Intramolecular [4 + 4] Photocycloaddition of 2-Pyridones Tethered by a Three-Carbon Chain: Studies on the Formation of Cycloadducts and Control of Stereogenesis. 3†,1

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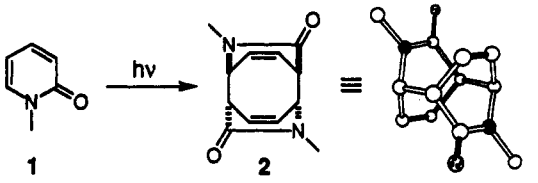
Irradiation of a pair of 2-pyridones tethered at the 3- and 6'-positions by a three-carbon chain initiates an efficient [4 + 4] cycloaddition to produce a densely functionalized, fused 5-8 carbocyclic ring system with the trans isomer predominant. An asymmetric center on the tether influences stereogenesis at the four new tetrahedral centers. This effect was probed with an alcohol substituent and its silyl ether as a function of solvent. A combination of inter- and intramolecular hydrogen-bonding can account for the observed levels of selectivity. Some of the cis products are unstable and undergo Cope rearrangement, yielding cyclobutane isomers.

The clinical efficacy of taxol[2] and the reticence of its tetracyclic ring system to yield to total synthesis[3] has brought eight-membered ring construction and manipulation to the forefront of the synthetic chemistry agenda.[4] Recent disclosures of new cyclooctane-containing natural products combining novel architecture and biological activity are further stimulation for this area of research.[5] Synthetic studies in both simple and complex systems have improved our understanding of cyclooctanoid synthesis, reactivity, and issues of stereogenic control;[6] however, the underlying issues have long been recognized. Studies of cyclization reactions conducted during the last 70 years have pointed to cyclooctane as the most difficult carbocycle to prepare.[7] Once formed, the conformational complexity[8] of cyclooctane challenges our ability to predict its chemistry.[9] Despite many synthetic endeavors in this arena, efficient construction and controlled manipulation of eight-membered rings remains an important methodology challenge.

Our laboratory is studying an intramolecular variation of the [4 + 4] photodimerization of 2-pyridones. This reaction forms an eight-membered carbocyclic ring with a high degree of regio- and stereogenic control in a single step from aromatic precursors (eq 1). While cycloaddition reactions are a primary method for construction of polycyclic molecules, preparatively useful cycloadditions leading directly to eight-membered rings are relatively rare.[10] Orbital symmetry allowed [4 + 4] photocycloaddition of simple 1,3-dienes could lead directly to 1,5-cyclooctadienes; however this is only a minor photochemical pathway.[11]



(1)

† Dedicated to Professor E. C. Taylor on the occasion of his 70th birthday.

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In contrast, [4 + 4] dimerization is the dominant photochemical reaction for 2-pyridones, a reaction reported by Taylor and Paudler more than 30 years ago.[12] The structure of the photoadduct was characterized the following year and was found to consist of a trans, head-to-tail product (2).[13] Although most reports of this reaction describe the formation of only this [4 + 4] isomer, Nakamura[14] showed that under some conditions the other three [4 + 4] isomers were also formed, albeit in low yield, and reported that photo-[4 + 2] and [2 + 2] products were not observed. Sharp and Hammond[15] demonstrated that a short-lived singlet excited state is responsible for the [4 + 4] reaction, and estimated that the lifetime for this intermediate was less than 200 ps. Several reports have shown that this photodimerization is compatible with chlorine and alkylpyridone substituents,[16,17] with only 6-chloro[18] or 4-alkoxy[19] substitution unsuitable for the transformation. Only one other study of the intramolecular photochemistry of two pyridones has been reported, Nakamura's triplet-sensitized photoreactions of *N,N'*-polymethylene bis(pyridones) (Figure 1), where the tether constraints combined with photosensitization produced only [2 + 2] and [4 + 2] photoproducts such as 4 and 5.[20]

Intriguingly, the carbon skeleton of the 2-pyridone photodimer 2 has substantial overlap with the cyclooctane component of natural products such as taxol and the fusicoccins, with alkenes located in regions of oxidation and carbonyl groups located where one-carbon substituents

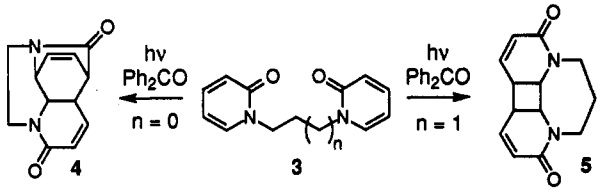
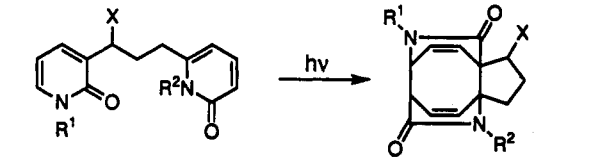


