Photoreactivity of 2-Pyridones with Furan, Benzene, and Naphthalene. Inter- and Intramolecular Photocycloadditions

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Pyridones, well-known for their ability to photodimerize, have been found to undergo [4 + 4] photocycloaddition with furan and naphthalene but not with benzene. In some cases these reactions can be highly regio- and stereospecific. Intramolecular reaction with furan produces both cis and trans [4 + 4] products. The cycloaddition with naphthalene can occur both inter- and intramolecularly. The intermolecular reaction yields primarily the cis isomer, whereas the trans isomer is the major product from the intramolecular reaction. A mixture of 4-methoxy-2-pyridone and 2-methoxynaphthalene that could form up to eight regio- and stereoisomers forms largely one [4 + 4] product.

Among the higher-order cycloadditions,[1−3] 2-pyridones have long been recognized for their propensity to photodimerize with a high level of regio- and stereoselectivity.[4] At concentrations above 0.1 M, most 2-pyridones will undergo photodimerization in high yield, forming exclusively the head-to-tail regioisomers **2** and **3**, with the trans isomer **3** dominating. A less-well studied reactivity of 2-pyridones is their photocycloaddition with other polyunsaturated molecules such as 1,3-dienes and triazolopyridines. Using an excess of a 1,3-diene, especially cyclopentadiene, [4 + 4] products such as cis **4** and trans **5** have been prepared by Sato et al.,[5] and intramolecular reactions proceed similarly.[6] Triazolopyridines, also known to photodimerize,[7] will yield cross [4 + 4] product **6** when irradiated in the presence of a 2-pyridone (Figure 1).[8]The symmetry of 2-pyridone photodimers **2** and **3**, with a C_2 axis and a center of inversion, respectively, limits the potential application of this efficient [4 + 4] cycloaddition because few synthetic targets are similarly symmetric. One approach to eliminating the symmetry of pyridone/pyridone photoproducts is to use pyridone mixtures.[9] These photoreactions can yield densely functionalized [4 + 4] products from simple and readily available aromatic substances.[10,11] Alternatively, new examples of 2-pyridone cross-photocycloaddition with polyunsaturated species would greatly expand the range of accessible products. As part of our continuing investigations of 2-pyridone photoreactivity, we have therefore surveyed its reactivity with furan, benzene, and naphthalene and report the results here.

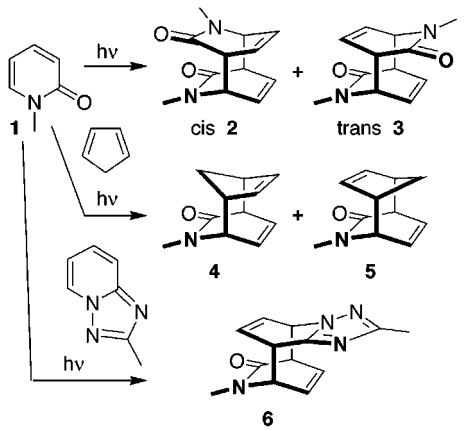

Figure 1. Photodimerization of 2-pyridones and cross-reaction wth 1.3-dienes and triazolopyridine.

Among this set of aromatics, furan, benzene, and naphthalene, only naphthalene will photodimerize to give structures such as **10** (Figure 2).[2,3,12] This photo-[4 + 4] reactivity is well-studied with three-atom tethered bis-1-naphthalenes,[13] and intermolecular photo-[4 + 4] dimerization can also occur readily, especially with 2-methoxynaphthalene.[14]

Furans (**7**) do not photodimerize, with the exception of isobenzofuran,[15] undergoing fragmentation and isomerization reactions instead.[16,17] West has found that furan will photochemically yield intramolecular [4 + 4] adducts

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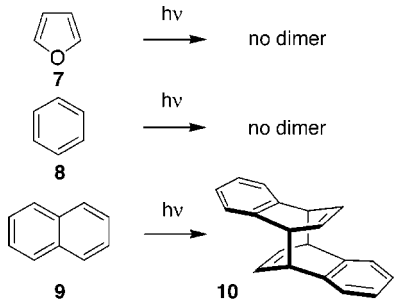

Figure 2. Naphalene will undergo [4 + 4] photodimerization, whereas benzene and furan will not.

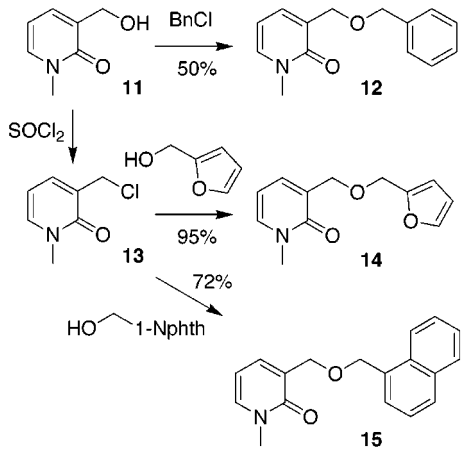

Figure 3. Photosubstrate synthesis.

