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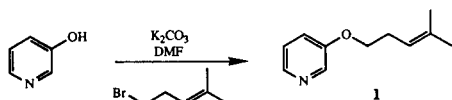
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Carbonyl 2+2 photoaddition occurs selectively to the alkene moiety of 3-(4-methyl-3-pentenoxypyridine). Photolysis of alkene containing pyridines in acetophenone gives rise to an oxetane which is obtained with extremely high diastereoselectivity as shown by analysis of the major 2+2 photoproduct. A second photoproduct, 2,3-dihydroxy-2,3-diphenylbutane, is obtained as a result of acetophenone coupling.

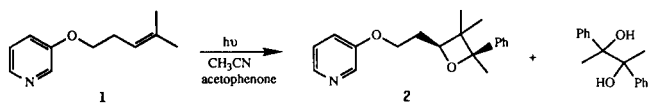
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We have been interested in photochemical reactions involving heterocyclic systems for utilization in the development of synthetic methodology. Recent literature is replete with examples of exploiting light-induced reactions for the ultimate synthesis of unnatural and natural heterocyclic compounds [1]. In our attempt to examine the chemistry available *via* sensitization of the pyridine moiety, we found that good yields of Paterno-Buchi products are obtained from photolysis of alkene-substituted pyridines in the presence of standard triplet sensitizers. We now report the results of this regio- and stereoselective photocycloaddition.

Synthesis of the typical pyridine compound **1** was accomplished in one step by alkylation of hydroxypyridine with 5-bromo-2-methyl-2-pentene under standard ether synthesis conditions [2]. Irradiation of this compound in



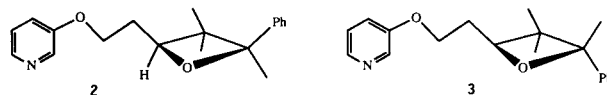
various photograde solvents (*e.g.* acetonitrile, *t*-butyl alcohol, tetrahydrofuran, or cyclohexane) with a high-pressure Hg lamp through quartz for 5 hours resulted in recovery of starting material. Our studies have shown that 2-methyl-6-(2-pyridyl)-2-pentene is also photoinert under these conditions. In the presence of acetophenone [3] (8 eq) in acetonitrile ( $10^{-3}$  M), photolysis of the pentenoxy-substituted pyridine **1** gave rise to *cis*-2,3,3-trimethyl-2-phenyl-4-[2-(3-pyridinoxy)ethyl]oxetane **2** in 61% yield [4]. Relative stereochemistry of the oxetane product was verified by 500



MHz NOE analysis and the assignment of chemical shifts was confirmed by lanthanide shift reagent (LSR) studies [5]. A significant by-product of the photoreaction was 2,3-dihydroxy-2,3-diphenylbutane [6]. The Paterno-Buchi photochemical reaction has also been observed upon photolysis

of the alkene-substituted pyridines in acetone [7].

The acetophenone cycloaddition results were interesting because although one would predict the high regioselectivity, the diastereoselectivity (>30:1) is not predictable [8]. The regiochemistry of the observed product is consistent with a stepwise-like mechanism which is typical for this photocycloaddition. The high stereoselectivity of the product, on the other hand, is not indicative of a stepwise process, especially in light of molecular mechanics calculation (MMX) [9] that show the two possible stereoisomers **2** and **3** vary in energy by only 0.3 kcal/mol. This energy difference is insufficient to justify the high selectivity resulting from irradiation at 30°.



If one assumes there is diradical nature in the intermediate of the oxetane formation [10], then the reaction appears to involve initial oxygen-carbon bonding. This type of process precludes parallel approach of the  $\pi$  systems since that pathway is symmetry forbidden. Thus, the likely mechanistic pathway involves perpendicular approach of triplet [11] acetophenone ( $n, \pi^*$ ) to the moderately electron-rich alkene followed by  $\pi$  (alkene)  $\rightarrow$   $n$  (ketone) interaction which results in oxygen-carbon bond formation. The observed stereoselectivity [12] would presumably result from the steric interaction inherent to the perpendicular approach since calculations rule out product control. Bond rotation prior to spin flip [13] may be inhibited by the excessive substitution on the putative radical centers.

An alternative explanation is that the oxetane formation is concerted. This mechanistic route would explain the high stereoselectivity. The regioselectivity is difficult to justify unless one invokes dipolar interactions. We are continuing our investigation in this area.

Acknowledgement.

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NOE experiment. We acknowledge Research Corporation and the BYU Development Fund for financial support. Instrumental nmr support from the National Science Foundation, Grant No. CHE 8712101 is also acknowledged.

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[1a] S. L. Schreiber, *Science*, **227**, 857 (1985); [b] J.-C. Gramain, R. Remuson and D. Vallée, *J. Org. Chem.*, **50**, 710 (1985); [c] R. W. Kavash and P. S. Mariano, *Tetrahedron Letters*, 4185 (1989); [d] A. Padwa, G. E. Fryxell, L. Zhi and S. F. Hornbuckle, *Tetrahedron Letters*, 6889 (1988); [e] M. A. Brumfield and W. C. Agosta, *J. Am. Chem. Soc.*, **110**, 6790 (1988); [f] R. Kiesewetter and P. Margaretha, *Helv. Chim. Acta*, **72**, 83 (1989); [g] J. Cossy and D. Belotti, *Tetrahedron Letters*, 6113 (1988).