Figure 1. Triplet-sensitized irradiation of *N,N'*-polymethylene bis(2-pyridones) yields only [4 + 2] and [2 + 2] cycloaddition products.[20]

are required.[21] Additionally, the polycyclic [4.2.2^{1,6}.2^{2,5}] ring system of the photoproduct locks the 1,5-cyclooctadiene into a well-defined conformation, consequentially leading to predictable synthetic elaboration. We were also impressed by the absence of reports concerning the chemistry of this photodimerization product, outside of the patented work of Paquette and Slomp at Upjohn.[13,22]

Our initial investigations[21] demonstrated that the reaction was compatible with both three- and four-carbon tether lengths. These intramolecular reactions can be run to complete conversion, whereas the intermolecular reaction requires high concentrations (>0.1 M) for [4 + 4] dimerization and unimolecular photoprocesses become significant as concentrations fall below this level.[14,17] The ring formed by the tether removes the inherent symmetry of the photodimerization product 2. We were particularly interested in determining how this asymmetry could be controlled by a center of asymmetry on the tether, analogous to other intramolecular photochemical,[23] thermal,[24] and radical[25] reactions.

This paper describes the preparation of the three-carbon-tethered bis(2-pyridones) 6–8 and their photochemical transformation to the carbocyclic [6.3.0] products 9–11 with a carbon skeleton common to a number of natural product classes.[4]



6 X = H
7 X = OH
8 X = OTBS

a $R^1 = R^2 = H$
b $R^1 = CH_3$, $R^2 = H$
c $R^1 = R^2 = CH_3$

9 X = H
10 X = OH
11 X = OTBS

Results

Preparation of Bis(2-pyridone) Photosubstrates. Our initial communication[21] described the synthesis of

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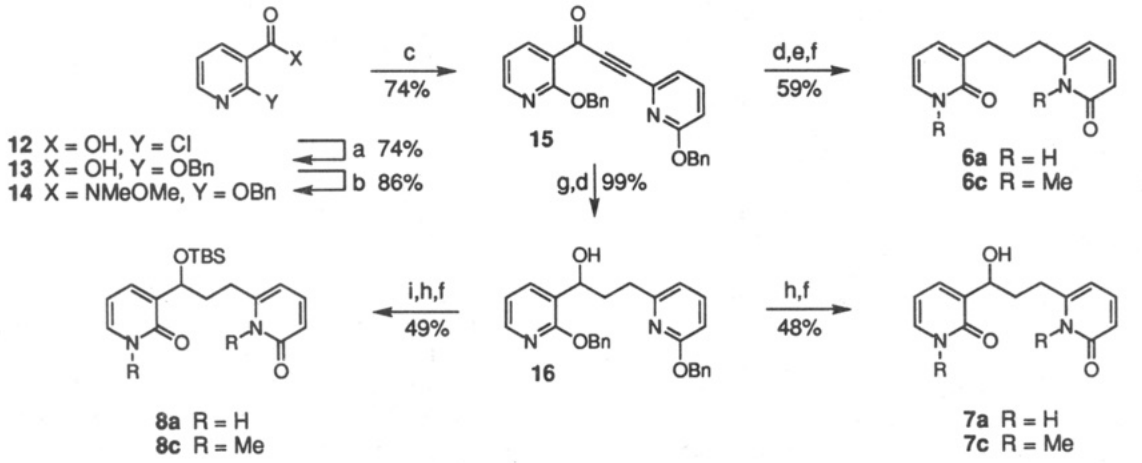
Scheme 1[a]



[a] (a) NaOBn, DMF; (b) CDI, MeONHMe; (c) 2-BnO(C_5H_3N)-6-C≡CMgBr; (d) $NaBH_4$; (e) H_2, Pd–C, Ac_2O, TFA; (f) MeI, K_2CO_3, MeOH; (g) H_2, Ra–Ni; (h) H_2, Pd–$CaCO_3$; (i) TBSCl, imidazole, MeCN.

the bis(2-pyridone) **7b**. A different sequence leading to **6**, **7**, and **8** is outlined in Scheme 1.

The commercially available 2-chloronicotinic acid (**12**), on treatment with sodium benzyloxide, yields 2-(benzyloxy)nicotinic acid (**13**), which is then converted to Weinreb amide[26] **14**. This amide couples with the bromomagnesium acetylide derived from 2-(benzyloxy)-6-ethynylpyridine,[27] to give the central ketone intermediate **15** (47% overall). Following reduction of the ketone to an alcohol with sodium borohydride, hydrogenation with palladium in a mixture of acetic anhydride and trifluoroacetic acid consumes 5 equiv of hydrogen to yield the very polar **6a**. N-Methylation[28] is best accomplished with iodomethane in methanol at ambient temperature to give **6c** (59% from **15**). Alternatively, hydrogenation of **15** with Raney nickel followed by ketone reduction gives **16** quantitatively. Hydrogenation over palladium followed by N-methylation then yields **7c** (48% overall from **16**). Silylation of alcohol **16** followed by hydrogenolysis of the benzyl groups and N-methylation gives **8c** (49% from **16**).