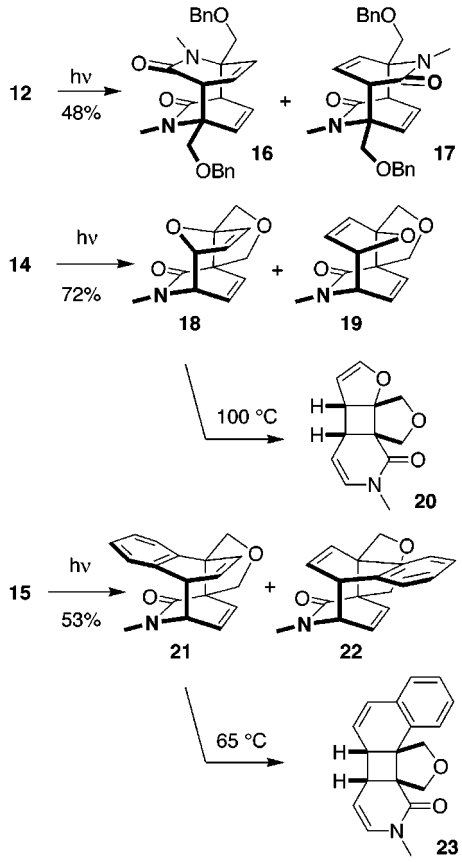

Figure 4. Photoreactions of pyridones tethered to phenyl (**12**), furyl (**14**), and naphthalene (**15**) and Cope rearrangement of the cis isomers.

with 2-pyrones.[18] Benzene **8** has a wide range of photoreactivity, including [4 + 4] photocycloadditions with 1,3-dienes and with furan, but it does not photodimerize.[2,19]

The photoreactivity of 2-pyridones with these three substrates has not been tested, although benzene has been used as a solvent. Nevertheless, the potential intramolecular reaction of benzene and pyridone was included in this study so that its reactivity could be compared with the other aromatics studied here.

Results and Discussion

Intramolecular Reactions. Photosubstrates, with a three-atom chain anchoring furan, benzene, and naphthalene at C-3 of 1-methyl-2-pyridone, were readily prepared from the known 3-hydroxymethyl-1-methyl-2-pyridone **11** (Figure 3).[20,21] During the course of this work, a new preparation of this useful intermediate was developed, and it is included here. Alcohol **11** was coupled directly with benzyl chloride using phase-transfer etherification conditions[22] to give ether **12**. Conversion of hydroxymethyl pyridone **11** to the corresponding chloromethyl pyridone **13**[20] using thionyl chloride, followed by phase-transfer mediated etherification with furfuryl alcohol and 1-(hydroxymethyl)naphthalene, gave ethers **14** and **15**, respectively. Each of these ethers was subjected to ambient temperature, Pyrex-filtered irradiation from a water-cooled 450 W medium-pressure mercury lamp and monitored at intervals by TLC and/or NMR.

Benzyl ether **12** was found to undergo a relatively slow photoreaction. After 8.5 h of irradiation, the product mixture was concentrated and purified by flash chromatography. In addition to residual **12**, only the cis and trans [4 + 4] dimers **16** and **17** were isolated, in a ratio of 2:3 (Figure 4); however, these had nearly identical R_f values and were not separated. This dimerization was not unexpected, as benzene has been found to be a suitable solvent for 2-pyridone photochemistry, but it establishes that even under ideal intramolecular circumstances, an unsubstituted phenyl group is inert to photocycloaddition with 2-pyridones.

In contrast to the phenyl group, the furan in **14** reacted completely within 3 h to give photoproducts **18** and **19**.[18] These two products were formed in a ratio of 3:10, favoring the trans isomer **19**. Changing the solvent from benzene to methanol did not alter significantly the rate of the photoreaction or the ratio of the products. The cis

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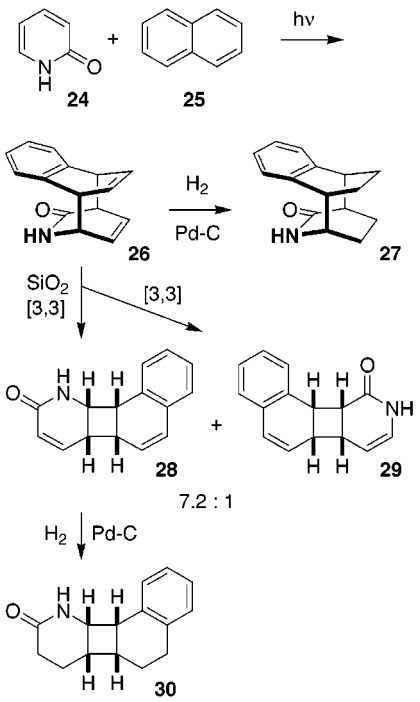

Figure 5. Intermolecular photocycloaddition of 2-pyridones and naphthalene can yield a single product.

isomer **18** was identified by heating benzene solutions of each isomer to 100 °C in a sealed tube. Under these conditions, the trans isomer **19** was unchanged but the cis isomer underwent a Cope rearrangement[23] to produce the cyclobutane product **20**.

Naphthylmethyl ether **15** proved to be similar in reactivity to furfuryl ether **14**. A solution of **15** in benzene-d_6 was completely converted to photoproducts after 1 h of irradiation. Two isomers **21** and **22** were formed in a ratio of 1:5, favoring the trans isomer. In methanol-d_4 the same isomers were produced, but this required a slightly longer reaction time (3.5 h) and gave a ratio of 1:2. Once again, the cis isomer was identified by its facile Cope rearrangement. In this case, the inseparable mixture of cis and trans isomers was heated to 65 °C for 4.5 h. The trans isomer **22** remained unchanged, and the cis isomer **21** was fully converted to cyclobutane **23**.

