

Steven A. Fleming* and Vance D. Bachelder

Department of Chemistry, Brigham Young University,
Provo, UT 84602

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Ethyl 3-(2-pyridyl)propionate formation results from irradiation of 3-(2-pyridyl)propanal diethylacetal in acetonitrile. This photoreaction is unique to the heteroaromatic pyridine and only occurs in acetonitrile. A minor product, 1-aza-2-methyl-3-(2-ethanal diethylacetal)-4-ethoxycycloocta-1,3,5,7-tetraene, is also obtained. The irradiation of 2-methyl-6-(2-pyridyl)-2-pentene in the presence of various sensitizers results in addition to the alkene side-chain to produce oxetanes.

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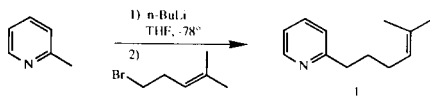
Cyclization reactions of radical intermediates has received intense investigation in the last few years [1]. The application of this synthetic methodology has allowed for the synthesis of many interesting and complex molecules. Stereocontrol, control of regioselectivity, and product control are challenges that have required attention in inter- and intra-molecular cyclizations. Many of the recent examples have successfully dealt with these issues. We are interested in the synthesis of heterocyclic systems using similar methodology with regiocontrolled side chain addition to heteroaromatic compounds.

We have previously reported on the unexpected stereoselectivity of the Paterno-Buchi reaction between alkeno-oxy-substituted pyridines and acetophenone [2]. We now report our results from photochemical investigation of alkenyl- and acetal-substituted pyridines.

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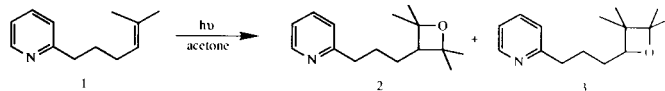
Synthesis of the alkenylpyridine compound **1** was accomplished in one step by alkylation of the anion of 2-methylpyridine with 5-bromo-2-methyl-2-pentene [3] (see Equation 1). Irradiation of this compound in various photograde solvents (*e.g.* acetonitrile, *t*-butyl alcohol, tetrahydrofuran, or cyclohexane) with a 450 W high-pressure Hg

Equation 1



lamp through quartz for extended periods of time resulted in recovery of starting material. Photolysis in the presence of hydrogen abstractable solvents (*e.g.* methanol or *i*-propyl alcohol) gave unidentifiable high MW non-aromatic material. When sensitizers were employed, photoaddition to the alkene moiety was observed. Thus, irradiation in acetone gave oxetane products **2** and **3** in a 26% yield (3:1 respectively) at 93% conversion [4] as shown in Equation 2. Pinacol was also obtained from coupling of the presumed acetone radical anion intermediate.

Equation 2



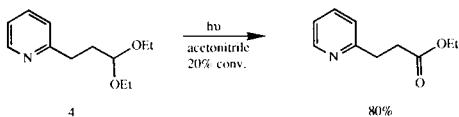
The photolysis of pyridine **1** and 5 equivalents of acetophenone [5] in acetonitrile ($10^{-3} M$) resulted in the formation of one major diastereomeric oxetane [6]. The acetone photoaddition to the side chain alkene proceeded with minimal regioselectivity which appears to have been dictated by steric factors. Acetophenone addition, on the other hand, occurred with much higher regioselectivity in this study which is consistent with our previous work [2]. The major stereoisomer, *cis*-2,3,3-trimethyl-2-phenyl-4-(3-(2-pyridyl)propyl)oxetane [7], was obtained in 65% yield after total conversion of hexenylpyridine **1**. A minor amount of the coupled 2,3-dihydroxy-2,3-diphenylbutane was also isolated. Identification of the Paterno-Buchi product was based on spectral data and comparison to the previously reported oxetane [2]. The reason for these efficient and selective photocycloadditions may be intermolecular aromatic ring interaction in the ground or excited state between the pyridine and the acetophenone.

Irradiation with xanthone also results in 2 + 2 reaction with the side chain alkene [8]. The product of this addition was primarily the regioisomer expected from steric control as in oxetane **2**. Attempts to promote electron transfer in photoreactions of the alkenyl pyridine by adding tetracyanoethylene were unsuccessful.