Photochemical Conditions. Irradiations employed a Hanovia 450-W medium-pressure mercury lamp in a water-cooled quartz jacket. The reactions were run at ambient temperature (ca. 28 °C) in Pyrex test tubes taped to the cooling jacket. Reactions were run with ca. 100 mg of substrate and at a concentration of 0.02–0.05 M. The solutions were routinely deoxygenated with a stream of nitrogen gas, although omitting this step did not appear to affect the results. The photoreactions were followed by TLC and stopped after all of the starting material had been consumed, typically 4–10 h.

Product Analysis. In the case of the unsubstituted tether **6**, only cis and trans [4 + 4] products are possible. Four products were anticipated for substrates **7** and **8**, resulting from cis/trans and syn/anti pairs (Figure 2). Trans and cis refers to the relative orientation of the lactams on the cyclooctadiene, and syn refers to the isomers in which

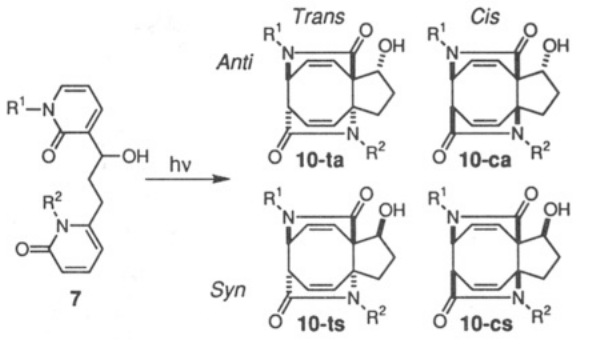


Figure 2. Stereogenic center on the tether yields four possible diastereomeric products.

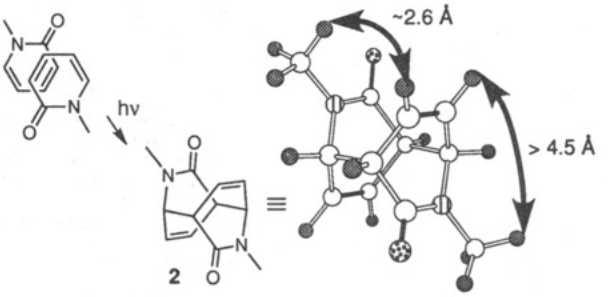


Figure 3. NOE enhancement of the vinyl protons, on irradiation of the *N*-methyl group, observed for trans isomers but not for cis isomers.

the alcohol (or silyl ether) is located on the same side of the cyclopentane as the adjacent lactam carbonyl.

Cis and trans products cannot be distinguished using NMR coupling constants, as the relevant protons in these isomers have identical dihedral angles. They can be readily distinguished, however, by observing NOE enhancements during irradiation of the *N*-methyl groups (Figure 3). This analysis relies on the proximity of the *N*-methyl groups to the vinyl protons *derived from the other pyridone ring in trans products*, whereas vinyl protons and the *N*-methyl group derived from the same pyridone are outside of the normal NOE range. Thus, NOE enhancement of vinyl protons, on irradiation of the methyl signals, is observed for the trans isomers but not for the cis isomers.

Identification of syn and anti products for **10b** and **10c** is a more difficult problem. The pairs of syn and anti isomers for the trans products (**ts** and **ta**) and the cis

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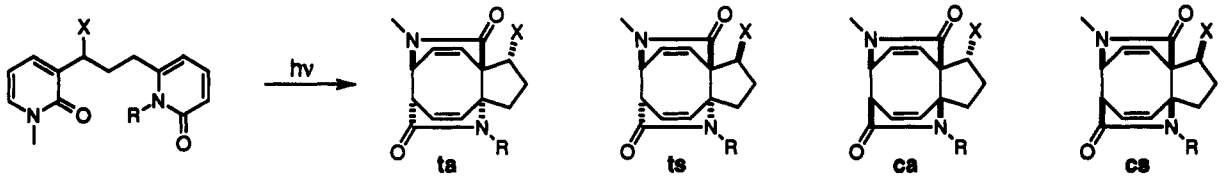
Table 1



entry	substr	X	R	solvent	product	ratio of products ta	ts	ca	cs	percent trans	percent anti	overall yield, %
1	**6c**	H	CH_3	CH_3OH	**9c**	2.1		1		68		84
2	**6c**			CH_2Cl_2	**9c**	3.8		1		79		63
3	**7b**	OH	H	EtOH	**10b**	17	1.5	3.5	1	81	89	93
4	**7b**			CH_2Cl_2	**10b**	4.7	6.3	1	2.2	78	40	85
5	**7c**	OH	CH_3	CH_3OH	**10c**	13	1.8	2.5	1	80	84	71
6	**7c**			THF	**10c**	11	5.7	1	1.3	88	64	58
7	**7c**			CH_2Cl_2	**10c**	5.0	4.8	1	2.8	72	44	82
8	**8c**	OTBS	CH_3	CH_3OH	**11c**	2	*a*	1[b]	*a*	66	99	89
9	**8c**			CH_2Cl_2	**11c**	2.9	*a*	1[b]	*a*	74	98	85

[a] Less than 1% of this isomer. [b] Refers to combined yield of cis-anti isomer and compound **23**.

products (**cs** and **ca**) were confirmed by oxidation of the alcohols to the same ketone using PDC in DMF, usually after hydrogenation of the alkenes with platinum oxide.[21] Designation of isomers as syn or anti relied on X-ray structure determination for trans-anti **10b–ta** and cis-syn **10c–cs**[29] and a clear correlation in the NMR spectra and relative TLC properties of these two closely related isomer sets. Desilylation of the isomers of **11c** with tetrabutylammonium fluoride allowed for direct correlation with the isomers of **10c**.

