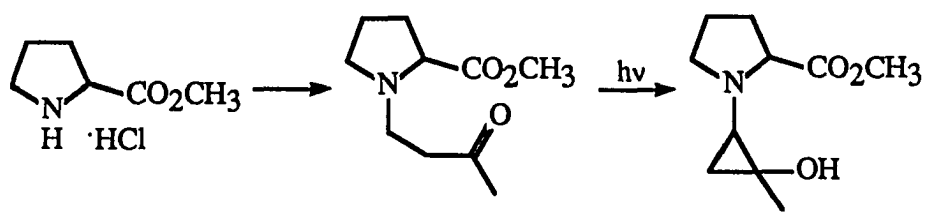


either increase the acidity of the δ-proton or stabilize a radical α to the nitrogen. Compound **36** was made with 1,2,3,6-tetrahydropyridine and MVK. It was thought that the unsaturation would increase the acidity of the δ-protons or would stabilize a radical at the δ-site. Irradiation



36 **37**

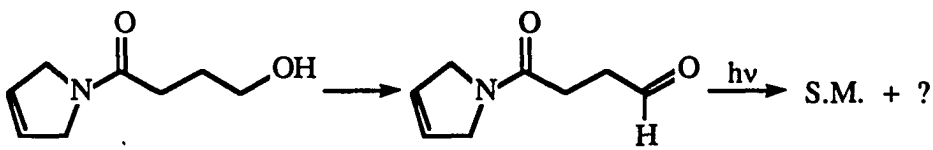
in benzene with a quartz filter resulted in cyclopropanol formation (**37**) as determined by examination of the NMR spectrum of the crude product. Irradiation of **36** in methanol with a quartz filter led to recovery of starting material. Irradiating the protonated amine was tried to see if eliminating electron transfer[43] would aid regioselectivity of hydrogen atom abstraction. Irradiation of the trifluoroacetate salt of **36**, made by adding an equimolar amount of trifluoroacetic acid to **36** in benzene, led only to recovery of starting material. Another way of increasing δ-proton acidity was tried: incorporating an ester α to the nitrogen atom. L-(-)-Proline was dissolved in methanol and was treated with thionyl chloride[66] at -10 °C to provide crude **38**. Triethylamine was added to a dichloromethane solution of **38** and filtered to remove triethylammonium chloride. MVK was added to the filtrate at 0 °C and was stirred



38 **39** **40**

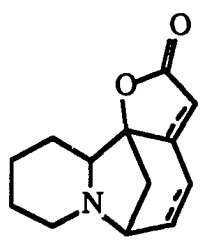
overnight. The ester **39** was isolated by silica gel chromatography in 63% yield from L-(-)-proline. Irradiation of **39** in benzene with a quartz filter gave cyclopropanol **40** in 35% yield. Other routes to indolizidine systems were pursued.

Cyclization onto a five-membered ring to make a 5,6-fused system was the next strategy. With swainsonine in mind we made compound **42**. 3-Pyrroline reacted with γ-butyrolactone in boiling THF to give crude lactam **41**. Compound **41** was oxidized without purification to the aldehyde **42** using Swern conditions (oxalyl chloride, DMSO, Et_3N). Two irradiations of **42**, 0.04 M in benzene with a quartz filter and 0.01 M in benzene with a quartz filter, gave starting material plus an unidentifiable product. The swainsonine project was abandoned.

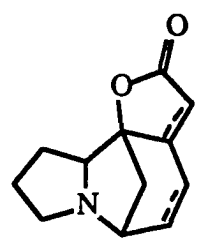


41 **42**

The next indolizidine project was the synthesis of the securinine alkaloids. The general structures are shown below. The securinine alkaloids are a group of approximately 18



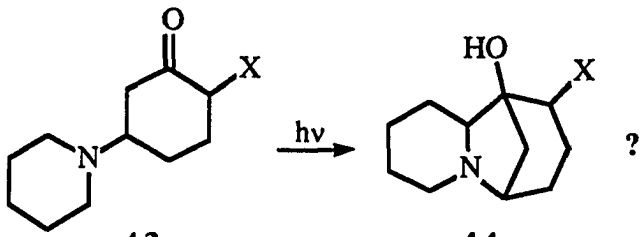
securinines



norsecurinines

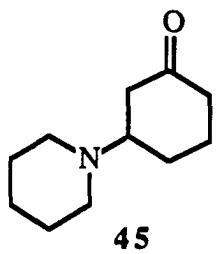
compounds that are GABA antagonists. Injection of securinine salts into laboratory animals caused central nervous system stimulation. Past syntheses of securinine and the pharmacology of the securinine alkaloids are detailed in the literature.[67] Irradiation of compound **43**

was expected to afford **44** through hydrogen atom abstraction or through electron transfer. If group **X** were an acetic acid unit or a masked ester, a γ-lactonization could then be performed



43 **44**

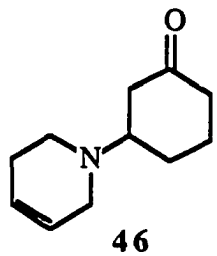
to give a securinine alkaloid. Compound **45** was made in 80% yield by addition of dry piperidine to distilled cyclohexenone[68] followed by vacuum distillation. Photolysis of **45**



45

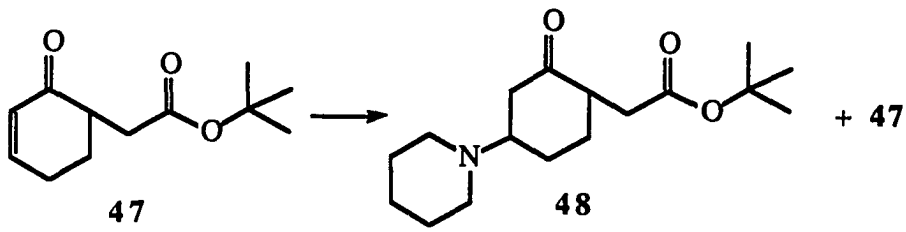
both in benzene with a quartz filter for eight hours and in benzene with a Pyrex filter for eight hours resulted in decomposition. Photolysis in 2-methyl-2-propanol with a quartz filter for three hours led to recovery of starting material and a trace of cyclohexenone. Photolysis of **45** in methanol with a quartz filter gave an unidentifiable product. Acylation of the crude material with acetic anhydride and pyridine in dichloromethane was tried to see if the O-acyl analogue of **44** could be isolated. The major product was N-acetylpiperidine; therefore, decomposition occurred. Photolyses of **45** in ether with a quartz filter and in THF with a quartz filter gave unidentifiable products. Acylation with acetic anhydride and pyridine gave unidentifiable products. It seemed logical to make the protons α to the nitrogen more acidic as was tried in

the swainsonine project. Addition of 1,2,3,6-tetrahydropyridine to cyclohexenone afforded **46** in 79% distilled yield. Photolysis of **46** in THF with a quartz filter and in THF with a



46

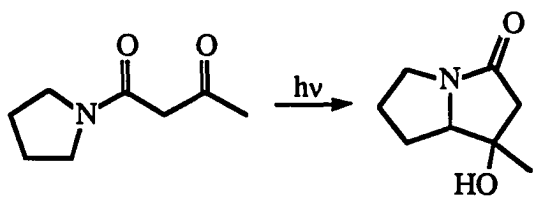
Pyrex filter followed by acetic anhydride and pyridine gave only decomposition products. The next strategy was irradiation of compound **48**. Deprotonation of cyclohexenone with LDA and alkylation with *t*-butyl iodoacetate[69] provided ketoester **47** in 79% yield. Addition



47 **48** + **47**

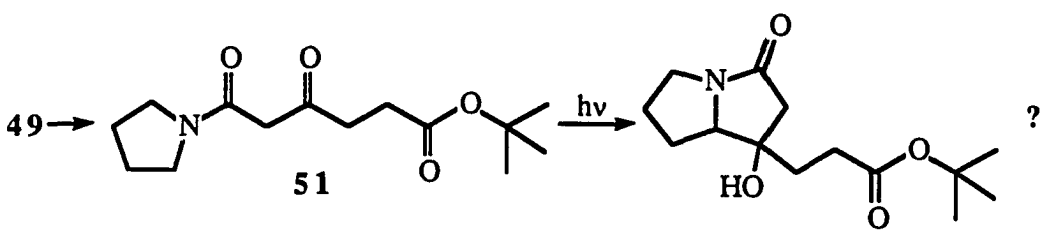
of piperidine to **47** and vacuum Kugelrohr distillation gave a 2.3 : 1 ratio of **48** and **47**. Irradiation of the mixture in THF with a quartz filter for four hours led to decomposition.

The norsecurinines were the next target. Photocyclization of an N,N-disubstituted β-ketoamide[44,45,70] would make two of the four rings of the norsecurinines. Irradiation of compound **51** was the goal. Treatment of diketene with distilled pyrrolidine gave β-ketoamide **49**, which was irradiated to check the chemistry. Irradiation of **49** in benzene with a Pyrex filter for 13 hours gave a 75% yield of **50** as a mixture of diastereomers. The dianion of **49** was made with two equivalents of LDA at 0 °C and was treated with *t*-butyl iodoacetate at -78 °C to afford **51** in 14% yield. Efforts to increase the yield of this step were fruitless.



49 50

Compound **51** was then irradiated in benzene with a Pyrex filter for 42 hours. The product tentatively was assigned structure **52**. The yield was 50% at 50% conversion. An attempt to increase the yield by using a quartz filter gave the same yield after eight hours. The next step was lactonization to afford a tricyclic molecule. A solution of **52** and catalytic p-toluene-sulfonic acid in benzene heated at reflux for two hours gave two unknown products. Milder conditions were tried to see if the product distribution changed. Treatment of **52** with pyridinium p-toluenesulfonate (PPTS) in boiling benzene gave a different unknown product.