We have also examined the photochemistry of 3-(2-pyridyl)propanal diethylacetal **4**. This compound was available in our lab as a precursor to 3-(2-pyridyl)-1-propanol which was needed for related studies. The synthesis of the acetal was performed in the same manner as the alkenyl pyridine using 2-bromoacetaldehyde diethylacetal as the electrophile [9]. At low conversions (*ca.* 20%), irradiation of the acetal substituted pyridine in acetonitrile ($10^{-3} M$) with a 450 W Hg lamp gave an 80% yield of ethyl 3-(2-

pyridyl)propionate [10] as shown in Equation 3. At higher conversions the yield of the ester photoproduct diminished and a minor photoproduct, 1-aza-2-methyl-3-(2-ethanal diethylacetal)-4-ethoxycycloocta-1,3,5,7-tetraene [11], appeared.

Equation 3



This photooxidation of the acetal to the ester was not observed when *t*-butyl alcohol or cyclohexane were employed as solvents. Formation of the ester is presumably a result of initial inter- or intramolecular hydrogen abstraction from the acetal followed by electron transfer from the radical species to form the stabilized cation. The cation would then undergo dealkylation to give the observed ester. Alternatively, the radical species could react with oxygen in solution to yield an orthoformate type intermediate that would ultimately result in formation of the ester and ethoxide. We note that this second pathway includes oxygen as a reactant, but ester formation was observed even in deoxygenated experiments [12]. The latter mechanism also results in ethoxide formation which is a fragment found in the minor photoadduct.

Independent irradiation of the pyridyl ethyl ester in acetonitrile established that it was indeed photolabile, since it was converted to intractable material. However, none of the minor photoproduct cyclooctatetraene was formed from the ester photolysis. In addition, time studies indicate that the minor product is not a result of secondary photochemistry. We are uncertain as to the mechanism involved in the formation of this compound.

Our discovery of the unexpected, but potentially useful, photooxidation of pyridine acetal **4** directed us to the study of other acetals. Synthesis and photolysis of 3-phenylpropanal diethylacetal in acetonitrile unfortunately gave no photooxidation. The all carbon analog was photostable even with prolonged irradiation and when pyridine was added to the photomixture. It should be noted that other methods for oxidation of acetals to esters have been reported [13]. We are continuing to investigate the generality and mechanism of this photochemical transformation.

Acknowledgement.