Photochemistry Results. Irradiation of **6c** in methanol results in the formation of two [4 + 4] products, the trans **9c–t** and the cis **9c–c**, in 57% and 27% isolated yields, respectively (68% trans, Table 1, entry 1). This ratio is fairly independent of the protic nature of the solvent: irradiation in methylene chloride gave **9c–t** and **9c–c** in yields of 50% and 13% (79% trans). Similarly, the *tert*-butyldimethylsilyl ether **8c** shows little change in product ratio with a change in solvent (entries 8 and 9) and a similar percentage of trans product (66% trans in methanol and 74% trans in methylene chloride). The selectivity for anti isomers **11c–ta** plus **11c–ca** with silyl ether **8c** is very high (98–99%) in both of these solvents.

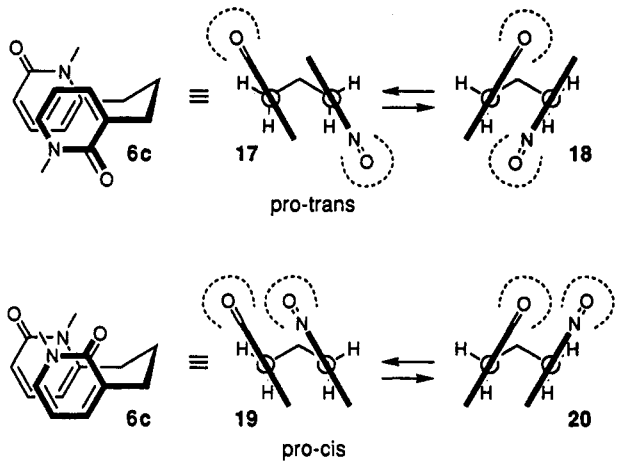
In contrast, alcohols **7b** and **7c** show large changes in the product ratios with changes in the solvent (entries 3–7). These changes in product distribution are due to a solvent dependence of the syn:anti ratio whereas the percentage of trans isomers remains relatively constant. Comparing entries 3 and 4 with entries 5 and 7 (**7b** vs **7c**) indicates that methylation of the pyridone nitrogen has no significant effect on either the yield or the ratio of products.[30]

Discussion

Trans:Cis Selectivity. For the intermolecular [4 + 4] dimerization of 2-pyridones, it has been proposed[17] that the trans, head-to-tail selectivity results from a preassociation of the pyridones with opposing ground-state dipole moments. If dipole interactions were the sole factor determining trans:cis selectivity, however, one would expect a significant enhancement of the trans selectivity on decreasing the dielectric constant of the solvent from methanol (ϵ = 32.7) to methylene chloride (ϵ = 9.1).[31] Only minor changes in trans selectivity are observed in these examples, and a similarly invariant trans selectivity (60–75% trans) was found for the intermolecular dimerization by Nakamura[14] in water (ϵ = 80.2) and in benzene (ϵ = 2.3).

A diminished dipole contribution to trans selectivity in polar solvents might be counterbalanced by the steric effects of solvation. The effect of a solvation sphere[32] around the amide group is illustrated in Scheme 2 for the intramolecular reaction of **6c**. Cycloaddition-conducive coplanar arrangements of the 2-pyridones that would minimize eclipsing interactions with the tether are shown as conformations **17–20**. Of the two conformations leading to trans isomers, the more extended one (**17**) would best accommodate the solvation of the amide. Both of the pro-cis conformations **19** and **20** would be destabilized by

Scheme 2



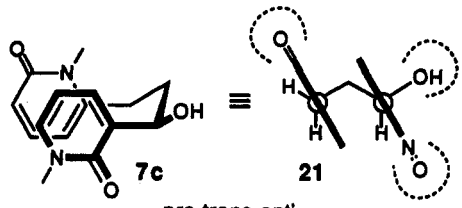
(29) The X-ray structure of **10a-ta** has been published.[21] Compound **10c-cs** crystallizes in the monoclinic space group $P2_1/c$ with a = 8.2451(6) Å, b = 12.1635(4) Å, c = 13.521(1) Å, β = 105.109(3)°, V = 1309.1(3) Å^3, and Z = 4. Final least-squares refinement using 1501 unique reflections with $I > 3\sigma(I)$ gave $R(R_w)$ = 0.074 (0.104). The authors have deposited atomic coordinates for this compound with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

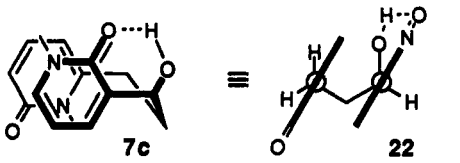
(30) Insensitivity of photoproduct isomer ratios to N-substitution has also been observed for the intermolecular case, see refs 14 and 17.