Intermolecular Reactions. The photocycloaddition of naphthalene with pyridone could also be performed without the tether, using a mixture of the commercially available substrates **24**[24] and **25** (Figure 5). The highly dissimilar solubilities limited the solvent choice; however, ethanol proved to be acceptable for both substrates. An initial survey of relative concentrations led to the finding that an excess of naphthalene **25** limited dimerization of **24** and resulted in formation of largely one new component. After irradiation of a 1:3 ratio of **24** and **25** in methanol (0.5 M in **25**) for 24 h, little of the pyridone remained. Unfortunately, purification of the resulting photoproduct proved to be troublesome.

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(24) Nitrogen substitution does not affect the photochemistry of 2-pyridones.

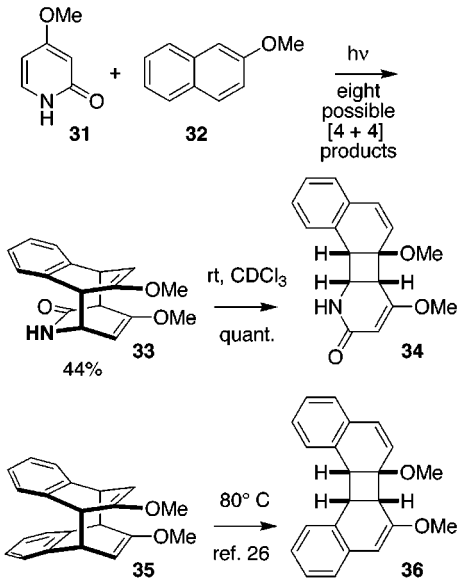

Figure 6. Methoxy substitution is tolerated in the cross-photocycloaddition of a pyridone and a naphthalene and yields a high level of regio- and stereoselectivity. Products **33** and **34** are comparable to the known **35**, a dimer of **32**, and its Cope rearrangement product **36**.

Product **26** was unstable and underwent Cope rearrangement during purification over silica gel. Cope rearrangement of *cis*-2-pyridone dimers (**2**) during silica gel chromatography has been reported by Nakamura.[25] Two alternative Cope rearrangements are possible for **26**, and the two isomeric cyclobutanes **28** and **29** were formed in this rearrangement, with the α,β-unsaturated amide **28** favored by more than a factor of 7.

Hydrogenation of the unpurified photoproduct mixture was readily accomplished, and the product **27** could then be chromatographically purified in 32% overall yield, based on pyridone **24** as the limiting reagent. Hydrogenation of the major Cope product **28** was also performed for comparison with **27**.

A complicating aspect of the intermolecular reaction of 2-pyridone with naphthalene (Figure 5), was the need to use an excess of naphthalene **25** to suppress photodimerization of pyridone **24**. Pyridone photodimerization can also be avoided by using 4-methoxy-2-pyridone **31** (Figure 6). Pyridone **31**[24] will not photodimerize but will undergo [4 + 4] photocycloaddition with other 2-pyridones,[9,10] and we anticipated that this reactivity might also be available with non-pyridone reactants such as naphthalene. Methoxynaphthalene **32** was chosen as a reaction partner for **31**.

Among the potential complications for photoreaction of **31** and **32** was the known [4 + 4] dimerization of naphthalene **32**, the first naphthalene photodimerization to be reported.[14] Perhaps more significantly, however, cross-photoreaction of **31** and **32**, assuming an exclusively [4 + 4] reaction manifold, could result in reaction at either aromatic ring, and each of these reaction sites has two possible regioisomers and two possible stereoisomers, for a total of eight (racemic) [4 + 4] products. A 1:1 ratio of **31** and **32** in methanol was irradiated for 72 h and produced largely a single isomeric product **33**. In contrast

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to **26**, product **33** was stable to silica gel chromatography and was isolated in 44% yield.

The proton NMR spectrum of **33** contained four aromatic protons, consistent with alkyl substitution (7.2−6.8 ppm), and two enol ether vinyl protons (5.1 and 5.0 ppm). The methoxy groups had identical chemical shifts (3.55 ppm), indicating that they were in similar environments and isolated from anisotropic influences of the amide group and aromatic ring. These chemical shifts are nearly identical to the corresponding data reported[26] for the cis 2-methoxynaphthalene dimer **35**, particularly the chemical shift of the methoxy singlet at 3.58 ppm. In chloroform-*d* at ambient temperature, this product underwent a slow, quantitative rearrangement to cyclobutane **34**, confirming the cis configuration of **33**, with the alkenes in close proximity as shown in Figure 6.

After this rearrangement, the chemical shift of the two methoxy groups shifted substantially, one upfield and one downfield (3.65 and 3.06 ppm). This pattern is identical to that observed for the Cope rearrangement product **36**, with two methoxy singlets at 3.71 and 3.07 ppm.[26] In addition, three vinyl protons were now present and were consistent with structure **34**, with two "normal" alkene protons (6.7 and 5.5 ppm) and a vinyl proton associated with a β-alkoxy-α,β-unsaturated amide group (4.9 ppm). Thermodynamically, this would be the expected product, with an α,β-unsaturated amide rather than the alternative *N*-alkenyl amide, and it is consistent with the major product formed upon rearrangement of **26** (Figure 5).