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- [1a] P. Renaud, J.-P. Vionnet and P. Vogel, *Tetrahedron Letters*, **32**, 3491 (1991); [b] J. Cossy and C. Leblanc, *Tetrahedron Letters*, **32**, 3051 (1991); [c] X.-M. Zhang and P. S. Mariano, *J. Org. Chem.*, **56**, 1655 (1991); [d] T. Hasegawa, T. Ogawa, K. Miyata, A. Karakizawa, M. Komiyama, K. Nishizawa and M. Yoshioka, *J. Chem. Soc. Perkin Trans. I*, 901 (1990); [e] P. Margaretha and W. C. Agosta, *Tetrahedron Letters*, **32**, 31 (1991).
- [2] S. A. Fleming and R. W. Jones, *J. Heterocyclic Chem.*, **27**, 1167 (1990).
- [3] Standard conditions (a. *n*-BuLi, THF, -78° ; b. RBr, 3 hours) gave an 75% yield of 2-methyl-6-(2-pyridyl)-2-pentene, bp $48^{\circ}/0.01$ Torr; ^1H nmr (deuteriochloroform): 200 MHz δ 8.49 (bt, J = 1.0 Hz, 1H, pyridine), 7.55 (bt, J = 5.1 Hz, 1H, pyridine), 7.08 (m, 2H, pyridine), 5.13 (bt, J = 7.2 Hz, 1H, C = CH), 2.75 (t, J = 8.0 Hz, 2H, pyridyl-CH₂), 2.01 (dq, J = 7.3 Hz, vinyl CH₂), 1.73 (m, 2H, CH₂), 1.66 (s, 3H, vinyl CH₃), 1.55 (s, 3H, vinyl CH₃); ^{13}C nmr (deuteriochloroform): 50 MHz δ 163.0, 149.8, 136.7, 132.4, 124.7, 123.1, 121.3, 38.2, 30.2, 28.0, 25.9, 17.9 ppm; ir (neat): 3007, 2925, 1590, 1569, 1474, 1434, 749 cm^{-1} ; uv (95% ethanol): λ max 205 (12 000), 261 (4 500).
- [4] *Anal. Calcd.* for C₁₂H₁₇N: C, 82.23; H, 9.77. Found: C, 82.12; H, 10.00.
- [4] Chromatographic separation (chloroform, silica gel) of the photomixture (450 W, quartz, 1.2 hours) gave 7% recovered starting material, 26% of an oxetane mixture (3:1), and 2,3-dimethyl-2,3-butane-diol. Spectral data for major oxetane **2**: ^1H nmr (deuteriochloroform): 200 MHz δ 8.50 (bd, J = 1.8 Hz, 1H, pyridine), 7.56 (bt, J = 4.0 Hz, 1H, pyridine), 7.10 (m, 2H, pyridine), 2.80 (m, 2H, pyridyl-CH₂), 1.5-1.8 (m, 4H, -CH₂CH₂-), 1.37 (s, 6H, 2 x CH₃), 1.25 (s, 6H, 2 x CH₃); ^{13}C nmr (deuteriochloroform): 50 MHz δ 163.5, 150.0, 136.8, 123.1, 121.4, 79.3, 38.5, 33.0, 29.0, 25.0, 18.3 ppm. Spectral data for **3**: ^1H nmr (deuteriochloroform): 200 MHz δ 8.50 (bd, J = 1.8 Hz, 1H, pyridine), 7.56 (bt, J = 4.0 Hz, 1H, pyridine), 7.10 (m, 2H, pyridine), 4.29 (t, J = 5 Hz, 1H, OCH), 2.80 (m, 2H, pyridyl-CH₂), 1.6-1.8 (m, 4H, -CH₂CH₂-), 1.35 (s, 3H, CH₃), 1.18 (s, 3H, CH₃), 1.05 (s, 6H, 2 x CH₃); ^{13}C nmr (deuteriochloroform): 50 MHz δ 164.0, 150.0, 136.8, 123.1, 121.4, 86.1, 38.3, 33.0, 32.0, 25.5, 25.4, 24.3, 23.5, 18.3 ppm.
- [5] Acetophenone was purified by double distillation.
- [6] A 9% combined yield of the two regioisomeric oxetanes was also formed.
- [7] Chromatographic separation (chloroform, silica gel) gave a 46% yield of *cis*-2,3,3-trimethyl-2-phenyl-4-(3-(2-pyridyl)propyl)oxetane. Spectral data are: ^1H nmr (deuteriochloroform): 200 MHz δ 8.47 (bd, J = 1.8 Hz, 1H, pyridine), 7.55 (bt, J = 8.0 Hz, 1H, pyridine), 7.1-7.3 (m, 7H, arom), 4.44 (t, J = 7.5 Hz, 1H, OCH), 2.80 (t, J = 8.0 Hz, 2H, pyridyl-CH₂), 1.4-1.9 (m, 4H, -CH₂CH₂-), 1.62 (s, 3H, CH₃), 1.20 (s, 3H, CH₃), 0.62 (s, 3H, CH₃); ^{13}C nmr (deuteriochloroform): 50 MHz δ 162.3, 149.6, 146.5, 136.8, 128.1 (2x), 126.7, 124.7 (2x), 123.2, 121.5, 88.3, 86.1, 43.7, 38.8, 31.8, 26.0, 25.7, 23.5, 21.0 ppm.
- [8] Spectral data for the major xanthone oxetane are: ^1H nmr (deuteriochloroform): 200 MHz δ 8.50 (m, 1H, pyridine), 7.56 (m, 1H, pyridine), 7.40 (m, 12H, arom), 2.90 (m, 2H, pyridyl-CH₂), 2.65 (m, 1H, oxetane CH), 1.5-1.8 (m, 4H, -CH₂CH₂-), 1.55 (s, 3H, CH₃), 1.25 (s, 3H, CH₃).
- [9] Standard conditions [3] were employed using 2-bromoacetaldehyde diethylacetal to give 62% of 3-(2-pyridyl)propanal diethylacetal, bp $62^{\circ}/0.01$ Torr; ^1H nmr (deuteriochloroform): 200 MHz δ 8.52 (bt, J = 1.0 Hz, 1H, pyridine), 7.58 (bt, J = 5.1 Hz, 1H, pyridine), 7.12 (m, 2H, pyridine), 4.52 (t, J = 7.2 Hz, 1H, CH(OEt)₂), 3.58 (m, 4H, 2 x OCH₂), 2.87 (t, J = 7.3 Hz, 2H, pyridyl-CH₂), 2.08 (m, 2H, CH₂), 1.20 (t, J = 7.0 Hz, 6H, 2 x CH₃); ^{13}C nmr (deuteriochloroform): 50 MHz δ 162.1, 149.8, 136.7, 123.2, 121.4, 61.4, 33.6, 33.5, 15.4 ppm; ir (neat): 2974, 1591, 1569, 1474, 1435, 1374, 1128, 1088, 1062, 750 cm^{-1} .
- [10] *Anal. Calcd.* for C₁₂H₁₉NO₂: C, 68.85; H, 9.15. Found: C, 68.73; H, 9.39.
- [10] Chromatographic isolation of ethyl 3-(2-pyridyl)propionate was accomplished with 5% ethyl acetate:pentane. The spectral data are: ^1H nmr (deuteriochloroform): 200 MHz δ 8.52 (bt, J = 1.0 Hz, 1H, pyridine), 7.59 (bt, J = 5.1 Hz, 1H, pyridine), 7.15 (m, 2H, pyridine), 4.12 (q, J =