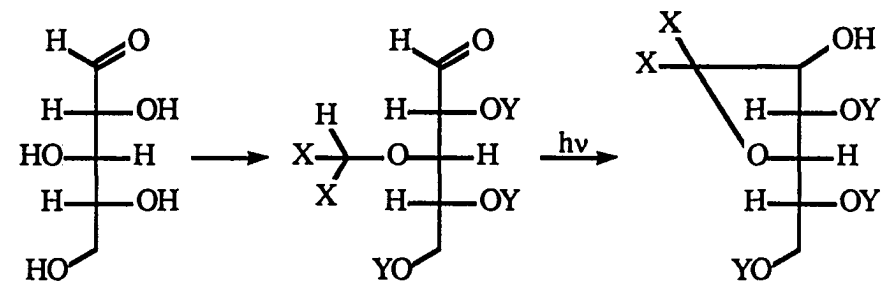
51 52

Starting material remained after boiling a solution of **52** in THF with catalytic potassium *t*-butoxide for two hours. Addition of sodium hydride and stirring at room temperature led to decomposition. It was concluded that **52** is not a desirable intermediate. Thus ended the study of the syntheses of indolizidine and pyrrolizidine alkaloids with the Norrish Type II photocyclization.

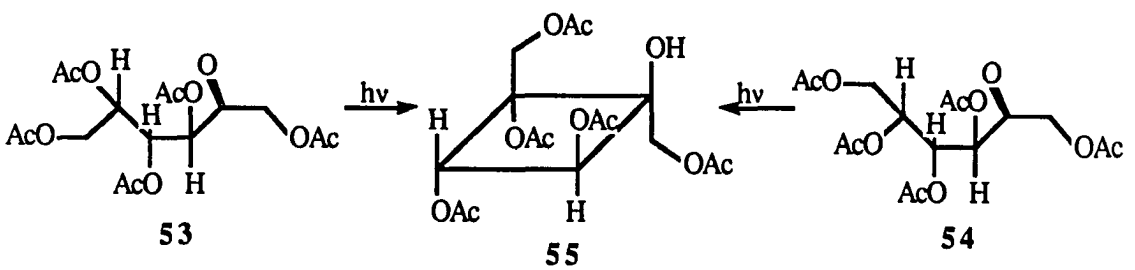
C. Sugar Derivatives

As part of our investigation into the synthetic potential of the Norrish Type II reaction, we explored syntheses of sugar derivatives. We wanted to develop a method by which a

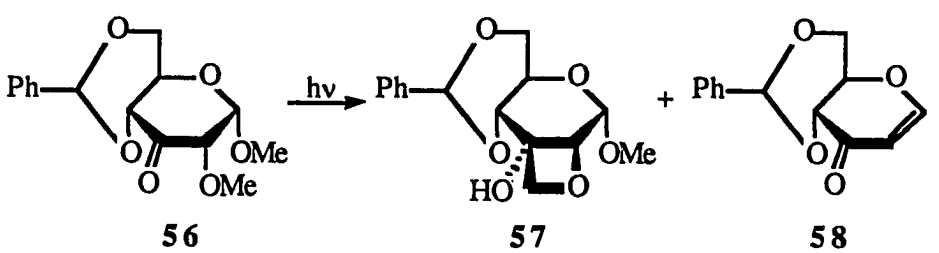
readily available aldose could be functionalized and irradiated to create a sugar derivative. We expected this methodology to add to known carbohydrate synthetic methods.



Many of the applications of photochemistry to carbohydrate chemistry[71] have been Norrish Type II photofragmentations[12-15]. However, there are reports of Norrish Type II photocyclizations in carbohydrates. Whistler and Doner[72] reported that ultraviolet irradiation of D-fructose derivative **53** and **54** (epimeric at the γ-carbon) afforded one product, **55**, in

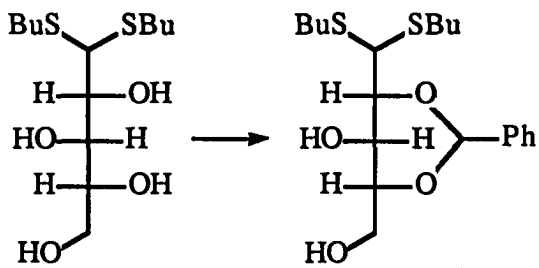


11.6% and 26.2% yields, respectively. This demonstrates the diastereoselectivity possible in these photoreactions. Collins et al.[73] observed both fragmentation and cyclization upon



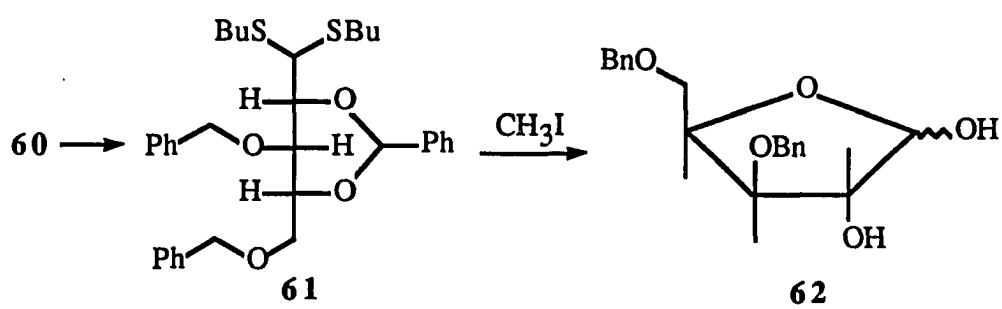
irradiation of **56** to give **57** and **58**, respectively. Our results which include total syntheses of penta-O-acetyl-D-gulopyranose and penta-O-acetyl-D-idopyranose are presented here.

D-Xylose was the starting material for all of the derivatives prepared in this study. Treatment of D-xylose with excess butanethiol and concentrated HCl at 0 °C[74] gave the thioacetal **59**. Compound **59** was treated with benzaldehyde and concentrated HCl in aqueous dioxane at 0 °C[75] to afford the acetal **60**. Many different aldehydes could be made from **60** by alkylation of the two hydroxyl groups and hydrolysis of the thioacetal. We conducted a survey of δ-hydrogen-bearing functional groups that we could incorporate into **60**.



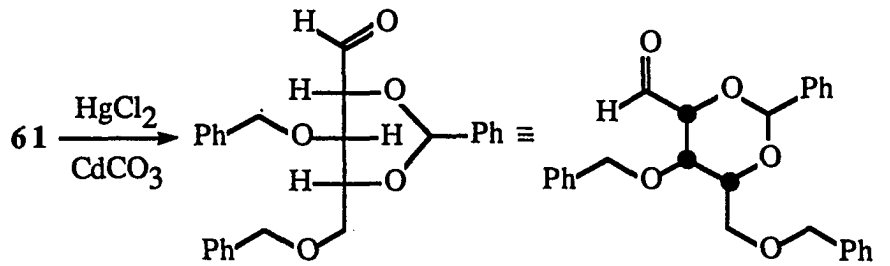
59 **60**

The dianion of **60** was made in DMF with two equivalents of NaH. Treatment with two equivalents of benzyl bromide at 0 °C and stirring overnight gave **61** in 62% yield. Hydrolysis of the thioacetal by stirring with excess methyl iodide in aqueous acetonitrile occurred with hydrolysis of the benzylidene acetal to afford **62**, because the solution became



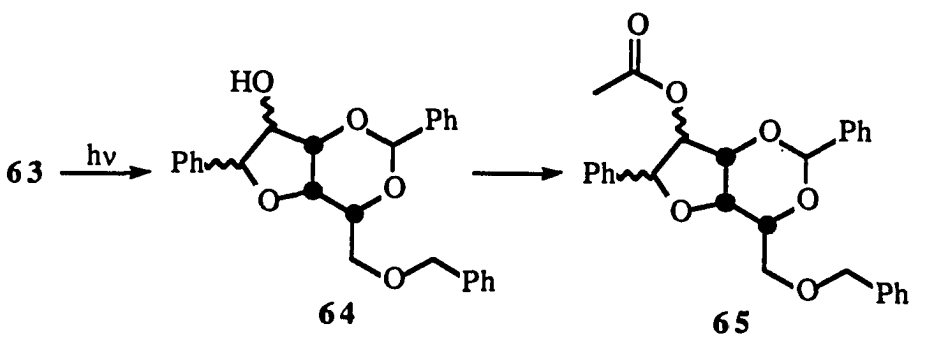
61 **62**

acidic. Repeating the reaction with $NaHCO_3$ led to decomposition. Attempted deprotection with $AgNO_3$ and Ag_2O in acetonitrile and water[76] led to recovery of starting material. Hydrolysis of the thioacetal was achieved with mercury(II) chloride and cadmium carbonate[77] in acetone and water. Purification afforded derivative **63** in 68% yield. We expected that in



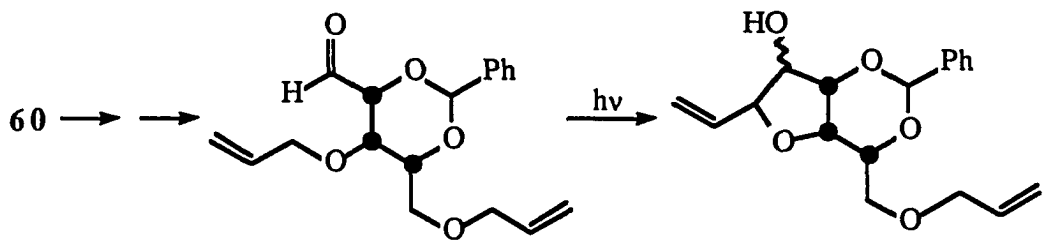
63

63 hydrogen atom abstraction would occur from the cis 2°-benzyloxy group. Irradiation in benzene with a quartz filter provided **64** in 57% yield as an inseparable mixture of diastereomers. To make proton NMR spectral assignments, **64** was acylated with acetic anhydride and 4-(N,N-dimethylamino)pyridine (DMAP) to give **65** as three distinct spots by



thin layer chromatography (TLC). Isolation of the major product was done by silica gel chromatography, but diastereomer identification was impossible.

