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LETTERS

INTRAMOLECULAR PHOTOCYCLOADDITION OF 1,3-DIENES WITH 2-PYRIDONES

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Abstract: Intramolecular photocycloaddition of a 2-pyridone and an acyclic 1,3-diene leads to formation of an apparent [2 + 2] product. This is presumably formed by an initial [4 + 4] cycloaddition followed by Cope rearrangement of the highly strained product. The isolated 1,2-divinylcyclobutane undergoes a Cope rearrangement at 120 °C to give a polycyclic cyclooctadiene. © 1999 Elsevier Science Ltd. All rights reserved.

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2-Pyridones are generally poor substrates for thermal cycloaddition chemistry, in part because of their aromatic character.[1] Nevertheless, they undergo photochemical reactions with themselves under mild conditions and with few side reactions, yielding Dewar pyridones and/or [4 + 4] dimerization products.[2] When these photoreactions are conducted in the presence of other unsaturated species, different cycloaddition products can form, including [2 + 2] products from acrylonitrile,[3] and [4 + 4] products from 1,3-dienes[4] as well as other heterocycles such as triazolopyridines.[5] We report here the first example of an intramolecular photocycloaddition of a pyridone and an acyclic 1,3-diene (**3**) that yields an apparent [2 + 2] cycloaddition product (**4**). Thermal rearrangement of this photoproduct yields a 1,5-cyclooctadiene, in a process that is similar to the rearrangement of the parent divinylcyclobutane[6] and contrasts with the Cope rearrangement of 2-pyridone dimers.[7,8]

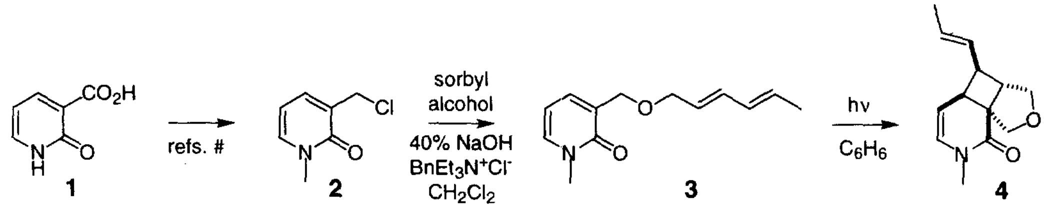

Figure 1. Synthesis of photosubstrate **3**. Photoreaction yields **4** as the major product.

Many examples of 2-pyridone photochemistry have been described. However, photoreaction of 2-pyridones with 1,3-dienes have only been reported by Sato and coworkers, and all examples have been intermolecular.[4] To test the viability of an intramolecular 1,3-diene/2-pyridone photoreaction as part of our continuing investigation of 2-pyridone photoreactions, we prepared ether **3** from 2-oxo-nicotinic acid **1** and sorbyl alcohol, by conversion of **1** to 3-chloromethyl-1-methyl-2-pyridone **2** and etherification using phase-transfer reaction conditions.[9,10] The resulting product **3**[11] was subjected to pyrex-filtered irradiation from a medium-pressure mercury lamp at ambient temperature, and the reaction was followed by TLC. In methanol,

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with an initial concentration of 0.05 M, eight hours of irradiation was required to fully convert all of the starting **3**. The major product formed, tentatively identified as **4**,[11] was isolated in 29% yield.

Based on the known photoreactions of acyclic 1,3-dienes with aromatics,[12] this reaction could involve a highly strained intermediate, with the potential for subsequent reaction with solvent. Consistent with this view, changing the reaction solvent to benzene resulted in a reaction that was faster (2.5 h) and cleaner, with product **4** isolated in 67% yield.

Sato et. al have described the photocycloaddition of 2-pyridones with both cyclic (*s*-cis) and acyclic (largely or exclusively *s*-trans) 1,3-dienes.[4] In both cases, [4 + 4] cycloaddition is the primary reaction pathway (Figure 2). Cyclopentadiene yields the trans [4 + 4] adduct **6** and cyclobutane **8**. The latter is believed to derive from cis [4 + 4] adduct **7**, which undergoes a facile Cope rearrangement. In the case of the *s*-trans 2,5-dimethyl-2,4-hexadiene, a strained product **9** is formed, with a trans alkene reflecting the ground-state structure of the 1,3-diene. This product rapidly isomerizes via Cope rearrangement to the more stable cyclobutane products **10** and **11**. Both of these Cope rearrangements (**7** → **8** and **9** → **10** + **11**) proceed in a manner opposite to the parent cis 1,2-divinylcyclobutane (**14**, Figure 4), which was found by Vogel to rearrange to 1,5-cyclooctadiene.