The high selectivity of this cycloaddition for the substituted ring of **32** mirrors the photodimerization of 2-substituted naphthalenes. A variety of 2-substituted naphthalenes undergo [4 + 4] photodimerization exclusively across the substituted ring (see **35**). Such head-to-tail selectivity has also been observed in suitably substituted anthracenes. Neither steric nor simple orbital interactions have been found to adequately account for the regioselectivity.[27]

Conclusions

Pyridones are stable and readily available aromatics, well-known for their [4 + 4] photocycloadditions, and the experiments described here reveal a richer diversity for this [4 + 4] reactivity. The readily available furans and naphthalenes, in combination with pyridones, yield novel and potentially useful new products. The high site, regio-, and stereoselectivities leading to **33** are especially intriguing and further studies are in progress.

Experimental Section

3-Hydroxymethyl-1-methyl-2-(1*H*)-pyridone 11.[20,21] Following the method of Deady,[28] to a solution of 2-hydroxy nicotinic acid (2.0 g, 14.4 mmol) in a mixture of methanol (20 mL) and water (3 mL) was added powdered potassium hydroxide (1.6 g, 28.6 mmol). This mixture was refluxed for 15 min. Iodomethane (10 mL, 161 mmol) was added, and the resulting mixture was refluxed for 2 h. The resulting clear solution was concentrated to half of its volume, and 10% hydrochloric acid (2 mL) was added. The resulting suspension was filtered to give 1-methyl 2-oxo-(1*H*)-pyridine-3-carboxylic acid[28−30] as a colorless solid (2.11 g, 96%): ^{1}H NMR (D_2O) δ 8.29 (d, J = 7.4 Hz, 1H), 7.91 (d, J = 6.6 Hz, 1H), 6.63 (dd, J = 7.4, 6.6 Hz, 1H), 3.59 (s, 3H).

This acid (439 mg, 2.87 mmol) was dissolved in thionyl chloride (6.5 mL) and refluxed for 1 h. After evaporation of the excess thionyl chloride, methanol (10 mL) was added, and the solution was refluxed for 0.5 h. The solvent was evaporated, the residue was dissolved in chloroform, and the solution was washed with saturated sodium bicarbonate solution and then water. Concentration gave methyl 1-methyl-2-oxo-(1*H*)-pyridine-3-carboxylate[28,31] as a light yellow solid (442 mg, 92%): ^{1}H NMR ($CDCl_3$) δ 8.06 (dd, J = 7.1, 2.2 Hz, 1H), 7.54 (dd, J = 6.6, 2.2 Hz, 1H), 6.17 (dd, J = 7.1, 6.6 Hz, 1H), 3.82 (s, 3H), 3.53 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 165.6, 159.3, 144.6, 143.1, 120.2, 104.4, 52.1, 38.2.

To a solution of methyl 1-methyl-2-oxo-(1*H*)-pyridine-3-carboxylate (410 mg, 2.45 mmol) in THF (25 mL) at −5 °C was added diisobutylaluminum hydride (5.40 mmol). After 3 h at 0 °C, methanol (1 mL), water (1 mL), sodium hydroxide (15%, 1 mL), and water (2 mL) were added. The resulting suspension was filtered, and the residue was washed with methanol. The filtrate was concentrated, and the product was purified by flash chromatography (3−5% gradient of methanol in methylene chloride) to afford alcohol **11**[20,21] as a colorless solid (160 mg, 47%): ^{1}H NMR ($CDCl_3$) δ 7.29 (d, J = 6.9 Hz, 1H), 7.20 (d, J = 6.9 Hz, 1H), 6.17 (t, J = 6.9 Hz, 1H), 4.50 (s, 2H), 3.49 (s, 3H).

Benzyl (3-[1-Methyl-2-oxo-(1*H*)-pyridinyl])-methyl Ether 12. To a solution of alcohol **11** (39 mg, 0.28 mmol) in methylene chloride (10 mL) at 0 °C was added benzyl chloride (79 mg, 0.56 mmol), benzyltriethylammonium chloride (83 mg, 0.37 mmol), and 40% sodium hydroxide (0.56 mL). The mixture was allowed to reach ambient temperature and stirred for 24 h. The aqueous phase was extracted with methylene chloride, and the combined organics were washed with water and then dried over anhydrous sodium sulfate. The organics were concentrated and purified by flash chromatography (3:97 methanol/methylene chloride) to give **12** as a colorless oil (34 mg, 50%): R_f = 0.21 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.50 (d, J = 6.9 Hz, 1H), 7.39−7.27 (m, 5H), 7.21 (d, J = 6.9 Hz, 1H), 6.18 (t, J = 6.9 Hz, 1H), 4.65 (s, 2H), 4.52 (s, 2H), 3.53 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.6, 138.2, 136.4, 135.4, 129.7, 128.3, 127.6, 127.5, 105.6, 73.0, 67.3, 37.4.