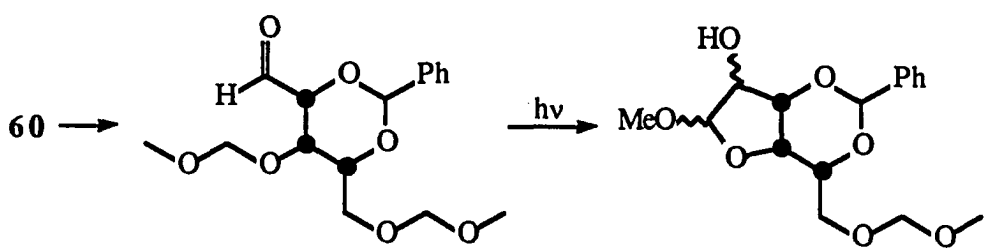
Alkylation of the dianion of **60** (NaH) with allyl bromide gave the diallylated product in 90% isolated yield. Deprotection ($HgCl_2$, $CdCO_3$, acetone, H_2O) gave **66** which was hydrolytically sensitive to silica gel chromatography. Isolation of **66** in 33% yield was accomplished by a short Florisil column. Irradiation of **66** in benzene with a quartz filter for 75 minutes followed by Florisil chromatography afforded a 37% yield of **67**. The low yields



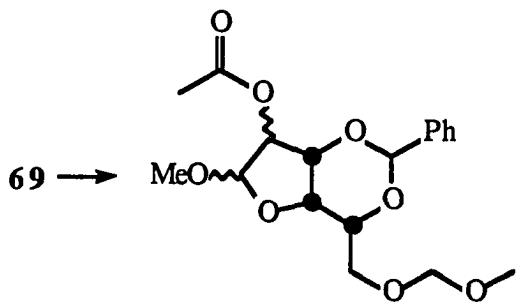
66 **67**

of **66** and **67** may reflect some hydrolytic instability on Florisil. Acylation of **67** (Ac_2O, DMAP) afforded a separable mixture of three spots on TLC. The major spot was one diastereomer by ^1H and ^{13}C NMR spectroscopy. Identifying diastereomers was impossible.

Next we made compound **68**, because the diastereomeric products of photolysis could be converted into two rare sugars: D-gulose and D-idose. The dianion of **60** was treated with two equivalents of chloromethyl methyl ether to give the desired product in 75% yield. Hydrolysis of the thioacetal ($HgCl_2$, $CdCO_3$, acetone, water) provided aldehyde **68** in 61% yield. Photolysis of **68** for 70 minutes in benzene with a quartz filter gave a 45% isolated

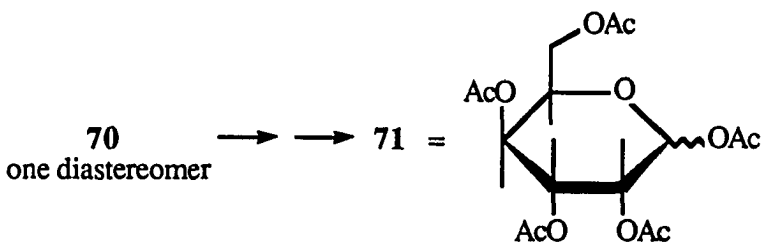


68 **69**



70

yield of **69** as an inseparable mixture of diastereomers. Acylation of **69** (Ac_2O, DMAP) gave **70** as a separable mixture of three spots on TLC, one of which looked like two diastereomers by proton NMR spectroscopy. The other two spots each looked like one diastereomer. All three spots had identical infrared and high resolution mass spectra. One of the diastereomers was then converted into a penta-O-acetyl-D-pyranose, because purification was easier on a small scale. The one diastereomer was heated at 50-55 °C in THF, water, and 6 N HCl[78] for five hours. The solvents were removed on a rotary evaporator. At this stage, the residue should be the monoacetate of D-gulose or D-idose. The residue was taken up in acetic anhydride, cooled to 0 °C, and treated with one drop of 70% perchloric acid. After workup and chromatography, the pentaacetate **71** (Table 1) was isolated in quantitative yield. A comparison of proton and carbon-13 NMR spectra with those of authentic samples of the pentaacetates of D-gulopyranose and D-idopyranose revealed **71** to be penta-O-acetyl-D-gulopyranose (**72**). Both synthetic and authentic samples of the pentaacetyl gulopyranoses were



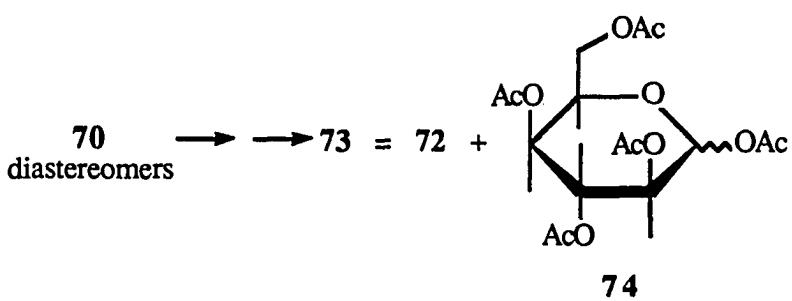
72

mixtures of two compounds, which could be both α and β anomers. Another sample of **68** was irradiated. Without separation of diastereomers, the product was hydrolyzed and acetylated as before to give the pentaacetate mixture **73** (Table 1). A comparison with proton

Table 1. ^{13}C-NMR Data for Pentaacetylpyranoses

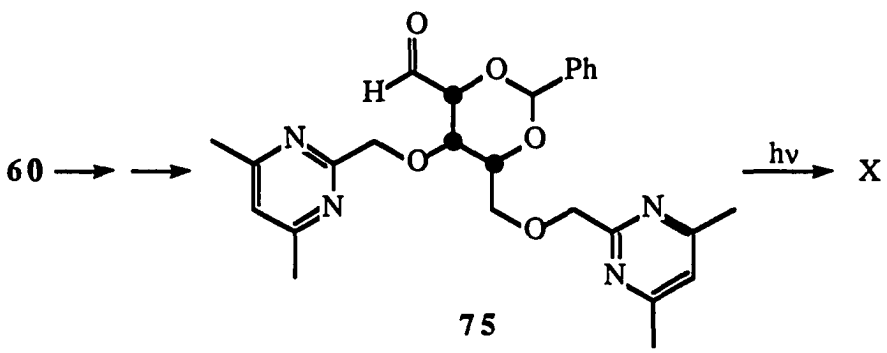
Compound		C-1	C-2 - C-5				
D-Gulo	major	89.86	71.30	67.46	67.28	67.20	61.46
	minor	88.64	67.62	65.76	65.58	64.62	61.60
D-Ido		90.63	66.75	66.35	66.30	66.20	61.76
71	major	89.90	71.34	67.52	67.33	67.26	61.50
	minor	88.68	67.66	65.81	65.65	64.68	61.63
73		89.90	71.34	67.52	67.32	67.27	61.50
		90.63	66.75	66.35	66.30	66.19	61.76

and carbon-13 NMR spectra with those of the authentic samples revealed the presence of both **72** and penta-O-acetyl-D-idopyranose (**74**). The synthetic and authentic samples of **74** were each one major compound. We have developed a method of converting a five-carbon sugar into a six-carbon sugar using the Norrish Type II reaction.



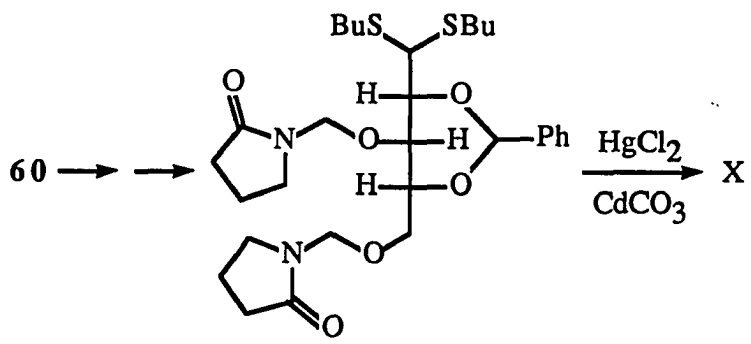
74

Next we decided to functionalize compound **60** with nitrogen-containing side chains. This extension of the project would allow us to make compounds resembling nucleosides (purine or pyrimidine glycosides). Treatment of the dianion of **60** with two equivalents of 2-chloromethyl-4,6-dimethylpyrimidine[79] afforded the dialkylated product in 67% yield. Deprotection of the aldehyde ($HgCl_2$, $CdCO_3$, acetone, water) and purification gave **75** in 61% yield. Photolysis of **75** for 80 minutes led to decomposition of the material. We think that an electron transfer process was involved.



75

The next compound we made was **76**. A side chain was needed that was less likely to engage in electron transfer chemistry. Alkylation of the dianion of **60** with two equivalents of N-chloromethyl-2-pyrrolidinone[80] gave a 47% yield of a mixture of monoalkylated products



76

and a 32% yield of product **76**. The thioacetal hydrolysis conditions ($HgCl_2$, $CdCO_3$, acetone, H_2O) led to decomposition.

The synthesis of sugar derivatives via Norrish Type II chemistry was successful. Unfortunately, we could not prepare nucleosides. We have presented preparations of diastereomeric mixtures of three sugar derivatives, one of which led to effective syntheses of D-gulose and D-idose.

IV. CONCLUSION

The Norrish Type II reaction has proven to be an effective means of synthesizing tetrahydrofuranols and dihydrobenzofuranols from β-alkoxy ketones.

Highlights of the strategy are the synthesis of **5** in only six steps from 1,3-dihydroxy-benzene. This bodes well for a direct photochemical entry into the aflatoxin family. Another highlight is the synthesis of sugar derivatives containing a tetrahydrofuranol moiety from a readily-available aldose. The usefulness of this strategy is demonstrated in the direct synthesis of a mixture of **71** and **73** in six steps from D-xylose.

Syntheses of pyrrolizidine and indolizidine alkaloids by ultraviolet irradiation of nitrogenous ketones demands more study.

Use of the Norrish Type II photocyclization will allow for the rapid formation of natural products containing di- and tetrahydrofuranol moieties.