(31) *Lange's Handbook of Chemistry*; 13th ed.; Dean, J. A., Ed.; McGraw-Hill: New York, 1985.

(32) Buslaeva, M. N.; Samoilov, O. Y. In *The Chemical Physics of Solvation. Pt. A. Theory of Solvation*; Dogonadze, R. R., Kálmám, E.; Kornyshev, A. A., Ulstrup, J., Eds.; Elsevier: New York, 1985; Vol. 38; pp 391–414. Jorgensen, W. L. *Acc. Chem. Res.* **1989**, *22*, 184–189.

Scheme 3

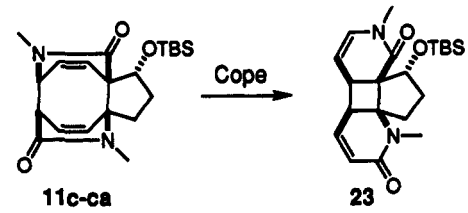




an increased solvation of the amide. Thus while increasing the polarity and hydrogen-bonding capacity of the solvent would attenuate the effect of dipole interactions, it would also engender trans selectivity through solvation.

Syn:Anti Selectivity. Whereas the ratio of trans:cis isomers is relatively insensitive to solvent, the syn:anti ratio shows a substantial solvent effect for the hydroxy-substituted tethers **7b** and **7c**. The anti isomers dominate in methanol for these substrates (84–89% anti) while the syn isomers are slightly favored in methylene chloride (40–44% anti); in THF the selectivity is intermediate (64% anti). This effect can be understood in the context of the solvation effects and the reactive conformations proposed in Scheme 3. External solvation of the alcohol, most significant in methanol and least significant in methylene chloride, is best accommodated by a pseudoequatorial alcohol conformation such as **21**, leading to anti isomers. In the absence of hydrogen bonding to solvent, an intramolecular hydrogen bond from the alcohol to the adjacent carbonyl group would stabilize conformation **22**, leading to syn isomers. The supposition that the anti selectivity for **7b** and **7c** is due to a steric effect of solvation is supported by the solvent-independent anti selectivity for the bulky *tert*-butyldimethylsilyl ether substituent of **8c**, for which the syn products represent less than 2% of the reaction mixture.

Product Stability. During some photochemistry runs in which inadvertent warming of the reaction vessels occurred, products in addition to those reported in Table 1 were observed. These were determined to be Cope rearrangement products derived from the cis isomers (eq 2). Maintaining adequate cooling was sufficient to suppress formation of these isomers in all cases except for the silyloxy substrate **8c**. The instability of the cis isomer derived from **8c** was readily apparent when a chromatographically isolated sample of **11c–ca** was found to have substantially (60%) rearranged to cyclobutane isomer **23** during acquisition of a ^{13}C NMR spectrum. Because isomer **23** is clearly derived from cis isomer **11c–ca**, the reported values for cis isomer **11c–ca** in Table 1 represent the combined yields of **11c–ca** and **23**. The details and implications of this facile rearrangement will be discussed elsewhere.



(2)

Conclusions

Two 2-pyridones tethered at the 3- and 6′-positions by a three-atom chain will efficiently undergo a [4 + 4] photocycloaddition to give a richly functionalized, fused 5–8 ring system, with a carbon skeleton found in a number of natural product families. A stereogenic center at the 1-position of the tether can be used to set the relative stereochemistry of the four new sp^3 centers of the photoproduct. Anti selectivity can be high (up to 99%) and for the alcohol was solvent dependent. The trans selectivity (up to 88%) was generally moderate and relatively independent of solvent effects.

Experimental Section

General. Melting points were obtained by using a Thomas-Hoover capillary melting point apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc. UV spectra were obtained using a Perkin-Elmer Lambda 5 or an HP Model 8452A spectrophotometer and methanol as solvent. IR spectra were obtained with a Perkin-Elmer Model 1600 FT-IR instrument. NMR spectra were recorded on a GE QE-300 (300 MHz ^1H) or a Bruker AC-250 (250 MHz ^1H) instrument. Mass spectra were recorded on a VG-7070ENF or VG-ZAB1FHF spectrometer. Column and thin layer chromatography were performed on silica gel with the indicated solvent system. Ether and THF were distilled from sodium benzophenone ketyl and methylene chloride was distilled from calcium hydride. All reactions requiring anhydrous conditions were performed under a positive pressure of nitrogen.