3-Chloromethyl-1-methyl-2-(1*H*)-pyridone 13.[20] To a solution of alcohol **11** (0.728 g, 5.24 mmol) in methylene chloride (15 mL) was added dropwise a solution of thionyl chloride (0.42 mL) in methylene chloride (6 mL). The mixture was stirred for 1.5 h, at which time TLC indicated an absence of starting **11**. The mixture was concentrated, and the resulting oil was purified by flash chromatography (5:95 methanol/methylene chloride) to give **13** as an oil (0.725 g, 88%):[20] R_f = 0.31 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.46 (dd, J = 6.9, 1.8 Hz, 1H), 7.28 (dd, J = 6.9, 1.8 Hz, 1H), 6.14 (t, J = 6.9 Hz, 1H), 4.51 (s, 2H), 3.52 (s, 3H).

2-Furylmethyl (3-[1-Methyl-2-oxo-(1*H*)-pyridinyl])-methyl Ether 14. To a solution of chloride **13** (82 mg, 0.52 mmol) in methylene chloride (15 mL) at 0 °C was added furfural alcohol (56 mg, 0.57 mmol), benzyltriethylammonium chloride (150 mg, 0.68 mmol), and sodium hydroxide (1.8 mL of a 40% aqueous solution). The mixture was allowed to reach ambient temperature and stirred for 24 h. The aqueous phase was extracted with methylene chloride, washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo. Purification by flash chromatography (3:97 methanol/methylene chloride) gave **14** (108 mg, 95%): R_f = 0.40 (3:97 methanol/

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methylene chloride); mp = 96.0−97.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.46 (dd, J = 6.9, 1.9 Hz, 1H), 7.39 (m, 1H), 7.20 (dd, J = 6.9, 1.9 Hz, 1H), 6.33 (m, 2H), 6.16 (t, J = 6.9 Hz, 1H), 4.57 (s, 2H), 4.50 (s, 2H), 3.53 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.7, 151.6, 142.8, 136.5, 135.6, 129.4, 110.2, 109.4, 105.6, 67.1, 64.8, 37.4; MS (DCI/NH_3) m/z 220 (MH^+, 66), 138 (10), 123 (100), 95 (19), 81 (38); exact mass (DCI/NH_3) calcd for $C_{12}H_{14}NO_3$ 220.0974, found 220.0963.

(3-[1-Methyl-2-oxo-(1*H*)-pyridinyl])-methyl 1-Naphthylmethyl Ether 15. To a solution of chloride **13** (78.1 mg, 0.496 mmol) in methylene chloride (15 mL) at 0 °C was added 1-hydroxymethylnaphthalene (94.1 mg, 0.595 mmol), benzyltriethylammonium chloride (147 mg, 0.645 mmol), and 40% sodium hydroxide (1.5 mL). The mixture was allowed to reach ambient temperature and stirred for 9 h. The aqueous phase was extracted with methylene chloride, washed with water, dried over anhydrous sodium sulfate, and concentrated. Purification by flash chromatography (3:97 methanol/methylene chloride) gave **15** as a colorless solid (99.5 mg, 72%): R_f = 0.33 (3:97 methanol/methylene chloride); mp = 102.4−103.4 °C; ^{1}H NMR ($CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 1H), 7.83 (m, 2H), 7.56−7.40 (m, 5H), 7.13 (dd, J = 6.9, 1.6 Hz, 1H), 6.09 (t, J = 6.9 Hz, 1H), 5.09 (s, 2H), 4.54 (s, 2H), 3.49 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 161.5, 136.3, 135.4, 133.6, 133.5, 131.6, 129.5, 128.4, 128.3, 126.3, 126.0, 125.6, 125.1, 123.9, 105.4, 71.4, 67.3, 37.2; MS (DCI/NH_3) m/z (%) 280 (MH^+, 100), 141 (60), 123 (82); exact mass (DCI/NH_3) calcd for $C_{18}H_{18}NO_2$ 280.1338, found 280.1327.

Photocycloaddition of Benzyl Ether 12. A stream of dry nitrogen was passed for 15 min through a solution of **12** (25.7 mg, 0.11 mmol) in benzene-d_6 (50 mM in **12**), and the Pyrex test tube was then sealed with a septum. This tube was taped to the side of a water-cooled quartz cooling jacket surrounding a 450 W medium-pressure mercury Hanovia lamp fitted with a Pyrex filter and irradiated for 8.5 h. The photoreaction was periodically monitored by ^{1}H NMR. The solvent was removed, and the crude mixture was purified with silica gel chromatography (3:97 methanol/methylene chloride) to give an inseparable mixture of **16** and **17** (12.3 mg, 48%): R_f = 0.43 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.37−7.27 (m, 10H), 6.64 (d, J = 2.4 Hz, 1.2H), 6.57 (m, 1.2H), 6.50 (m, 0.8H), 6.20 (d, J = 8.4 Hz, 0.8H), 4.60 (m, 4H), 4.27 (d, J = 2.4 Hz, 1.2H), 3.94−3.88 (m, 2H), 3.81−3.74 (m 2H), 3.68 (d, J = 9.9 Hz, 0.8H), 2.80 (s, 3.6H), 2.76 (s, 2.4H).