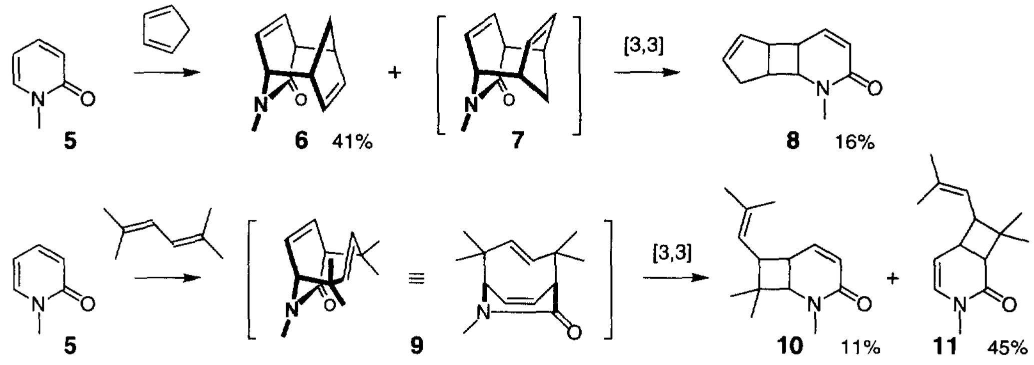

Figure 2. Sato's photoreactions of pyridones with cyclic and acyclic 1,3-dienes.[4]

We assume that the intramolecular reaction of the diene and the 2-pyridone in **3** follows a similar path. Photoreaction of **3** yields **12**, retaining the lowest energy *s*-trans conformation of the 1,3-diene. Cope rearrangement of the intermediate [4 + 4] product **12** results in the observed cyclobutane **4**. In an attempt to intercept **12**, photoreaction of **3** was repeated in the presence of three equivalents of furan. No evidence for formation of Diels-Alder product **13** was found, therefore if **12** is an intermediate, rearrangement must be rapid.[13]

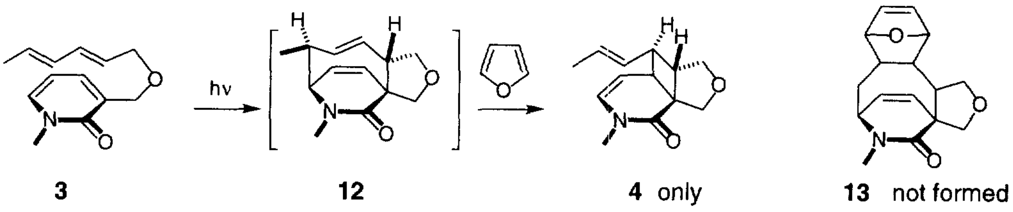

Figure 3. Photocycloaddition of **3** may involve **12** but it was not trapped by furan.

Rearrangement of cis-1,2-divinylcyclobutane **14** to 1,5-cyclooctadiene **15**[6] is promoted by relief of ring strain, occurring at the modest temperature of 120 °C.[6] The opposite rearrangement is found for polycyclic cyclooctadienes, such as the bis-2-pyridone [4 + 4] cycloadduct **16** which rearranges to cyclobutane **17** at 60 °C, with a half life of ca. 45 minutes.[8] In view of these diametrically opposed reactivities, it was of interest to test the potential of **4** for Cope rearrangement. The proposed cis orientation of the two alkenes in **4** was based on its presumed origin from **12** (Figure 3). Few Cope rearrangements of acyclic diene-derived cyclobutanes such as **4** have been reported.[14] In the event, heating a benzene-d_6 solution of **4** to 120 °C (sealed tube), and monitoring by proton NMR, gave a clean rearrangement of **4** to cyclooctadiene **18**,[11] with a half life of 45 minutes (66% yield after column chromatography). Therefore, the thermodynamics of the [3,3] rearrangement of **4** to **18** resembles that of the parent cyclobutane **14**/cyclooctadiene **15**, and not the photoadduct **16**/cyclobutane **17**.