2-(Benzyloxy)nicotinic Acid (13). To a 0 °C suspension of NaH (7.02 g, 60% in mineral oil, 175 mmol, washed 3× with hexane) in dry DMF (100 mL) was added 2-chloronicotinic acid (**12**) (10.0 g, 63.5 mmol) in portions. The resulting mixture was stirred for 0.5 h and then benzyl alcohol (7.62 g, 70.5 mmol) was added dropwise over 10 min. The mixture was allowed to warm to rt over a period of 3 h and then heated to 75 °C for 16 h. The resulting mixture was poured into aqueous HCl (1 M, 250 mL) and extracted with four 125-mL portions of ether. Concentration of the combined organic extracts gave a yellow solid residue (12.3 g). Recrystallization from ethyl acetate afforded **13** (10.8 g, 74%) as colorless crystals: mp 134.5–136 °C; ^1H NMR ($CDCl_3$) δ 8.50 (dd, 1H, J = 7.4, 2.1 Hz), 8.42 (dd, 1H, J = 4.6, 2.1 Hz), 7.51–7.35 (m, 5H), 7.16 (dd, 1H, J = 7.4, 5.0 Hz), 5.65 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 160.9, 151.8, 151.7, 143.1, 135.3, 128.8, 128.7, 128.2, 118.4, 112.7, 69.4; IR (KBr) 2920, 2589, 1953, 1718, 1579, 1372, 1321, 1233, 1142, 1097, 1078, 1062, 878 cm^{-1}; MS (EI) 229 (8, M^+), 211 (41), 183 (41), 155 (22), 154 (36), 75 (100). Anal. Calcd for $C_{13}H_{11}N_1O_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 67.44; H, 4.82; N, 5.97.

***N*-Methoxy-*N*-methyl-2-(benzyloxy)nicotinamide (14).** To a mixture of 2-(benzyloxy)nicotinic acid (**13**) (8.30 g, 36.2 mmol) and CH_2Cl_2 (45 mL) was added carbonyldiimidazole (5.83 g, 36.0 mmol). The solution was stirred for 15 min and then transferred to a stirred suspension of *N,O*-dimethylhydroxylamine hydrochloride (3.85 g, 39.5 mmol) in CH_2Cl_2 (15 mL). After the solution was stirred at room temperature for 24 h, the solution was diluted with ether (150 mL) and extracted twice with 75-mL portions of 0.25 N HCl. The aqueous phase was extracted with CH_2Cl_2 (100 mL) and the combined organics were washed twice with 75-mL portions of saturated aqueous $NaHCO_3$. Concentration and Kugelrohr distillation (185 °C, 0.65 Torr) afforded **14** (8.47 g, 86%) as a clear viscous oil: R_f = 0.22 (1/1 ethyl acetate:hexanes); ^1H NMR ($CDCl_3$) δ 8.22 (dd, 1H, J = 5.0, 1.7 Hz), 7.64 (d, 1H, J = 7.0 Hz), 7.55–7.25 (m, 5H), 6.95 (dd, 1H, J = 7.0, 5.0 Hz), 5.43 (s, 2H), 3.48 (3H, br s), 3.29 (3H, br s); ^{13}C NMR ($CDCl_3$) δ 159.1, 147.7, 136.9, 136.8, 128.1, 127.6, 127.5, 127.4, 119.4, 116.4, 77.2, 67.5, 6 0.9; IR (neat) 3298, 3062, 3032, 2936, 1655, 1583,

1362, 1302, 1260, 987, 893, 778, 738 cm^{-1}; MS (EI) 272 (0.10, M$^+$), 212 (61.9), 135 (15.4), 122 (4.0), 91 (100); HRMS (CI/NH_3) calcd for $C_{15}H_{17}N_2O_3$ 273.1244, found 273.1239. Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 66.01; H, 5.90; N, 10.09.

1-(3-(2-(Benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-2-propyn-1-one (15). To a 0 °C solution of 2-(benzyloxy)-6-ethynylpyridine[27] (3.26 g, 15.6 mmol) in THF (50 mL) was added vinylmagnesium bromide (22 mL of an 0.8 M solution in THF, 18 mmol), and the solution was allowed to warm to ambient temperature over 1 h. A solution of amide 14 (2.70 g, 9.92 mmol) in THF (50 mL) was added and the mixture heated to a gentle reflux for 4 h. The mixture was poured into a mixture of ethanol (200 mL) and 1 N HCl (100 mL) and extracted with three 400-mL portions of CH_2Cl_2. The combined organics were washed with saturated aqueous NaCl (500 mL), dried over Na_2SO_4, and concentrated to give 5.67 g of a brown oil. Column chromatography over silica gel (300 g, 0–20% ether in petroleum ether) gave ketone 15 as a light yellow solid (3.09 g, 74%): R_f = 0.53 (1/1 ether:hexanes); mp 92.5–94.5 °C; ^{1}H NMR ($CDCl_3$) δ 8.43–8.35 (m, 2H), 7.6–7.2 (m, 11 H), 7.05 (dd, 1H, J = 7.2, 5.1 Hz), 6.96 (d, 1H, J = 7.2 Hz), 6.85 (d, 1H, J = 8.2 Hz), 5.58 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 192.7, 182.9, 163.5, 162.0, 152.0, 141.2, 138.5, 137.9, 137.0, 136.8, 131. 9, 128.4, 128.3, 128.1, 127.9, 127.8, 127.6, 122.5, 120.9, 116.9, 113.4, 68.4, 68.0; IR (KBr) 3060, 3030, 2926, 2206, 1613, 1584, 1454, 1440, 1251, 1050, 982, 773, 702 cm^{-1}; MS (EI) 420 (1.04, M$^+$), 419 (2.7), 329 (21.9), 212 (7.81), 208 (15.5), 122 (14.7), 91 (100). Anal. Calcd for $C_{27}H_{20}N_2O_3$: C, 77.13; H, 4.79; N, 6.66. Found: C, 77.05; H, 4.83; N, 6.67.