Photocycloaddition of 14. A stream of dry nitrogen was passed for 15 min through a solution of **14** (51.6 mg, 0.235 mmol) in benzene-d_6 (50 mM in **14**), and the Pyrex test tube was then sealed with a septum. This tube was taped to the side of a water-cooled quartz cooling jacket surrounding a 450 W medium-pressure mercury lamp inside of a Pyrex filter and irradiated. After 3 h, ^{1}H NMR indicated that all of **14** had been consumed. The solution was concentrated and purified by flash chromatography (3:97 methanol/methylene chloride) to give a difficultly separable 3.4:1 mixture (NMR) of **18** and **19** (37.2 mg, 72%). **Cis isomer 18:** R_f = 0.34 (3:97 methanol/methylene chloride); mp = 129.5−130.5 °C; ^{1}H NMR ($CDCl_3$) δ 6.49 (dd, J = 5.8, 1.9 Hz, 1H), 6.44 (t, J = 7.8 Hz, 1H), 5.97 (d, J = 5.8 Hz, 1H), 5.87 (dd, J = 7.8, 1.6 Hz, 1H), 4.84 (d, J = 9.3 Hz, 1H), 4.62 (dd, J = 6.3, 1.9 Hz, 1H), 3.96 (d, J = 9.9 Hz, 1H), 3.82 (d, J = 9.9 Hz, 1H), 3.73 (dt, J = 6.3, 1.6 Hz, 1H), 3.65 (d, J = 9.3 Hz, 1H), 3.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.0, 136.8, 135.8, 135.2, 134.7, 96.7, 78.2, 71.4, 70.8, 65.5, 61.9, 33.9; MS (DEI) m/z (%) 220 (MH^+, 9), 138 (32), 123 (100), 95 (63), 81 (48); exact mass (DEI) calcd for $C_{12}H_{14}NO_3$ 220.0974, found 220.0982. **Trans isomer 19:** mp = 129.2−130.4 °C; R_f = 0.36 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 6.60 (dd, J = 7.5, 6.6 Hz, 1H), 6.41 (d, J = 5.6 Hz, 1H), 6.36 (dd, J = 5.6, 1.6 Hz, 1H), 6.14 (dd, J = 7.5, 1.4 Hz, 1H), 4.58 (dd, J = 5.6, 1.6 Hz, 1H), 4.44 (d, J = 9.7 Hz, 1H), 3.94 (d, J = 9.7 Hz, 1H), 3.86 (d, J = 10.1 Hz, 1H), 3.74 (d, J = 10.1 Hz, 1H), 3.67 (dt, J = 6.6, 1.4 Hz, 1H), 2.77 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.9, 137.2, 135.2, 132.6, 130.8, 91.4, 77.9, 72.2, 71.7, 65.5, 62.6, 35.3; MS (DEI) m/z (%) 220 (MH^+, 4), 138 (20), 123 (100), 95 (55), 81 (40); exact mass (DEI) calcd for $C_{12}H_{14}NO_3$ 220.0974, found 220.0984.

Cope Rearrangement of 18. Photoproduct **18** (6.9 mg) was dissolved in benzene-d_6 and heated at 100 °C (sealed tube) for 8 h. Flash chromatography (3:97 methanol/methylene chloride) gave **20** (2.7 mg, 39%): mp = 168.5−169.5 °C; R_f = 0.49 (5:95 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 6.41 (m, 1H), 5.97 (d, J = 8.2 Hz, 1H), 5.16 (m, 1H), 4.76 (dd, J = 8.2, 5.2 Hz, 1H), 4.29 (d, J = 9.1 Hz, 1H), 4.05 (d, J = 9.6 Hz, 1H), 4.00 (d, J = 9.1 Hz, 1H), 3.81 (d, J = 9.6 Hz, 1H), 3.54 (m, 1H), 3.10 (dd, J = 7.0, 5.2 Hz, 1H), 3.02(s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.1, 147.9, 131.0, 103.7, 101.7, 99.2, 77.2, 71.8, 56.6, 52.0, 39.7, 34.8. MS (DEI) m/z (%) 220 (MH^+, 5), 138 (36), 123 (79), 122 (100).

Photocycloaddition of 15. A solution of **15** (60.0 mg, 0.215 mmol) in benzene-d_6 (4.3 mL, 50 mM in **15**) was irradiated with a Pyrex-filtered 450 W medium-pressure mercury lamp for 1 h. The resulting mixture was purified by flash chromatography (3:97 methanol/methylene chloride) to give an inseparable 1:5 mixture of **21** and **22** (31.8 mg, 53%).

Irradiation of a solution of **15** (35.1 mg, 0.126 mmol) in methanol-d_4 (2.52 mL, 50 mM in **15**) for 3.5 h under the conditions described above, followed by flash chromatography, gave a 1:2 mixture of **21** and **22** (18.8 mg, 53%).