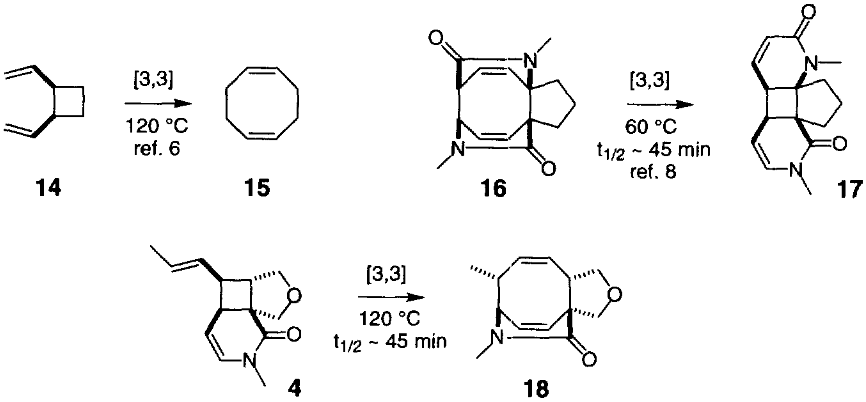

Figure 4. Cope rearrangement of **4** is like the parent divinylcyclobutane **14** rather than the pyridone-pyridone photoadduct **16**.

This intramolecular 1,3-diene/2-pyridone route to polycyclic cyclooctadienes may begin with a [2 + 2] cycloaddition, or a [4 + 4]/Cope rearrangement equivalent. In either case, this simple system leads to a complex product with four new stereogenic centers, as a single diastereomer. This reaction complements the intramolecular reactions of tethered 1,3-dienes[15,16] and those of tethered heterocycles.[17]

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11 Selected data:

3: ^{1}H NMR ($CDCl_3$) δ 7.42 (d, J = 6.9 Hz, 1H), 7.19 (d, J = 6.9 Hz, 1H), 6.21 (dd, J = 15.0, 10.4 Hz, 1H), 6.15 (t, J = 6.9 Hz, 1H), 6.03 (dd, J = 15.0, 10.4 Hz, 1H), 5.73-5.59 (m, 2H), 4.42 (s, 2H), 4.08 (d, J = 6.0 Hz, 2H), 3.51 (s, 3H), 1.71 (d, J = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 161.6, 136.3, 135.3, 133.2, 130.7, 129.9, 129.8, 126.4, 105.5, 71.3, 67.0, 37.3, 18.0.

4: ^{1}H NMR ($CDCl_3$) δ 5.94 (d, J = 8.1 Hz, 1H), 5.50 (m, 2H), 4.74 (dd, J = 8.1, 4.4 Hz, 1H), 4.25 (d, J = 9.0 Hz, 1H), 3.98 (d, J = 9.0 Hz, 1H), 3.79 (dd, J = 9.3, 4.7 Hz, 1H), 3.64 (m, 1H), 3.05 (s, 3H), 1.64 (d, J = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 169.1, 130.1, 129.4, 126.6, 104.4, 77.1, 73.5, 55.5, 49.0, 44.2, 40.9, 34.7, 17.8.

18: ^{1}H NMR ($CDCl_3$) δ 6.20 (dd, J = 9.3, 5.8 Hz, 1H), 6.04 (d, J = 9.3 Hz, 1H), 5.07 (q, J = 13.4 Hz, 2H), 4.60 (d, J = 8.5 Hz, 1H), 4.12 (t, J = 8.0 Hz, 1H), 3.89 (d, J = 8.5 Hz, 1H), 3.70 (dd, J = 5.8, 3.7 Hz, 1H), 3.51 (m, 1H), 3.37 (m, 1H), 3.03 (s, 3H), 2.97 (m, 1H), 1.14 (d, J = 7.7 Hz, 1H). ^{13}C NMR: ($CDCl_3$) δ 170.2, 130.9, 130.8, 126.3, 121.3, 75.8, 72.5, 63.9, 56.6, .52.2, 41.9, 33.3, 20.9.

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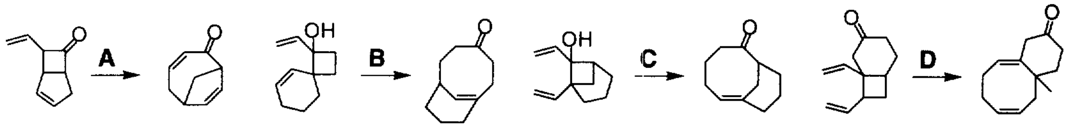

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