3-[3-(1,6-Dihydro-1-methyl-6-oxo-2-pyridinyl)propyl]-1-methyl-2(1*H*)-pyridone (6c). To a solution of ketone 15 (939.8 mg, 2.24 mmol) in ethanol (5 mL) at ambient temperature was added sodium borohydride (169.1 mg, 4.47 mmol). After 2 h of stirring, the mixture was concentrated under vacuum and then partitioned between water (50 mL) and ether (50 mL). The organic layer was washed with 10% HCl (50 mL) and saturated aqueous NaCl (50 mL), dried over $MgSO_4$, and concentrated to give a yellow oil (966.8 mg). Flash chromatography (1/9 ethyl acetate:hexane) gave 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-2-propyn-1-ol as a colorless oil (757 mg, 80%): R_f = 0.44 (1/1 ether:hexanes); ^{1}H NMR ($CDCl_3$) δ 8.17 (dd, 1H, J = 5.0, 1.8 Hz), 7.92 (dd, 1H, J = 7.3, 1.8 Hz), 7.6–7.3 (m, 11H), 7.03 (d, 1H, J = 7.4 Hz), 6.97 (dd, 1H, J = 7.4, 5.0 Hz), 6.77 (d, 1H, J = 8.1 Hz), 5.88 (d, 1H, J = 6.1 Hz), 5.52 (s, 2H), 5.36 (s, 2H), 3 .16 (d, 1H, J = 6.1 Hz); ^{13}C NMR ($CDCl_3$) 163.3, 160.5, 146.7, 139.5, 138.5, 137.1, 136.5, 130.3, 128.5, 128.4, 128.3, 128.1, 127.83, 127.77, 122.9, 120.9, 117.3, 111.7, 86.9, 85.7, 77.0, 67.8, 61.1; IR (neat) 3380, 3063, 3031, 2936, 2232, 1587, 1569, 1440, 1319, 1252, 1235, 1019, 984 cm^{-1}; MS (CI/NH_3) 423 (100, MH$^+$), 313 (20), 210 (55), 91 (83); HRMS (CI/NH_3) calcd for $C_{27}H_{23}N_2O_3$ 423.1709, found 423.1701.

To a solution of 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-2-propyn-1-ol (757.5 mg, 1.79 mmol) in acetic anhydride (5 mL) were added 10% palladium on carbon (75 mg) and two drops of trifluoroacetic acid. After 36 h of vigorous stirring at rt under H_2 (1 atm), the reaction mixture was filtered and concentrated under reduced pressure to give a brown oil. Addition of methanol (15 mL), potassium carbonate (5 g, 36 mmol), and iodomethane (1.2 mL, 19.3 mmol) was followed by heating to reflux for 10 h. The reaction mixture was cooled, concentrated, and partitioned between water (50 mL) and CH_2Cl_2 (50 mL). The organic layer was washed twice with 10% HCl (50 mL), dried over $MgSO_4$, and concentrated to give an oil. Flash chromatography (1/19 methanol:ethyl acetate) afforded 6c as a colorless solid (341.8 mg, 74%): R_f = 0.34 (1/4 methanol:ethyl acetate); mp 185.0–187.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.15–7.21 (m, 3 H), 6.40 (d, 1 H, J = 9 Hz), 6.07 (dd, 2 H, J = 6.8, 13.6 Hz), 3.51 (s, 3 H), 3.48 (s, 3 H), 2.57–2.66 (m, 4 H), 1.87–1.95 (m, 2 H); ^{13}C NMR δ 164, 162.8, 149.8, 138.5, 136.4, 136.2, 132.2, 117.2, 105.5, 105.4, 37.6, 33.3, 30.7, 30.6, 26.5; IR (KBr) 3486, 3072, 3044, 2970, 2344, 1980, 1873, 1853, 1820, 1645, 1610, 1577, 1474, 1432, 1408, 1378, 1332, 1309, 1280, 1227, 1196, 1175, 1148, 1134, 1107, 1035 cm^{-1}; UV 232 nm (ϵ = 10 300), 308 nm (ϵ = 14 300); MS (EI) 258 (20, M$^+$), 137 (10), 136 (100), 134 (8), 123 (11), 94 (6), 85 (20), 83 (29); HRMS (EI) calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1362.