Cope Rearrangement of 21. The 1:2 mixture of **21** and **22** was dissolved in chloroform-d_1 and heated to 65 °C for 4.5 h. The resulting mixture was purified by flash chromatography (3:97 methanol/methylene chloride) to give trans isomer **22** (36%) and Cope product **23** (23%). **Photoproduct 22:** R_f = 0.39 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 1H), 7.17−7.09 (m, 3H), 6.57 (t, J = 7.5 Hz, 1H), 6.27 (d, J = 8.2 Hz, 1H), 5.81 (t, J = 7.3 Hz, 1H), 5.38 (d, J = 8.2 Hz, 1H), 4.76 (d, J = 9.1 Hz, 1H), 4.63 (d, J = 9.6 Hz, 1H), 4.00−3.81 (m, 4H), 2.94 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 173.9, 144.3, 143.9, 140.2, 137.0, 134.8, 133.1, 126.2, 125.9, 125.9, 123.7, 75.5, 75.4, 65.0, 62.0, 60.8. 47.8, 35.9; MS (DCI/NH_3) m/z (%) 280 (MH^+, 84), 141 (53), 123 (100); exact mass (DCI/NH_3) calcd for $C_{18}H_{18}NO_2$ 280.1338, found 280.1329. **Cope product 23:** R_f = 0.57 (3:97 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.11−7.06 (m, 3H), 6.95−6.92 (m, 1H), 6.38 (d, J = 9.9 Hz, 1H), 5.72 (dd, J = 8.2, 1.4 Hz, 1H), 5.54 (dd, J = 9.9, 5.2 Hz, 1H), 4.83 (d, J = 9.3 Hz, 1H), 4.76 (dd, J = 8.2, 3.8 Hz, 1H), 4.13 (d, J = 9.1 Hz, 1H), 3.98 (d, J = 9.3 Hz, 1H), 3.70 (d, J = 9.3 Hz, 1H), 3.62 (dd, J = 9.1, 5.2 Hz, 1H), 3.22 (ddd, J = 9.1, 3.8, 1.4 Hz, 1H), 2.70 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.5, 133.6, 130.2, 129.6, 128.3, 127.6, 127.5, 127.4, 127.4, 123.8, 104.4, 80.1, 78.1, 61.6, 59.1, 43.4, 42.2, 34.6; MS (DCI/NH_3) m/z (%) 280 (MH^+, 100), 141 (66), 123 (69); exact mass (DCI/NH_3) calcd for $C_{18}H_{18}NO_2$ 280.1338, found 280.1340.

Intermolecular Photocycloaddition of 2-Pyridone 24 and Naphthalene 25. A solution of naphthalene (239.7 mg, 1.87 mmol) and 2-pyridone **2** (59.4 mg, 0.625 mmol) in methanol (5 mL, overall 0.5 M in **24** + **25**) was irradiated for 24 h with a water-cooled Pyrex-filtered 450 W medium-pressure mercury lamp. The crude mixture was cooled to 0 °C overnight, and the crystalline naphthalene **25** was removed by filtration. Concentration of the filtrate gave a mixture containing largely photoproduct **26** plus residual **25**. **Photoproduct 26:** R_f = 0.71 (1:9 methanol/methylene chloride). In addition to absorbances due to naphthalene, the ^{1}H NMR exhibited the following ($CDCl_3$): δ 7.25 (m, 1 H), 7.03 (m, 2 H), 6.94 (m, 1 H), 6.60 (t, J = 8.1 Hz, 1 H), 6.40 (t, J = 7.2 Hz, 1 H), 6.27 (bs, 1 H, NH), 6.24 (t, J = 7.2 Hz, 1 H), 6.05 (t, J = 7.5 Hz, 1 H), 4.03−3.96 (m, 1 H), 3.83−3.73 (m, 2 H), 3.45−3.39 (m, 1 H). MS (FAB+) m/z (%) 224 (MH^+, 30), 128 (13), 96 (100); exact mass (CI) calcd for $C_{15}H_{14}NO$ 224.1075, found 224.1077.

Hydrogenation of Photoproduct 26. To a degassed solution of crude photoproduct **26** (558 mg, 2.5 mmol) in methanol (20 mL) was added 10% Pd/C (56 mg), and the flask was fitted with a hydrogen balloon. After stirring for 19 h the solution was filtered through Celite, concentrated in vacuo, and purified by flash chromatography (1:9 methanol/methylene chloride) to give 183.8 mg (32%) of **27** as an eggshell white solid: R_f = 0.73 (1:9 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.20−7.16 (m, 2 H), 6.97−6.94 (m, 2H), 5.46 (bs, 1H, NH), 3.87 (m, 1H), 3.44 (d, J = 3.6 Hz, 1H), 3.40 (d, J = 3.9

Hz, 1H), 3.04 (dd, J = 10.5, 4.2 Hz, 1H), 2.32−2.24 (m, 4H), 1.88−1.80 (m, 2H), 1.61−1.53 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 176.4, 141.5, 140.1, 127.4, 127.1, 126.9, 126.8, 51.2, 45.4, 43.0, 38.6, 23.8, 23.2, 21.7, 20.4; MS (CI) *m/z* (%) 227 (M^+, 13), 130 (33), 99 (100); exact mass (CI) calcd for $C_{15}H_{17}NO$ 227.1310, found 227.1311.