V. EXPERIMENTAL

Unless otherwise noted, materials were obtained from commercial suppliers and were used without purification. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. N,N-Dimethylformamide (DMF) was dried by azeotropic distillation with benzene, followed by vacuum distillation. Benzene was distilled from lithium aluminum hydride. Dichloromethane (CH_2Cl_2), 1,2-dimethoxyethane, (DME), and acetonitrile were distilled from calcium hydride. All reactions were conducted under an argon atmosphere, and all extracts were dried over anhydrous sodium sulfate. Apparatus for experiments requiring anhydrous conditions were flame-dried under a stream of argon or were dried in a 150 ^{o}C oven for 12 h. Flash chromatography was performed on Kieselgel 60, mesh 230-400. Infrared spectra were obtained on a Perkin-Elmer 1320 spectrophotometer and are reported in cm^{-1}. Proton nuclear magnetic resonance spectra (300 MHz) were obtained using a Nicolet Magnetics Corporation NMC-1280 spectrometer. All chemical shifts are reported in δ relative to tetramethylsilane as an internal standard. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and ABq (AB quartet); addition of br indicates a broadened pattern. Carbon-13 NMR spectra (75 MHz) were obtained on a Nicolet NMC-1280 spectrometer and are reported in δ relative to $CDCl_3$ (77.0 ppm). Ultraviolet spectra were obtained on a Perkin-Elmer 320 UV-Vis spectrophotometer. High resolution mass spectra were recorded on a Kratos model MS-50 spectrometer. Low resolution mass spectra were recorded on a Finnegan 4023 mass spectrometer. The purity of all title compounds was judged to be $\geq$ 90% by ^{1}H NMR spectral determinations.

General Procedure for Photolyses of Carbonyl Compounds. A solution of the carbonyl compound in solvent (0.01 - 0.05 M) was charged into a tube (quartz, Pyrex).

The tube was sealed with a rubber septum, and the solution was degassed by bubbling argon through it (argon passed through Drierite) for 15-30 min. The solution was irradiated with a Hanovia 450 watt medium-pressure mercury lamp placed in a water-cooled quartz jacket. The solvent was removed in vacuo. The product was purified by silica gel chromatography to afford the pure product.

Ethyl 2,6-bis[(methoxymethyl)oxy]-α-oxobenzeneacetate (7). To a 0 °C solution of **6** (6.93 g, 35.0 mmol) in 50 mL of ether was added 16.0 mL (38.6 mmol) of a 2.41 M solution of *n*-butyllithium in hexane. The solution was heated to reflux for two days. The reaction mixture was cooled to -78 °C. Ethyl oxalyl chloride was added rapidly with rapid stirring and was stirred for 4 h. The solution was quenched at -78 °C with saturated aqueous NH_4Cl, poured into water, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water and with brine, dried, and concentrated. The crude product was purified by flash chromatography with 3:1 hexanes-ethyl acetate (3:1 H:EA) to afford 5.25 g of glyoxalate **7** (50% yield).: R_f 0.22 (3:1 H:EA); ^1H NMR ($CDCl_3$) δ 1.37 (t, J=7 Hz, 3H), 3.45 (s, 6H), 4.35 (q, J=7.1 Hz, 2H), 5.16 (s, 4H), 6.84 (d, J=8.4 Hz, 1H), 7.36 (t, J=8.4 Hz, 2H). Yellow oil.

Ethyl 2,6-dimethoxy-α-oxobenzenepropanoate (8). To a solution of $SnCl_2 \cdot 2H_2O$ (0.19 g, 0.84 mmol) and ethyl diazoacetate (0.23 g, 2.0 mmol) in 5 mL of CH_2Cl_2 (green solution) was added 0.5 mL of a solution of 2,6-dimethoxybenzaldehyde (0.29 g, 1.7 mmol) in 3 mL CH_2Cl_2. When N_2 evolution started, the remaining aldehyde solution was added dropwise over 10 min. The reaction mixture was still green, and the reaction was incomplete by TLC. Another 0.20 g (0.89 mmol) of $SnCl_2 \cdot 2H_2O$ was added and caused more N_2 evolution. The solution was stirred for 10 min. The reaction mixture was poured into brine and extracted with ethyl acetate. The combined organic layers were

concentrated, diluted with ether, washed with 10% KF, filtered, dried, and concentrated. The crude product was purified by flash chromatography with 2:1 hexanes-ethyl acetate to afford 0.24 g of ketoester **8** (54% yield).: R_f 0.33 (2:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, J=7.2 Hz, 3H), 3.81 (s, 6H), 4.16 (q, J=7.2 Hz, 2H), 6.55 (d, J=8.4 Hz, 1H), 7.29 (t, J=8.4 Hz, 2H); IR (film) 2980, 1740, 1705, 1590, 1470. Yellow oil.

Ethyl 4-methoxy-3-benzofuranacetate (9).: R_f 0.16 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J=7.2 Hz, 3H), 3.84 (d, J=0.9 Hz, 2H), 3.87 (s, 3H), 4.20 (q, J=7.2 Hz, 2H), 6.61 (d, J=8.1 Hz, 1H), 7.08 (d, J=8.4 Hz, 1H), 7.18 (t, J=8.1 Hz, 1H), 7.48 (d, J=0.9 Hz, 1H). Colorless oil.

2,6-Bis[(methoxymethyl)oxy]benzaldehyde (10). To a solution of **6** (3.20 g, 16.1 mmol) in 20 mL ether was added 7.7 mL (19.2 mmol) of a 2.50 M solution of *n*-butyl-lithium in hexane dropwise over 10 min. The reaction mixture was heated to reflux for 1 h, and was cooled to room temperature. DMF was added dropwise. The solution was stirred for 30 min. The reaction mixture was poured into water, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed sequentially with saturated NH_4Cl(aq), 1N NaOH(aq), water, and brine, were dried and concentrated. The crude product was purified by flash column chromatography with 3:2 hexanes-ethyl acetate to afford 2.65 g of aldehyde **10** (72.6% yield).: R_f 0.20 (3:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.51 (s, 6H), 5.27 (s, 4H), 6.84 (d, J=8.4 Hz, 2H), 7.40 (t, J=8.4 Hz, 1H),10.54 (s, 1H). Yellow solid.

Ethyl 2,6-bis[(methoxymethyl)oxy]-β-diazo-α-hydroxybenzenepropanoate (11). To a -78 °C solution of **10** (0.23 g, 1.0 mmol) and ethyl diazoacetate (0.12 g, 1.0 mmol) in 2.5 mL THF was added a 0 °C solution of LDA (1.2 mmol) in THF dropwise over 5 minutes. The reaction mixture was stirred for 30 minutes. A solution of acetic acid (0.2

mL, 3.5 mmol) in 1 mL of ether was added, and the reaction mixture was warmed to room temperature. The resulting solution was poured into water, and the aqueous layer was extracted with ether. The combined organic layers were washed with saturated $NaHCO_3$(aq), water, and brine, dried, and concentrated. The crude product was purified by a 6" Florisil column with 3:1 hexanes-ethyl acetate to afford 0.30 g of ester **11** (85% yield).: R_f 0.25 (2:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J=6.9 Hz, 3H), 3.50 (s, 6H), 4.12 (d, J=10.2 Hz, 1H), 4.21-4.32 (m, 1H), 5.22 (s, 4H), 6.31 (d, J=10.8 Hz, 1H), 6.85 (d, J=8.4 Hz, 2H), 7.20 (t, J=8.4 Hz, 1H); IR (film) 3490, 2950, 2100, 1690, 1600, 1470. Yellow oil.

Ethyl 2,6-bis[(methoxymethyl)oxy]-α-oxobenzenepropanoate (12). To a solution of **11** (0.17 g, 0.50 mmol) in 2 mL of DME was added rhodium(II) acetate (2 mg, 0.004 mmol) at ambient temperature. The reaction mixture was stirred for 30 minutes and concentrated. The crude product was purified by flash column chromatography with 2:1 hexanes-ethyl acetate to afford 0.15 g of ketoester **12** (96% yield).: R_f 0.31 (2:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, J=7.2 Hz, 3H), 3.47 (s, 6H), 3.84 (s, 2H), 4.16 (q, J=7.2 Hz, 2H), 5.17 (s, 4H), 6.81 (d, J=8.4 Hz, 2H), 7.25 (t, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.92, 50.99, 56.16, 60.89, 94.54, 108.19, 120.74, 131.30, 154.42, 166.74, 195.23; IR (film) 2940, 1740, 1710, 1590, 1470; UV-Vis (CH_2Cl_2) λmax 218, 254. Colorless oil.

3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]propanal (15). To a -78 °C solution of oxalyl chloride (3.5 mL, 40 mmol) in 140 mL of CH_2Cl_2 was added a solution of DMSO (5.7 mL, 80 mmol) in 10 mL CH_2Cl_2. The solution was stirred 2 - 5 min. To the resulting solution, a solution of **14** (7.00 g, 36.8 mmol) in 15 mL CH_2Cl_2 was added, and the reaction mixture was stirred for 25 min. Triethylamine (25 mL, 179 mmol) was added, and the solution was stirred 5 min. The reaction mixture was warmed to room temperature

and poured into water, and 1N HCl was added to neutralize the layers. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water and with brine, dried, and concentrated. Distillation at reduced pressure (75 °C / 1 mm Hg) afforded 5.76 g of aldehyde **15** (83% yield).: R_f 0.53 (4:1 H:EA); ^1H NMR ($CDCl_3$) δ 0.07 (s, 6H), 0.89 (s, 9H), 2.60 (dt, J=2.1, 6.0 Hz, 2H), 3.99 (t, J=6.0 Hz, 2H), 9.80 (t, J=2.1 Hz, 1H); IR (film) 2940, 2720, 1725, 1250, 1100. Colorless oil.

1,3-Bis[(methoxymethyl)oxy]-2-[3-[(1,1-dimethylethyl)dimethylsilyl]-oxy-1-hydroxypropyl]benzene (16). To a solution of **6** (3.99 g, 20.1 mmol) in 40 mL ether was added 8.10 mL (20 mmol) of a 2.50 M solution of *n*-butyllithium in hexane. The resulting solution was heated to reflux for 1 h. The reaction mixture was cooled to 0 °C, and **15** (3.79 g, 20.1 mmol) was added dropwise. The solution was stirred for 45 min. and was poured into water and 1N HCl to neutralize the layers. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with water and with brine, dried, and concentrated. The crude product was purified by flash column chromatography with 4:1 hexanes-ethyl acetate to afford 5.33 g of **16** (69% yield).: R_f 0.31 (3:1 H:EA); ^1H NMR ($CDCl_3$) δ 0.06 (s, 3H), 0.07 (s, 3H), 0.91 (s, 9H), 1.85-1.96 (m, 1H), 2.12-2.23 (m, 1H), 3.48 (s, 6H), 3.79-3.84 (m, 2H), 5.20 (s, 2H), 5.21 (s, 2H), 5.35 (dd, J=3.9, 9.3 Hz, 1H), 6.79 (d, J=8.4 Hz, 2H), 7.12 (t, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -5.37, 18.19, 25.83, 40.47, 56.13, 60.25, 64.78, 94.31, 94.42, 108.12, 121.38, 128.24, 155.26; IR (film) 3560, 2940, 1595, 1470, 1150. Yellow oil.