7.1 Hz, 2H, OCH₂), 3.12 (t, J = 7.3 Hz, 2H, CH₂CO); 2.80 (t, J = 7.3 Hz, pyridyl-CH₂), 1.23 (t, 3H, J = 7.1 Hz, CH₃); ir (neat): 2980, 1732, 1593, 1569, 1476, 1437, 1374, 1259, 1173, 1041, 754 cm⁻¹.

Anal. Calcd. for C₁₀H₁₃NO₂: C, 67.05; H, 7.31; N, 7.82. Found: C, 66.89; H, 7.51; N, 7.54.

[11] Spectral data for the minor photoproduct cyclooctatetraene are: ¹H nmr (deuteriochloroform): 500 MHz δ 7.25 (dd, J = 1.5, 8.0 Hz, 1H, vinyl CH), 7.14 (dt, J = 1.6, 7.5 Hz, 1H, vinyl CH), 6.98 (dt, J = 1.5, 8.0 Hz, 1H, vinyl CH), 6.63 (dd, J = 1.6, 7.5 Hz, 1H, vinyl CH), 4.64 (t, J = 6.0 Hz, 1H, CH(OEt)₂), 4.26 (q, J = 7.5 Hz, 2H, OCH₂), 3.54 (m, 4H, 2 x

OCH₂), 2.81 (d, J = 6.0 Hz, 2H, vinyl CH₂), 1.80 (s, 3H, vinyl CH₃), 1.34 (t, J = 7.5 Hz, 3H, CH₃), 1.15 (t, J = 7.4 Hz, 6H, 2 x CH₃); ¹³C nmr (deuteriochloroform): 50 MHz δ 161 (s), 148 (s), 131 (d), 128 (s), 127 (d), 123 (d), 121 (d), 103 (d), 62 (t, 2 x CH₂), 61 (t), 36 (t), 16 (q), 15 (q, 2 x CH₃), 14 (q) ppm; HETCOR studies indicate 161 and 16 ppm carbons are directly bonded; ir (neat): 2975, 1675, 1598, 1486, 1372, 1242, 1118, 747 cm⁻¹; ms: m/e (%) 279 (M⁺, 40), 250 (-C₂H₆, 100).

[12] The sample deoxygenation with purified nitrogen may still allow for the presence of sufficient oxygen for this reaction to occur.

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