The Photochemistry of Pyrylium Salts: New Photohydrations and Photoamidations of Heterocycles Leading to Bicyclic Oxazolines and Functionalized Cyclopentenes

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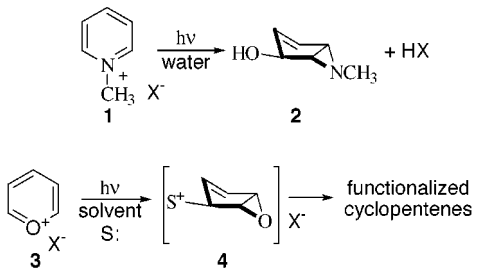
Photochemical studies of arenes have elucidated several important valence bond isomerizations and led to the discovery of the synthetically significant arene−alkene meta-cycloaddition reaction.[1,2] Although n−π* excitation precludes such processes in pyridines, Kaplan et al. reported in 1972 that photolysis of *N*-methylpyridinium chloride (**1**) in H_2O furnished 6-methylazabicyclo-[3.1.0]hex-3-en-2-ol (**2**) exclusively as the exo-isomer (Scheme 1).[3] The synthetic utility of such aziridinyl cyclopentenes has prompted additional work on related photoalcoholyses of pyridinium salts.[4]

By contrast, photochemical studies on pyrylium salts have been limited to a few highly substituted examples,[5] and to 4-pyranones that have hydroxypyrylium resonance structures.[6] As part of our continuing interest in the design and synthesis of cyclopentane-based glycomimetics,[7] we report that under appropriate conditions, irradiation of pyrylium perchlorate (**3**) at 254 nm generates solvolysis products **4** that undergo in situ epoxide opening to afford stereochemically well-defined cyclopentenes. By using acetonitrile as solvent, we show that the photosolvolysis of both **3** and **1** followed by regioselective epoxide or aziridine opening affords bicyclic oxazolines whose synthetic utility is illustrated by a new peracid-mediated ring-opening oxidation to functionalized cyclopentenone oximes.

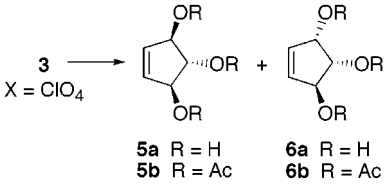
Pyrylium perchlorate was synthesized according to the published method.[8] Basic hydrolysis of pyridine−SO_3 complex afforded the sodium salt of glutaconaldehyde, which cyclized upon acidification with $HClO_4$ in methanol−ether. Recrystallization of the crude product from 0.1 M $HClO_4$ afforded the perchlorate salt of **3** as a tan solid that was stable at pH <0. By using this procedure, multigram quantities of **3** could be prepared.

Photolysis of the perchlorate salt of **3** (600 mg scale, 0.02 M, 90 min) in 15% $DClO_4/D_2O$ with NMR monitoring revealed new resonances consistent with the formation of *meso*-**5a** and (±)-**6a**. Since the water solubility of both triols complicated isolation and purification, the photolysis of **3** (X = ClO_4) was performed in acetic acid containing acetic anhydride (5 equiv). The corresponding triacetates **5b** and **6b** were obtained in a 5:2 ratio and in 60% isolated yield. Saponification of the mixture afforded **5a** and **6a**.

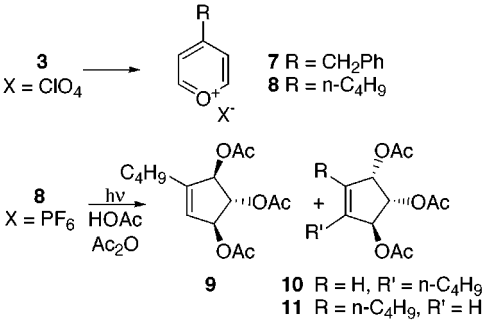
Scheme 1



Scheme 2



Scheme 3



The synthesis and photosolvolysis of ring-substituted pyrylium salts was also examined. Following the protocol reported by Taylor et al.,[9] the parent pyrylium salt **3** (X = ClO_4) was treated with dibenzylcopperlithium and di-*n*-butylcopperlithium. A subsequent oxidation with trityl hexafluorophosphate afforded 4-benzyl and 4-butylpyrylium PF_6 salts **7** (35%) and **8** (45%), respectively.

Irradiation of **7** led to no recognizable products, perhaps because of interfering electron transfer between the phenyl group and the electron-deficient pyrylium ring. However, photolysis of **8** in HOAc−Ac_2O afforded three triacetates in 60% overall yield. A sample of the predominant trans,trans-isomer **9** could be obtained pure by chromatography, but the two cis,trans-isomers **10** and **11** were inseparable. After saponification, the triol corresponding to **9** formed no cyclic acetal with 2-methoxypropene, whereas both triols corresponding to **10** and **11** furnished acetonide derivatives.