3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-1-[2,6-bis[(methoxymethyl)-oxy]]phenyl-1-propanone (17). To a suspension of activated MnO_2 (27.1 g) in 100 mL of ether was added **16** (2.71 g, 7.01 mmol). The reaction mixture was stirred 17 h, filtered through Celite, and concentrated. The crude material was purified by flash column

chromatography with 5:1 hexanes-ethyl acetate to afford 2.11 g of ketone **17** (78% yield).: R_f 0.41 (3:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 0.069 (s, 6H), 0.88 (s, 9H), 3.04 (t, J=6.9 Hz, 2H), 3.45 (s, 6H), 4.02 (t, J=6.9 Hz, 2H), 5.14 (s, 4H), 6.80 (d, J=8.4 Hz, 2H), 7.21 (t, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -5.43, 18.20, 25.81, 47.95, 56.12, 57.97, 94.45, 108.18, 122.28, 130.44, 154.07, 202.42; IR (film) 2940, 1705, 1595, 1465, 1040; MS m/e 353, 327, 295, 251, 221, 161.

1-[2,6-Bis[(methoxymethyl)oxy]]phenyl-3-hydroxy-1-propanone (3). To a solution of triethylammonium fluoride (0.49 g, 4.0 mmol) in 2 mL of THF was added a solution of **17** (0.50 g, 1.3 mmol) in 2 mL of THF. The solution was heated to 70 - 75 °C for 5 h. The resulting solution was diluted with ether, washed with water and with brine, dried, and concentrated. The crude material was purified by flash column chromatography with 1:2 hexanes-ethyl acetate to afford 0.19 g of the ketone **3** (54% yield).: R_f 0.17 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.05 (t, J=5.4 Hz, 2H), 3.46 (s, 6H), 3.98 (q, J=5.4 Hz, 2H), 5.16 (s, 4H), 6.81 (d, J=8.4 Hz, 2H), 7.24 (t, J=8.4 Hz, 1H); IR (film) 3470, 2920, 1700, 1595, 1465; UV-Vis (CH_2Cl_2) λmax 232, 250, 270; MS m/e calcd for $C_{13}H_{18}O_6$: 270.110344, found 270.1101; 225, 194, 177, 164, 136, 122. Colorless oil.

2,3-Dihydro-3-hydroxy-3-(2-hydroxyethyl)-2-methoxy-4-(methoxy-methyl)oxybenzofuran (5).: R_f 0.20 (1:5 H:EA); ^{1}H NMR ($CDCl_3$) δ 2.03-2.11 (m, 1H), 2.35-2.43 (m, 1H), 2.66 (t, J=5.8 Hz, 1H, exchangeable by D_2O), 3.51 (s, 3H), 3.63 (s, 3H), 3.78-3.96 (m, 2H), 5.21 (s, 1H), 5.22 and 5.27 (ABq, J=6.6 Hz, 2H), 6.51 (d, J=8.4 Hz, 1H), 6.71 (d, J=8.4 Hz, 1H), 7.15 (t, J=8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 39.25, 56.25, 56.72, 59.24, 81.35, 94.19, 104.66, 107.79, 108.73, 117.55, 130.99, 154.91, 158.13; IR ($CDCl_3$) 3540, 2940, 1605, 1480, 1250, 1150, 1040; MS m/e calcd for

$C_{13}H_{18}O_6$: 270.11034, found 270.1095; 252, 220, 208, 190, 177, 163, 147, 121. Colorless oil.

4,6-Dichloro-1,3-dihydroxybenzene (19). To a solution of 1,3-dihydroxybenzene (3.30 g, 30.0 mmol) in 30 mL of ether in a 100 mL flask equipped with a reflux condenser, $CaCl_2$ drying tube, and NaOH(aq) trap was added sulfuryl chloride (2.5 mL, 31 mmol). The solution was heated to reflux for 1 h. HCl gas in the resulting solution was removed under aspirator pressure for 5 min., and the solution was concentrated in vacuo. The crude product was the monochlorinated benzene. The above procedure was repeated with the monochlorinated product. After concentration in vacuo the crude product was purified by flash column chromatography with 3:2 hexanes-ethyl acetate to afford 5.37 g of **19** (100% yield).: mp 110-112 °C (sublimes); R_f 0.27 (2:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 5.64 (s, 2H), 6.71 (s, 1H), 7.28 (s, 1H). White solid.

1,3-Bis[(methoxymethyl)oxy]-4,6-dichlorobenzene (20). To a 0 °C suspension of hexane-washed NaH (0.88 g, 36.8 mmol) in 15 ml of DMF was added a solution of **19** (3.00 g, 16.8 mmol) in 15 mL of DMF. The reaction mixture was stirred for 1 h at room temperature and then was cooled to 0 °C. Freshly distilled chloromethyl methyl ether (2.8 mL, 36.9 mmol) was added dropwise, and the resulting solution was warmed to room temperature over 14 h. The reaction mixture was poured into water, and the aqueous layer was extracted with benzene. The combined organic layers were washed sequentially with 1N NaOH, water, and brine, and then were dried and concentrated. Purification by flash column chromatography with 5:1 hexanes-ethyl acetate afforded 3.77 g of **20** (84% yield).: mp 58-60 °C; R_f 0.40 (2:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.52 (s, 6H), 5.22 (s, 4H), 7.06 (s, 1H), 7.37 (s, 1H). White solid.

1-[2,6-Bis[(methoxymethyl)oxy]-4,6-dichloro]phenyl-1-ethanone (21). To a 0 °C solution of **20** (0.13 g, 0.49 mmol) in 2 mL of ether was added a 2.52 M solution of *n*-butyllithium (0.29 mL, 0.73 mmol) in hexane, and the reaction mixture was stirred for 1 h. Freshly distilled acetaldehyde (0.10 mL, 1.8 mmol) was added with a syringe cooled by dry ice, and the reaction was warmed to room temperature. The resulting solution was stirred 2 h and then was poured into 1N HCl and water to neutralize the layers. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried, and concentrated. The crude product was purified by flash column chromatography with 3:1 hexanes-ethyl acetate to afford 90 mg of the carbinol (59% yield). A solution of the carbinol (90 mg, 0.3 mmol) in 4 mL of ether was added to a suspension of activated MnO_2 (0.90 g) in 5 mL of ether, and the reaction mixture was stirred for 5 h. The reaction mixture was filtered through Celite and concentrated. Purification by flash column chromatography afforded 0.06 g of **21** (70% yield).: R_f 0.41 (3:1 H:EA); ^1H NMR ($CDCl_3$) δ 2.56 (s, 3H), 3.52 (s, 6H), 5.05 (s, 4H), 7.47 (s, 1H). Colorless oil.

3-(Methoxymethyl)oxy-1-propanal (22). To a 0 °C suspension of hexane-washed NaH (1.21 g, 50.2 mmol) in 100 mL of THF was added 1,3-propanediol (3.80 g, 49.9 mmol). The reaction mixture was warmed to room temperature and stirred 50 min. Freshly distilled chloromethyl methyl ether (3.6 mL, 47 mmol) was added rapidly, and the solution was stirred 14 h. The resulting mixture was poured into a solution of NH_4Cl(aq) and water. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, and concentrated. The crude product was purified by flash column chromatography with ether to afford 2.92 g of the monohydroxy compound (51% yield). To 50 mL of CH_2Cl_2 was added Florisil (9.6 g) and PCC (4.80 g, 22.3 mmol) and the mixture was stirred for 1 h. To this mixture was added a solution of the monohydroxy compound

(1.34 g, 11.2 mmol) in 10 mL of CH_2Cl_2, and the resulting mixture was stirred for 2 h. The reaction mixture was diluted with 50 mL of ether and was filtered through Celite with a 100 mL ether rinse. The filtrate was concentrated and was purified by flash column chromatography with 1:1 ether-hexanes to afford 0.83 g of **22** (63% yield).: R_f 0.38 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 2.70 (dt, J=1.8, 6.0 Hz, 2H), 3.36 (s, 3H), 3.89 (t, J=6.0 Hz, 2H), 4.63 (s, 2H), 9.81 (t, J=1.8 Hz, 1H).

1-[2,6-Bis[(methoxymethyl)oxy]]phenyl-3-(methoxymethyl)oxy-1-propanone (23). Compound **6** (0.35 g, 1.8 mmol) was lithiated as before. To the 0 °C solution of lithiated **6** in 5 mL of ether was added a solution of aldehyde **22** (0.22 g, 1.9 mmol) in 1 mL of ether. The resulting solution was stirred 15 min. and then was poured into saturated NH_4Cl(aq) and water. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried, and concentrated. Purification by flash column chromatography afforded 0.30 g of the carbinol (51% yield). To a suspension of activated MnO_2 (3.5 g) in 30 mL of ether was added the carbinol (0.30 g, 0.95 mmol). The mixture was stirred for 5 h. The resulting mixture was filtered through Celite, and concentrated. Purification by flash column chromatography with 2:1 hexanes-ethyl acetate afforded 0.14 g of ketone **23** (47% yield).: R_f 0.42 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.10 (t, J=6.6 Hz, 2H), 3.36 (s, 3H), 3.45 (s, 6H), 3.92 (t, J=6.6 Hz, 2H), 4.63 (s, 2H), 5.15 (s, 4H), 6.80 (d, J=8.7 Hz, 2H), 7.22 (t, J=8.7 Hz, 1H). Colorless oil.