Cope Rearrangement of Photoproduct 26. A solution of 2-pyridone **24** (59.4 mg, 0.625 mmol) and naphthalene **25** (239.7 mg, 1.87 mmol) in methanol (5 mL, overall 0.5 M in **24** + **25**) was irradiated for 24 h with a water-cooled, Pyrex-filtered 450 W medium-pressure mercury lamp. The crude mixture was purified by flash chromatography (1:9 methanol/methylene chloride) to give 16.5 mg of **28** and 2.3 mg of **29** (7.2:1, 13% from **24**) as a light brown solid. **28:** R_f = 0.65 (1:9 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.08−7.04 (m, 2 H), 6.90 (dd, J = 5.1, 3.6 Hz, 1H), 6.80 (m, 1H), 6.40 (dd, J = 9.9, 3.6 Hz, 1H), 6.35 (d, J = 9.9 Hz, 1H), 5.91 (bs, 1H, NH), 5.58 (m, 2H), 4.51 (t, J = 2.7 Hz, 1H), 3.96 (m, 1H), 3.60 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 164.8, 139.6, 129.2, 128.8, 127.8, 127.7, 127.3, 125.7, 123.7, 53.8, 42.4, 40.1, 38.2; MS (CI) *m/z* (%) 224 (MH^+, 28), 128 (20), 96 (100); exact mass (CI) calcd for $C_{15}H_{14}NO$ 224.1075, found 224.1076. **29:** R_f = 0.79 (1:9 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.10−7.05 (m, 2 H), 6.98 (m, 1H), 6.90 (m, 1H), 6.36 (d, J = 9.6 Hz, 1H), 6.3 (bs, 1H), 5.79 (dd, J = 7.8, 5.1 Hz, 1H), 5.66 (dd, J = 4.5, 9.9 Hz, 1H), 4.80 (dd, J = 4.2, 8.1 Hz, 1H), 4.21 (bt, J = 9.9 Hz, 1H), 3.65 (m, 2H).

Hydrogenation of 28. Following the procedure described for hydrogenation of **26**, Cope rearrangement product **28** was reduced to give **30**: R_f = 0.83 (1:9 methanol/methylene chloride); ^{1}H NMR ($CDCl_3$) δ 7.11−7.09 (m, 2 H), 6.96−6.93 (m, 2H), 5.35 (bs, 1H, NH), 4.19 (dt, J = 7.5, 2.1 Hz, 1H), 3.86 (t, J = 8.4 Hz, 1H), 3.09−3.03 (m, 1H), 2.88−2.82 (m, 1H), 2.73−2.66 (m, 1H), 2.58−2.48 (m, 1H), 2.30 (t, J = 3.3 Hz, 1H), 2.25 (t, J = 3.3 Hz, 1H), 2.08−1.73 (m, 4H); MS (EI) *m/z* (%) 228 (MH^+, 100), 130 (16); exact mass (CI) calcd for $C_{15}H_{18}NO$ 228.1388, found 228.1379.

Photocycloaddition of 4-Methoxy-2-pyridone 31 and 2-Methoxynaphthalene 32. A stream of dry nitrogen was passed for several minutes through a solution of 2-methoxynaphthalene (127 mg, 0.8 mmol) and 4-methoxy-2-pyridone (100 mg, 0.8 mmol) in methanol (6 mL), and the Pyrex test tube was then sealed with a septum. This solution was irradiated with a 450 W medium-pressure mercury lamp for 20 h, at which time all of the 2-methoxynaphthalene had been consumed (TLC). The solution was concentrated and purified by preparative TLC (2:1 ethyl acetate/hexanes) to give recovered **31** (28 mg) and adduct **33** (72 mg, 32%, 44% based on recovered **30**): R_f = 0.52 (2:1 ethyl acetate/hexane); ^{1}H NMR (CDC_{l3}) δ 7.18 (m, 1H), 7.00 (m, 2H), 6.89 (m, 1H), 5.29 (bs, 1H), 5.13 (d, J = 7.2 Hz, 1H), 5.01 (d, J = 7.2 Hz, 1H), 3.98 (m, 1H), 3.74 (m, 1H), 3.55 (m, 1H), 3.55 (s, 6H), 3.30 (m, 1H); IR (KBr) 3300, 3245, 2934, 1677, 1652, 1216 cm^{-1}.

Photoproduct **33** rearranged on standing in $CDCl_3$ at ambient temperature to give cyclobutane product **34**: R_f = 0.35 (2:1 ethyl acetate/ hexanes); ^{1}H NMR ($CDCl_3$) δ 7.17 (m, 2H), 7.05 (m, 1H), 6.96 (m, 1H), 6.67 (d, J = 10.2 Hz, 1H), 5.45 (d, J = 10.2 Hz, 1H), 4.93 (s, 1H), 4.57 (br, 1H), 4.27 (dd., J = 9.0 Hz, 7.5 Hz, 1H), 3.80 (d, J = 7.5 Hz, 1H), 3.65 (s, 3H), 3.50 (d, J = 9.0 Hz, 1H), 3.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.6, 133.8, 132.7, 128.6, 128.4, 128.1, 127.6, 126.3, 123.2, 93.4, 78.7, 55.4, 50.8, 47.7, 46.7, 46.5, 29.7; IR (KBr) 3504, 3448, 3231, 1667, 1221 cm^{-1}; MS (DEI) *m/z* (%) 282 (M^+ − H, 0.5), 158 (100), 115 (82); exact mass (DEI) calcd for $C_{17}H_{16}NO_3$ 282.1130, found 282.1118.

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Supporting Information Available: ^{1}H NMR spectra for **11**−**20**, **22**, **23**, **26**−**30**, **33**, and **34**; COSY spectra for **18**, **20**, **22**, **23**, **27**−**30**, **33** and **34**; and ^{13}C NMR spectra for **27** and **28**. This material is available free of charge via the Internet at http://pubs.acs.org.

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