It was also of interest to examine the use of other nucleophilic solvents in the photoreaction. When **3** (X = ClO_4) was photolyzed in wet acetonitrile (0.1% H_2O by volume), a single product was isolated, whose structure was identified by X-ray crystallography as oxazoline **14** (Scheme 4). Compound **14** likely arises by hydration of the initially formed nitrilium ion **12**, and subsequent cyclization of **13** with S_N2' opening of the epoxide. Under similar conditions, the photolysis of **1** (X = ClO_4, 0.25% H_2O present)

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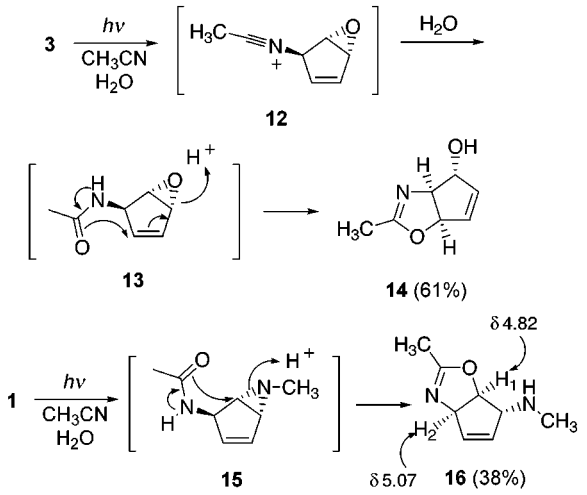
Scheme 4

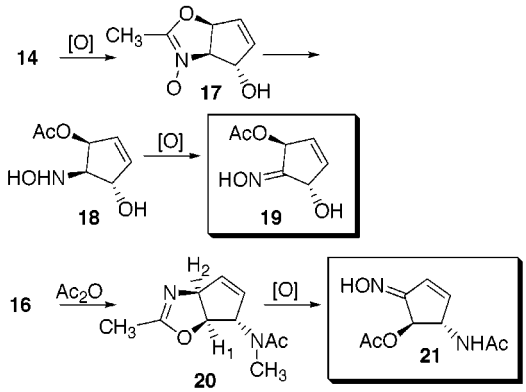


gave aminooxazoline **16**, the product of direct S_N2 opening of the aziridine **15**. The structure of **16** was assigned on the basis of NMR chemical shift comparisons with **14** and with other, known 4,5-dialkyloxazolines.[10,11]

The differing cyclization modes leading to oxazolines **14** and **16** were probed by using PM3 semiempirical energy minimizations (MOPAC6 code) on both the protonated epoxide and *N*-methyl aziridine of cyclopentadiene as model systems. Bond distortions in the protonated epoxide led to significant positive charge delocalization onto the allylic carbon, which would favor S_N2' opening of **13**. By contrast, C−N bond lengths in the protonated aziridine remained undistorted, so that least atomic motion would favor direct nucleophilic opening in **15** by the neighboring acetamide group.

Oxazolines **14** and **16** represent useful precursors to cyclopentitol-based glycomimetics. Toward that end, oxidation of the cyclopentene double bond in **14** was attempted by using excess *m*-chloroperoxybenzoic acid (MCPBA). Instead of the expected epoxide, a new cyclopentenol, identified spectroscopically as **19**, was obtained as the exclusive product in 53% yield (Scheme 5). This new reaction likely occurs by hydrolysis of the *N*-oxide **17** (a known MCPBA oxidation product of oxazolines[12] and other iminoethers[13]) and subsequent oxidation of the intermediate hydroxylamine **18**.

Scheme 5



This unexpected transformation of oxazolines to α-acetoxy oximes was also observed with the bicyclic oxazolidine **16**. After first protecting the *N*-methylamino group in **16** as its acetamide, reaction with MCPBA transformed **20** to the α,β-unsaturated oxime **21**. It should be noted that the adventitious, peracid-mediated *N*-demethylation of the amide in **20** has been observed with other tertiary carboxamides.[14] Moreover, the characteristic chemical shift pattern for the vinylic hydrogens in the conjugated oxime **21** provided additional support for the assignment of structure **16**.

Overall, the new chemistry of pyrylium salts reported here extends the regime of heteroaromatic photosolvolyses. Furthermore, the unprecedented use of acetonitrile in pyrylium and pyridinium photolyses and the versatile new chemistry of derived bicyclic oxazolines provide exceptionally easy access to intermediates for the synthesis of monosaccharide mimics and other structures of interest in modern glycobiology.

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Supporting Information Available: Representative experimental procedures, as well as analytical and spectroscopic characterization data for **5a**, **5b**, **9**, **14**, **16**, **19**−**21**, X-ray crystallographic data for **14**, and energy minimization files (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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