2,3-Dihydro-3-(3,5-dioxahexyl)-3-hydroxy-2-methoxy-4-(methoxy-methyl)oxybenzofuran (25).: R_f 0.31 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 2.15-2.25 (m, 1H), 2.44-2.52 (m, 1H), 3.32 (s, 3H), 3.48 (s, 3H), 3.64 (s, 3H), 3.70-3.81 (m, 2H), 4.62 (s, 2H), 5.21 (s, 2H), 5.40 (s, 1H), 6.49 (d, J=8.1 Hz, 1H), 6.68 (d, J=8.1 Hz, 1H), 7.14 (t, J=8.1 Hz, 1H).

3-(Methoxymethyl)oxy-1-(2,4,6-trimethoxy)phenyl-1-propanone (27). To a solution of **26** (0.25 g, 1.5 mmol) in 3 mL of ether was added a 2.47 M solution *n*-butyllithium (0.63 mL, 1.6 mmol), and the resulting mixture was heated to reflux for 1h. The reaction mixture was cooled to 0 °C, and a solution of **22** (0.18 g, 1.5 mmol) in 3 mL of ether was added dropwise. The solution was stirred 1 h. The reaction was poured into 1:1 saturated NH_4Cl(aq):H_2O. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried, and concentrated. The crude product was purified by flash column chromatography with 1:1 hexanes-ethyl acetate to afford 0.15 g of the carbinol (35% yield). To a suspension of activated MnO_2 (1.80 g) in 10 mL of ether was added the carbinol (0.15 g, 0.52 mmol). The mixture was stirred for 23 h. The mixture was filtered through Celite, and the Celite was rinsed with 25 mL of ether. The filtrate was concentrated and purified by flash column chromatography with 2:1 hexanes-ethyl acetate to afford 73 mg of ketone **27** (49% yield).: ^{1}H NMR ($CDCl_3$) δ 3.07 (t, J=6.6 Hz, 2H), 3.35 (s, 3H), 3.78 (s, 6H), 3.82 (s, 3H), 3.87 (t, J=6.6 Hz, 2H), 4.62 (s, 2H), 6.10 (s, 2H).

4,6-Dimethoxy-3-(3,5-dioxahexyl)benzofuran (28).: ^{1}H NMR ($CDCl_3$) δ 3.03 (dt, J=0.9, 6.9 Hz, 2H), 3.34 (s, 3H), 3.82 (t, J=6.9 Hz, 2H), 3.83 (s, 3H), 3.87 (s, 3H), 4.65 (s, 2H), 6.28 (d, J=2.1 Hz, 1H), 6.59 (d, J=2.1 Hz, 1H), 7.27 (t, J=0.9 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 25.49, 55.11, 55.32, 55.71, 67.51, 88.21, 93.87, 96.35, 118.99, 139.58, 139.62, 154.65, 157.27, 159.95.

1-(3-Diethoxypropyl)-2-piperidinone (32). To a suspension of powdered KOH (dried by heating in vacuo) (3.08 g, 54.9 mmol) and tetra-*n*-butylammonium bromide (3.22 g, 10 mmol) in 50 mL of THF was added a solution of δ-valerolactam (4.95 g, 50 mmol) and 3-chloropropionaldehyde diethyl acetal (8.4 mL, 50 mmol) in 30 mL of THF dropwise over 1 h with rapid stirring. The reaction mixture was heated to reflux for 3 h. The cooled mixture

was filtered, concentrated, and diluted with CH_2Cl_2. The organic solution was washed with water and with brine, dried, and concentrated. Flash column chromatography with 5:1 ethyl acetate-acetone afforded 6.17 g of lactam **32** (54% yield).: R_f 0.33 (5:1 EA: acetone); ^1H NMR ($CDCl_3$) δ 1.20 (t, J=7.2 Hz, 6H), 1.78 (m, 4H), 1.88 (m, 2H), 2.36 (br t, J=5.2 Hz, 2H), 3.28 (br t, J=5.8 Hz, 2H), 3.41 (t, J=7.5 Hz, 2H), 3.49 (q, J=7.2 Hz, 1H), 3.52 (q, J=7.2 Hz, 1H), 3.64 (q, J=7.2 Hz, 1H), 3.68 (q, J=7.2 Hz, 1H), 4.54 (t, J=5.7 Hz, 1H). Colorless oil.

3-(2-Oxopiperidino)propanal (33). To a solution of acetone (16 mL), water (5 mL) and 10% H_2SO_4 (0.5 mL) was added **32** (2.69 g, 11.7 mmol), and the resulting solution was stirred for 4 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried, and concentrated. Purification by Florisil chromatography (27 g Florisil) with ethyl acetate afforded 0.75 g of aldehyde **33** (41% yield).: R_f 0.33 (1:1 EA: acetone); ^1H NMR ($CDCl_3$) δ 1.78 (m, 4H), 2.35 (t, J=5.8 Hz, 2H), 2.77 (dt, J=1.5, 6.4 Hz, 2H), 3.34 (m, 2H), 3.64 (t, J=6.4 Hz, 2H), 9.80 (t, J=1.5 Hz, 1H); IR (film) 2940, 2720, 1720, 1640, 1490, 1350; MS m/e 55, 84, 98, 112, 127, 155. Colorless oil.

4-Piperidino-2-butanone (34). To MVK (2.55 mL, 30.6 mmol) at 0 °C was added piperidine (distilled over CaH_2) (3.0 mL, 30.3 mmol) with stirring. The reaction mixture was warmed slowly to room temperature. The crude product was distilled twice at reduced pressure (90 °C / 12.5 mm Hg) to afford 4.03 g of ketone **34** (85.6% yield).: ^1H NMR ($CDCl_3$) δ 1.43 (m, 2H), 1.57 (m, 4H), 2.17 (s, 3H), 2.37 (br t, J=4.5 Hz, 4H), 2.62 (t, J=2.6 Hz, 4H); IR (film) 2930, 1715, 1355, 1155, 1120. Colorless oil.

1-Methyl-2-piperidino-1-cyclopropanol (35).: R_f 0.30 (EA); ^1H NMR ($CDCl_3$) δ 0.35 (dd, J=4.2, 6.6 Hz, 1H), 0.55 (dd, J=6.6, 7.6 Hz, 1H), 1.37 (s, 3H), 1.44-1.57 (m, 6H), 2.53 (br s, 4H); ^{13}C NMR ($CDCl_3$) δ 19.02, 22.39, 23.82, 25.43, 47.12, 54.07, 54.21; IR ($CDCl_3$) 3400, 2940, 1335, 1270. Colorless oil.

4-(1,2,3,6-tetrahydropyridino)-2-butanone (36). To MVK (2.3 mL, 27.6 mmol) at 0 °C was added 1,2,3,6-tetrahydropyridine (2.5 mL, 27.4 mmol) with stirring. The reaction mixture was warmed slowly to room temperature. The crude product was distilled at reduced pressure (88 °C / 12 mm Hg) to afford 3.58 g of ketone **36** (85% yield).: ^1H NMR ($CDCl_3$) δ 2.18 (m, 5H), 2.56 (t, J=5.3 Hz, 2H), 2.69 and 2.71 (ABq, J=4.5 Hz, 4H), 2.96 (quintet, J=2.7 Hz, 2H), 5.62-5.68 (m, 1H), 5.71-5.78 (m, 1H); IR (film) 2900, 2800, 1715, 1360, 1135. Colorless oil.

Methyl N-(3-oxobutyl)-L-(-)-proline (39). To a -10 °C solution of L-(-)-proline in absolute methanol was added thionyl chloride dropwise. The solution was warmed to room temperature and stirred 2.5 h. Solvent was removed in vacuo to afford crude **38** as a viscous oil. To a solution of crude **38** (0.73 g, 4 mmol) in 10 mL of CH_2Cl_2 was added triethyl-amine (1.45 mL, 10.4 mmol). The solution was filtered and concentrated to a white, wet solid. The solid was dissolved in 10 mL of CH_2Cl_2 and cooled to 0 °C. MVK was added to the solution, and the resulting solution was slowly warmed to room temperature over 14 h. The reaction mixture was poured into water, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried, and concentrated. The crude product was purified by flash column chromatography in ethyl acetate to afford 0.55 g of **39** (63% yield).: R_f 0.30 (EA); ^1H NMR ($CDCl_3$) δ 1.78-1.96 (m, 2H), 2.07-2.16 (m, 2H), 2.18 (s, 3H), 2.34 (q, J=8.2 Hz, 2H), 2.63-2.75 (m, 2H), 2.99-3.10

(m, 1H), 3.14-3.20 (m, 2H), 3.72 (s, 3H); IR (film) 2950, 2820, 1740, 1720, 1360, 1170. Clear oil with green tint.

Methyl N-(2-hydroxy-2-methylcyclopropyl)-L-(-)-proline (40).: R_f 0.51 (EA); ^1H NMR ($CDCl_3$) δ 0.50-0.89 (m, 2H), 1.30 and 1.35 (s, 3H), 1.77-2.00 (m, 4H), 2.17-2.24 (m, 2H), 2.62 and 2.74 (m, 1H), 3.13-3.23 (m, 1H), 3.38 and 3.59 (m, 1H),3.70 and 3.74 (s, 3H); IR (film) 3430, 2950, 1735, 1440, 1200.

4-(3-Pyrrolino)-4-oxo-1-butanal (42). A solution of γ-butyrolactone (1.40 mL, 18.2 mmol) and 3-pyrroline (1.52 mL, 20.0 mmol) in 15 mL of THF was heated to reflux for 5 h. The resulting solution was poured into brine and water. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried and concentrated to yield 2.32 g of crude lactam **41**.

To a -78 °C solution of oxalyl chloride (0.32 mL,3.7 mmol) in 8 mL CH_2Cl_2 was added a solution of DMSO (0.51 mL, 7.2 mmol) in 3 mL of CH_2Cl_2. The solution was stirred 2 - 5 min., and a solution of crude lactam **41** (0.51 g, 3 mmol) in 3 mL of CH_2Cl_2 was added dropwise. The reaction mixture was stirred 30 min. Triethylamine (2.3 mL, 16 mmol) was added dropwise, and the resulting mixture was stirred for 45 min. before warming to room temperature. The resulting solution was poured into water and 1N HCl to neutralize the layers. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with water and with brine, dried and concentrated. Purification by flash column chromatography with ethyl acetate afforded 0.16 g of aldehyde **42** (32% yield).: R_f 0.24 (EA); ^1H NMR ($CDCl_3$) δ 2.59 (t, J=6.6 Hz, 2H), 2.88 (t, J=6.6 Hz, 2H), 4.23-4.24 (m, 2H), 4.27-4.30 (m, 2H), 5.81 and 5.88 (ABqt, J=2.1, 6.6 Hz, 2H), 9.87 (s, 1H); IR (film) 2850, 2720, 1715, 1640, 1620, 1440.