[2] Standard conditions (potassium carbonate, DMF, 125°, 10 hours) gave a 39% yield of 3-(4-methyl-3-pentenoxy)pyridine, bp 65°/0.025 Torr; <sup>1</sup>H nmr (deuteriochloroform): 200 MHz δ 8.31 (t, J = 1.5 Hz, 1H, pyridine), 8.20 (t, J = 3.7 Hz, 1H, pyridine), 7.18 (m, 2H, pyridine), 5.20 (bt, J = 8.6 Hz, 1H, C=CH), 3.97 (t, J = 7.0 Hz, 2H, O-CH<sub>2</sub>), 2.49 (bg, J = 7.0 Hz, vinyl-CH<sub>2</sub>), 1.73 (s, 3H, vinyl-CH<sub>3</sub>), 1.66 (s, 3H, vinyl-CH<sub>3</sub>); ir (neat): 2916, 1585, 1574, 1471, 1425, 1384, 1279, 1230, 707 cm<sup>-1</sup>.

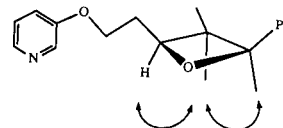
*Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>NO: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.66; H, 8.41; N, 8.01.

[3] Acetophenone was purified by double distillation.

[4] Chromatography (pentane, silica gel) of the photomixture gave 71% recovery of acetophenone, the second fraction (30% ethyl ether-pentane) yielded 2,3-dihydroxy-2,3-diphenylbutane (6%), the third fraction (ethyl ether) gave trace amounts of a minor oxetane (<2%), the fourth fraction contained oxetane **2** (61%), bp 205°/0.02 Torr; spectral data for the major oxetane: <sup>1</sup>H nmr (deuteriochloroform): 200 MHz δ 8.33 (t, J = 1.8 Hz, 1H, pyridine-H), 8.21 (t, J = 3.0 Hz, 1H, pyridine-H), 7.30 (m, 2H, pyridine-H), 7.23 (m, 5H, phenyl), 4.82 (dd, J = 5.5, 8.0 Hz, 1H, methine), 4.13 (bt, 2H, OCH<sub>2</sub>), 2.06 (m, 2H, methylene), 1.69 (s, 3H, methyl), 1.29 (s, 3H, methyl *trans*-to-Ph), 0.73 (s, 3H, methyl *cis*-to-Ph); ir (neat): 3057, 2970, 1574, 1490, 1470, 1278, 1230, 1048, 704 cm<sup>-1</sup>.

*Anal.* Calcd. for C<sub>19</sub>H<sub>23</sub>NO<sub>2</sub>: C, 76.74; H, 7.80. Found: C, 76.54; H, 8.04.

[5] NOE <sup>1</sup>H nmr (deuteriochloroform): 500 MHz shows strong interaction between a) the methyl *trans* to the phenyl and the methine and



b) the methyl *trans* to the phenyl and the C-1 methyl; LSR experiment [(deuteriochloroform): 200 MHz tris(dipivalomethane)europium complex] resulted in complexation to the pyridine, the methyl at δ 1.69 and remote phenyl had minimal change. See M. J. C. M. Koppes, A. M. Crabbendam and H. Cerfontain, *Rec. Trav. Chim.*, **107**, 676 (1988) for recent use of NOE and LSR for stereochemical assignments on a similar small ring compound.

[6] Formation of the pinacol-type compound is a result of hydrogen abstraction by the excited state acetophenone followed by coupling of two radical species. Possible hydrogen atom sources include the OCH<sub>2</sub> of the alkenoxy pyridine or acetonitrile. Identity of the 2,3-dihydroxy-2,3-diphenylbutane is based on comparison with known material (<sup>1</sup>H nmr, ir, ms and mp) H.-D. Becker, *J. Org. Chem.*, **32**, 2140 (1967). A 1:1 ratio of the two diastereomers was obtained. For a recent example of phenyl ketone coupling see: B. Guérin and L. J. Johnston, *J. Org. Chem.*, **54**, 3176 (1989).

[7] The same conditions with acetone as the solvent and sensitizer give a low conversion of substituted alkene to oxetane.

[8] Diastereoselectivity in the Paterno-Buchi reaction using chiral phenylglyoxalates has been reported: H. Buschmann, H.-D. Scharf, N. Hoffmann, M. W. Plath and J. Runsink, *J. Am. Chem. Soc.*, **111**, 5367 (1989).

[9] MMX calculations gave 67.12 kcal/mol strain energy for the *cis* product **2** and 67.40 kcal/mol strain energy for the *trans* isomer **3**.

[10] N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings, Menlo Park, 1978, p 432. The Paterno-Buchi diradical intermediate has been trapped recently by W. Adam, U. Kliem and V. Luccini, *Liebigs Ann. Chem.*, 867 (1988).

[11] Intersystem crossing of the aromatic carbonyl is too rapid for singlet reactivity. Quenching studies confirm the involvement of only the triplet state in oxetane formation, see D. R. Arnold, *Adv. Photochem.*, **6**, 301 (1968).

[12] A. Ohno, Y. Ohnishi and G. Tsuchishi, *Tetrahedron Letters*, 283 (1969). For a recent example of selectivity see: Y. Kubo, M. Suto, T. Araki, P. H. Mazzocchi, L. Klingler, D. Shook and C. Somich, *J. Org. Chem.*, **51**, 4404 (1986). For a discussion of steric demands in 2+2 photocycloadditions see: J. H. Penn, L.-X. Gan, E. Y. Chan and P. D. Loesel, *J. Org. Chem.*, **54**, 601 (1989).

[13] Lifetime of triplet species is long, therefore rotation is likely: R. A. Firestone, *Tetrahedron*, **33**, 3009 (1977).