3-(1,2,3,6-Tetrahydropyridino)cyclohexan-1-one (46). 1,2,3,6-Tetrahydropyridine (2.3 mL, 25 mmol) was added dropwise to distilled cyclohexenone (2.4 mL, 25 mmol) with stirring. The reaction mixture was stirred for 7 h. Distillation at reduced pressure (105 °C / 1 mm Hg) afforded 3.50 g of ketone **46** (78.7% yield).: ^{1}H NMR ($CDCl_3$) δ 1.52-1.78 (m, 2H), 2.03-2.45 (m, 6H), 2.58-2.72 (m, 4H), 2.75-2.86 (m, 1H), 3.09-3.14 (m, 2H), 5.64-5.78 (m, 2H); IR (film) 3020, 2940, 1710, 1565, 1220, 650. Colorless oil.

***t*-Butyl 5-cyclohexen-1-one-2-acetate (47).** To a -78 °C solution of LDA (23 mmol) in 40 mL of THF was added distilled cyclohexenone dropwise slowly. The solution was stirred for 1 h. To the reaction mixture was added *t*-butyl iodoacetate dropwise rapidly. The solution was stirred 3.5 h. Saturated NH_4Cl(aq) (50 mL) was added to the reaction mixture, and the reaction flask was warmed to room temperature. The quenched reaction mixture was poured into water. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with water and with brine, dried, and concentrated. Purification by flash column chromatography afforded 3.44 g of **47** (79% yield).: R_f 0.30 (3:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 9H), 1.74-1.88 (m, 1H), 2.19 (q, J=8.8 Hz, 2H), 2.40-2.47 (m, 2H), 2.76-2.87 (m, 2H), 6.00 and 6.03 (dd, J=1.4, 2.6 Hz, 1H), 6.92-6.98 (m, 1H).

***t*-Butyl 5-piperidinocyclohexan-1-one-2-acetate (48).** To neat ketoester **47** (1.13 g, 5.37 mmol) was added piperidine (distilled over CaH_2) (0.54 mL, 5.5 mmol) with stirring. The mixture was stirred for 12 h. Distillation under reduced pressure (160 °C / 0.035 mm Hg) afforded a mixture of **48** and enone **47** in a 2.3:1 ratio. The calculated yield of **48** was approximately 48%.: ^{1}H NMR ($CDCl_3$) δ 1.44 (s, 9H), 1.50-1.90 (m, 10H), 2.00-2.25 (m, 3H), 2.36-2.50 (m, 2H), 2.52-2.80 (m, 5H). Yellow oil.

4-Pyrrolidino-4-oxo-2-butanone (49). To a 0 °C solution of pyrrolidine (distilled over CaH_2) (1.39 mL, 16.6 mmol) in 30 mL of THF was added diketene (1.28 mL, 16.6 mmol) dropwise. The resulting solution was warmed to room temperature and stirred 1 h. The reaction mixture was concentrated in vacuo and purified by flash column chromatography with ethyl acetate to afford 1.97 g of **49** (76% yield).: R_f 0.23 (EA); ^{1}H NMR ($CDCl_3$) δ 1.86-1.98 (m, 4H), 2.29 (s, 3H), 3.41 (t, J=6.4 Hz, 2H), 3.48-3.51 (m, 5H); IR (film) 2970, 2880, 1720, 1635, 1160. Colorless oil.

4-Aza-1-hydroxy-1-methyl-3-oxobicyclo[3.3.0]octane (50).: R_f 0.16 (4:1 EA/ acetone); ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.41 (s, 3H), 1.50-1.62 (m, 1H), 1.84-1.95 (m, 1H), 1.95-2.07 (m, 2H), 2.41 and 2.45 (d, J=16.2 Hz, 1H), 2.80 and 2.91 (d, J=16.2 Hz, 1H), 2.98-3.12 (m, 1H), 3.52-3.63 (m, 1H), 3.78-3.91 (m, 1H); IR (film) 3370, 2970, 2880, 1670, 1435; MS m/e 155, 112, 70, 58, 43.

***t*-Butyl 4,6-dioxo-6-pyrrolidinohexanoate (51).** To a -78 °C solution of LDA (4.2 mmol) in 7 mL of THF was added **49** (0.31 g, 2.0 mmol) diluted in 3 mL of THF. The solution was warmed to room temperature and stirred for 1 h. The solution was cooled to -78 °C, and *t*-butyl iodoacetate was added slowly dropwise. The solution was warmed to room temperature over 1 h, and was poured into 1N HCl and water to neutralize the layers. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and concentrated. The crude product was purified by flash column chromatography with 5:2 ethyl acetate-acetone to afford 74 mg of **51** (14% yield).: R_f 0.41 (5:2 EA/ acetone); ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 9H), 1.84-1.96 (m, 4H), 2.52 (t, J=6.6 Hz, 2H), 2.82 (t, J=6.6 Hz, 2H), 3.41 (t, J=6.6 Hz, 2H), 3.48 (t, J=6.6 Hz, 2H), 3.52 (s, 2H). Colorless oil.

General Procedure for Diol Alkylation. To a 0 °C suspension of hexane-washed NaH (6.6 mmol) in 3 mL of DMF was added a solution of **60** (3 mmol) in 10 mL of DMF dropwise. The ice bath was removed, and the mixture was stirred 45 min. The reaction mixture was cooled to 0 °C, and the alkylating agent (6.3 mmol) was added neat or as a solution in 3 mL of DMF dropwise slowly. The ice bath was removed, and the reaction solution was stirred 14 h. The resulting solution was poured into water. The aqueous layer was extracted with ethyl acetate, and the combined organic layers were washed twice with water and once with brine, dried with Na_2SO_4, and concentrated in vacuo. The crude product was purified by silica gel chromatography.

General Procedure for Hydrolysis of Thioacetals. To a solution of thioacetal in acetone (0.17 M) and water (0.5 M) was added $CdCO_3$ (excess, ≥2 equiv) and a solution of $HgCl_2$ (3.6 equiv) in acetone (0.4 M). The mixture was stirred 14 h at ambient temperature, was heated to 50 °C for 15 min., and was heated to reflux for 15 min. The resulting mixture was filtered through Celite, and a small amount of fresh $CdCO_3$ was added to the filtrate. The solvents were removed in vacuo. The residue was taken up in $CHCl_3$ and swirled vigorously with Na_2SO_4 for abrasiveness and drying. The resulting solution was filtered through Celite and concentrated. The crude product was purified by either silica gel or Florisil chromatography.

General Procedure for Acetylation of Photolysis Products. To a 0 °C solution of photolysis product in CH_2Cl_2 (0.1 M) was added DMAP (1.5 equiv) and Ac_2O (3 equiv). The ice bath was removed, and the solution was stirred for 1 h. The resulting solution was poured into a 1:1 saturated $NaHCO_3$(aq):water solution. The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over

Na_2SO_4, and concentrated in vacuo. The product was purified by silica gel chromatography.

General Procedure for Hydrolysis and Acetylation of Photolysis Products. A solution of photolysis product in THF (0.1 M), water (0.03 M), and 6N HCl (0.01 M) was heated to 50-55 °C for 5 h. The resulting solution was concentrated in vacuo. To the 0 °C residue was added acetic anhydride (0.01 M) and catalytic 70% $HClO_4$ (one drop), and the solution was stirred 1 h. The resulting solution was poured into water, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$(aq), dried over $MgSO_4$, and concentrated. The crude product was purified by silica gel chromatography.

General Procedure for Preparation of Authentic Pentaacetylpyranoses. To an authentic sugar (5 mg) (Sigma) cooled to 0 °C was added 1 mL of acetic anhydride and 1 drop of 70% $HClO_4$. The solution was stirred for 45 min. The reaction mixture was diluted with ethyl acetate. The resulting solution was poured into water, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated $NaHCO_3$(aq) and with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by silica gel chromatography.

2,4-O-Benzylidene-D-xylose di-*n*-butyl dithioacetal (60).: mp 102-103 °C; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J=7.2 Hz, 3H), 0.93 (t, J=7.2 Hz, 3H), 1.33-1.49 (m, 4H), 1.49-1.66 (m, 4H), 2.65-284 (m, 4H), 3.82 (dd, J=0.9, 9.6 Hz, 1H), 3.86-3.91 (m, 1H), 3.96-4.00 (m, 2H), 4.12-4.16 (m, 2H), 5.64 (s, 1H), 7.34-7.40 (m, 3H), 7.52-7.55 (m, 2H). White solid.

3,5-Di-O-phenylmethyl-2,4-O-benzylidene-D-xylose di-*n*-butyl dithioacetal (61).: R_f 0.35 (9:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 0.85 (t, J=7.5 Hz, 3H), 0.88

(t, J=7.5 Hz, 3H), 1.31-1.45 (m, 4H), 1.45-1.58 (m, 4H), 2.63-2.72 (m, 4H), 3.68 (d, J=6.3 Hz, 2H), 3.81 (dd, J=1.2, 10.5 Hz, 1H), 4.05 (s, 1H), 4.10 (m, 1H), 4.22 (d, J=10.5 Hz, 1H), 4.47-4.56 (m, 2H), 4.77 and 4.86 (ABq, J=11.7 Hz, 2H), 5.61 (s, 1H), 7.28-7.37 (m, 13H), 7.51-7.54 (m, 2H). Colorless oil.

3,5-Di-O-phenylmethyl-2,4-O-benzylidene-D-xylose (63).: mp 109-111 °C; R_f 0.47 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.64-3.75 (m, 2H), 4.03 (t, J=1.8 Hz, 1H), 4.14-4.19 (m, 1H), 4.34 (d, J=1.8 Hz, 1H), 4.48-4.56 (m, 2H), 4.56 (s, 2H), 5.68 (s, 1H), 7.25-7.38 (m, 13H), 7.55-7.58 (m, 2H), 9.68 (s, 1H). White solid.

3,8-Diphenyl-9-hydroxy-5-phenylmethoxymethyl-2,4,7-trioxabicyclo-[4.3.0]nonane (64).: R_f 0.40 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.92-3.98 (m, 2H), 4.32 (dd, J=2.1, 12.3 Hz, 1H), 4.37 (dt, J=1.8, 6.3 Hz, 1H), 4.43 (dd, J=2.1, 4.5 Hz, 1H), 4.58-4.67 (m, 2H), 4.73 (dd, J=4.5, 8.7 Hz, 1H), 5.22 (d, J=8.7 Hz, 1H), 5.63 (s, 1H), 7.27-7.42 (m, 13H), 7.52-7.56 (m, 2H); IR ($CDCl_3$) 3560, 2910, 2880, 1455, 1050; MS m/e calcd for $C_{26}H_{26}O_5$: 418.17802, found 418.17825; 311, 179, 162, 133, 120, 107, 91. Colorless oil.

9-Acetoxy-3,8-diphenyl-5-phenylmethoxymethyl-2,4,7-trioxabicyclo-[4.3.0]nonane (65).: R_f 0.54 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 1.73 (s, 3H), 3.83-3.94 (m, 2H), 3.96 (t, J=1.8 Hz, 1H), 4.39 (dt, J=1.8, 6.2 Hz, 1H), 4.55-4.65 (m, 3H), 5.30 (d, J=8.7 Hz, 1H), 5.53 (dd, J=4.8, 8.7 Hz, 1H), 5.62 (s, 1H), 7.25-7.40 (m, 13H), 7.48-7.53 (m, 2H). Colorless oil.

3,5-Di-O-(2-propenyl)-2,4-O-benzylidene-D-xylose (66).: R_f 0.38 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ 3.69 (t, J=6.3 Hz, 2H), 3.91 (s, 1H), 4.02-4.16 (m, 5H), 4.33 (d, J=2.1 Hz, 1H), 5.14-5.33 (m, 4H), 5.69 (s, 1H), 5.70-5.97 (m, 2H), 7.32-7.40 (m, 3H), 7.51-7.60 (m, 2H), 9.74 (s, 1H). White solid.

8-Ethenyl-9-hydroxy-3-phenyl-5-(2-propenyloxymethyl-2,4,7-trioxabicyclo[4.3.0]nonane (67).: R_f 0.16 (3:2 H:EA); ^1H NMR ($CDCl_3$) δ 3.75-3.89 (m, 2H), 4.04-4.08 (m, 3H), 4.18-4.40 (m, 3H), 4.51-4.63 (m, 1H), 5.16-5.43 (m, 4H), 5.50 and 5.59 (s, 1H), 5.85-6.05 (m, 2H), 7.34-7.40 (m, 3H), 7.45-7.50 (m, 2H). Colorless oil.

3,5-Di-O-methoxymethyl-2,4-O-benzylidene-D-xylose (68).: R_f 0.25 (1:2 H:EA); ^1H NMR ($CDCl_3$) δ 3.36 (s, 3H), 3.38 (s, 3H), 3.74-3.85 (m, 2H), 4.08 (t, J=1.5 Hz, 1H), 4.14 (dq, J=1.5, 6.3 Hz, 1H), 4.37 (d, J=1.8 Hz, 1H), 4.67 (d, J=1.5 Hz, 4H), 5.72 (s, 1H), 7.36-7.40 (m, 3H), 7.55-7.60 (m, 2H), 9.69 (s, 1H). White solid.

9-Hydroxy-8-methoxy-5-[(methoxymethyl)oxy]methyl-3-phenyl-2,4,7-trioxabicyclo[4.3.0]nonane (69).: R_f 0.35 (1:2 H:EA); ^1H NMR ($CDCl_3$) δ 3.37 and 3.38 and 3.39 and 3.43 and 3.51 and 3.55 (s, 6H), 3.82-3.92 (m, 2H), 4.06-4.30 (m, 2H), 4.37-4.44 (m, 1H), 4.67-4.70 (m, 3H), 4.94-5.00 (m, 1H), 5.50 and 5.54 and 5.65 (s, 1H), 7.32-7.38 (m, 3H), 7.46-7.50 (m, 2H). Colorless oil.

9-Acetoxy-8-methoxy-5-[(methoxymethyl)oxy]methyl-3-phenyl-2,4,7-trioxabicyclo[4.3.0]nonane (70).: R_f 0.22 (1:1 H:EA); ^1H NMR ($CDCl_3$) δ 2.16 (s, 3H), 3.38 (s, 3H), 3.48 (s, 3H), 3.81-3.94 (m, 3H), 4.24 (dt, J=2.1, 6.3 Hz, 1H), 4.62 (dd, J=4.2, 3.0 Hz, 1H), 4.68 (s, 2H), 5.02 (dd, J=4.6, 5.7 Hz, 1H), 5.18 (d, J=5.1 Hz, 1H), 5.51 (s, 1H), 7.34-7.37 (m, 3H), 7.50-7.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.88, 55.39, 55.71, 66.58, 70.41, 72.94, 74.21, 75.61, 96.90, 99.55, 100.88, 126.73, 128.18, 128.98, 137.66, 170.73; IR ($CDCl_3$) 2930, 1735, 1370, 1240, 1030; MS m/e calcd for $C_{18}H_{24}O_8$: 368.14712, found 368.14664; 293, 215, 155, 145, 126, 105. Colorless oil.

Penta-O-acetyl-D-gulopyranose (71).: R_f 0.34 (1:1 H:EA); ^1H NMR ($CDCl_3$) δ (acetates are not presented)(relative integrations) 4.07-4.22 (m, 3H), 4.34-4.39 (m, 1H),

4.49-4.54 (m, 0.5 H), 5.00 (dd, J=1.5, 3.9 Hz, 1H), 5.07 (dd, J=1.8, 3.6 Hz, 0.5H), 5.12 (dd, J=3.3, 8.7 Hz, 1H), 5.28 (t, J=3.9 Hz, 0.5H), 5.32 (dd, J=0.60, 3.9 Hz, 0.5H), 5.44 (t, J=3.6 Hz, 1H), 6.00 (d, J=8.7 Hz, 1H), 6.25 (d, J=3.9 Hz, 0.5H). Viscous oil.

Penta-O-acetyl-D-gulopyranose (72).: R_f 0.34 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ (acetates are not presented)(relative integrations) 4.06-4.20 (m, 3H), 4.36 (dt, J=1.5, 6.3 Hz, 1H), 4.48-4.51 (m, 0.5H), 4.99 (dd, J=1.5, 3.9 Hz, 1H), 5.06 (dd, J=1.5, 3.9 Hz, 0.5H), 5.10 (dd, J=3.3, 8.4 Hz, 1H), 5.26 (t, J=3.9 Hz, 0.5H), 5.29-5.32 (m, 0.5H), 5.43 (t, J=3.6 Hz, 1H), 5.99 (d, J=8.4 Hz, 1H), 6.24 (d, J=4.8 Hz, 0.5H). Viscous oil.

Penta-O-acetyl-D-gulopyranose and Penta-O-acetyl-D-idopyranose (73).: R_f 0.34 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ (acetates are not presented)(relative integrations) 4.06-4.26 (m,4H), 4.33-4.38 (m, 1H), 4.44-4.50 (m, 1H), 4.88 (dd, J= 1.8, 3.9 Hz, 1H), 4.92-4.95 (m,1H), 4.99 (dd, J=1.5, 3.9 Hz, 1H), 5.05-5.12 (m, 2H), 5.29-5.32 (m, 1H), 5.43 (t, J=3.9 Hz, 1H), 5.99 (d, J=8.4 Hz, 1H), 6.05-6.08 (m, 1H). Viscous oil.

Penta-O-acetyl-D-idopyranose (74).: R_f 0.34 (1:1 H:EA); ^{1}H NMR ($CDCl_3$) δ (acetates are not presented)(relative integrations) 4.19 (dd, J=1.8, 6.3 Hz, 1H), 4.26 (d, J=6.6 Hz, 1H),4.44-4.49 (m, 1H), 4.87-4.90 (m, 1H), 4.93-4.95 (m, 1H), 5.07 (dt, J=0.60, 3.9 Hz, 1H), 6.05-6.08 (m, 1H). Viscous oil.

3,5-Di-O-(3,5-dimethylpyrimidinomethyl)-2,4-O-benzylidene-D-xylose (75).: R_f 0.25 (1:1 EA: acetone); ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 6H), 2.47 (s, 6H), 3.86-3.94 (m, 2H), 4.05-4.13 (m, 1H), 4.27 (t, J=1.8 Hz, 1H), 4.30-4.36 (m, 1H), 4.75 (s, 2H), 4.79 (s, 2H), 5.70 (s, 1H), 6.88 (s, 1H), 6.91 (s, 1H), 7.35-7.37 (m, 3H), 7.57-7.60 (m, 2H), 9.80 (s, 1H); IR ($CDCl_3$) 2930, 1735, 1590, 1545, 1105. White solid.

3,5-Di-O-(2-oxopyrrolidinomethyl)-2,4-O-benzylidene-D-xylose (76).: R_f 0.13 (1:4 H:EA); ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J=7.2 Hz, 3H), 0.93 (t, J=7.2 Hz, 3H),

1.34-1.48 (m, 4H), 1.50-1.66 (m, 4H), 1.98-2.11 (m, 4H), 2.38-2.45 (m, 4H), 2.63-2.77 (m, 3H), 2.80-2.89 (m, 1H),3.45-3.64 (m, 4H), 3.68-3.82 (m, 3H), 4.02-4.07 (m, 2H), 4.18 (d, J=10.2 Hz, 1H), 4.75 and 4.88 (ABq, J=10.5 Hz, 2H), 4.89 and 5.02 (ABq, J=9.6 Hz, 2H), 5.60 (s, 1H), 7.29-7.35 (m, 3H), 7.50-7.54 (m, 2H). Colorless oil.

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