1-(3-(2-(Benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanol (16). To a solution of ynone 15 (500 mg, 1.19 mmol) in ethanol:THF (1/1, 22 mL) was added Raney nickel (16 drops of a commercial 50% aqueous slurry), and the mixture was stirred under 1 atm of hydrogen for 3 h. Filtration through Celite and concentration gave 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanone (503 mg, 99.6%) as a pale yellow gum which was homogeneous by TLC and NMR: R_f = 0.59 (1/1 ether:hexanes); ^{1}H NMR ($CDCl_3$) δ 8.30 (dd, 1H, J = 4.8, 1.9 Hz), 8.15 (dd, 1H, J = 7.5, 1.9 Hz), 7.46–7.22 (m, 11H), 6.98 (dd, 1H, J = 7.5, 4.8 Hz), 6.67 (d, 1H, J = 7.2 Hz), 6.59 (d, 1H, J = 8.2 Hz), 5.50 (s, 2H), 5.18 (s, 2H), 5.50 (t, 2H, J = 7.2 Hz), 3.09 (t, 2H, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 199.8, 162.9, 161.4, 158.3, 150.5, 140.0, 138.8, 137.6, 136.7, 128.4, 128.3, 128.1, 127.9, 127.6, 121.7, 117.3, 117.2, 115.4, 108.0, 68.3, 67.1, 42.4, 31.7; IR (KBr) 3057, 3032, 2959, 2940, 2882, 1670, 1578, 1450, 1428, 1314, 1245, 1003 cm^{-1}; MS (CI/NH_3) 425 (62, MH$^+$), 300 (26), 256 (100), 239 (51), 212 (65), 195 (36), 168 (45); HRMS (CI/NH_3) calcd for $C_{27}H_{25}N_2O_3$ 425.1865, found 425.1854.

To a solution of 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanone (460 mg, 1.08 mmol) in ethanol:THF (2/1, 15 mL) was added $NaBH_4$ (46 mg, 1.22 mmol). The solution was stirred for 4.5 h, cooled to 0 °C, and quenched with 1 N HCl (10 mL). Water (50 mL) was added and the mixture was extracted with five 50-mL portions of ether. Saturated aqueous NaCl (75 mL) was added to the aqueous phase and it was further extracted with three 75-mL portions of CH_2Cl_2. The combined organics were dried over $MgSO_4$ and concentrated to give 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanol (16) as a yellow semisolid (457 mg, 99%): R_f = 0.39 (1/1 ether:hexanes); ^{1}H NMR ($CDCl_3$) δ 8.07 (d, 1H, J = 4.9 Hz), 7.75 (d, 1H, J = 7.0 Hz), 7.5–7.25 (m, 11H), 6.92 (t, 1H, J = 5.7 Hz), 6.71 (d, 1H, J = 7.0 Hz), 6.64 (d, 1H, J = 8.2 Hz), 5.42 (s, 2H), 5.35 (s, 2H), 5.01 (m, 1H), 4.6 (bs, 1H), 2.87 (t, 2H, J = 6.4 Hz), 2.29 (m, 1H), 2.11 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 163.1, 160.0, 159.1, 145.0, 139.2, 137.5, 137.3, 135.4, 128.4, 127.9, 127.8, 127.7, 127.6, 127.5, 127.3, 117.2, 115.7, 108.5, 68.7, 67.6, 67.4, 35.5, 33.9; IR (neat) 3372, 3065, 3033, 2931, 2359, 1591, 1577, 1448, 1355, 1303, 1247, 1019, 786 cm^{-1}; MS (CI/NH_3) 427 (100, MH$^+$), 411 (16), 319 (17), 199 (16), 91 (49); HRMS (CI/NH_3) calcd for $C_{27}H_{27}N_2O_3$ 427.2022, found 427.2037.

3-[3-(1,6-Dihydro-1-methyl-6-oxo-2-pyridinyl)-1-hydroxypropyl]-1-methyl-2(1*H*)-pyridone (7c). To a solution of 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanol (16) (102 mg, 0.239 mmol) in ethanol:THF (1/1, 4 mL) was added 10% Pd on $CaCO_3$ (12 mg). After 14 h of stirring at rt under 1 atm of hydrogen, the mixture was filtered through Celite. Concentration gave 3-[3-(1,6-dihydro-6-oxo-2-pyridinyl)-1-hydroxypropyl]-2(1*H*)-pyridone (7a) (53 mg) as a hygroscopic, nearly colorless foam. An analytical sample was prepared by recrystallization from methanol/heptane: R_f = 0.23 (1/9 methanol:CH_2Cl_2); mp 182 °C; ^{1}H NMR (1/1 methanol-d_4:$CDCl_3$) δ 7.69 (dd, 1H, J = 6.6, 1.2 Hz), 7.45 (dd, 1H, J = 9.0, 7.0 Hz), 7.32 (dd, 1H, J = 6.4, 1.8 Hz), 6.43–6.37 (m, 2H), 4.84 (dd, 1H, J = 8.3, 3.4 Hz), 4.53 (s, 1H), 2.81–2.75 (m, 2H), 2.23–2.09 (m, 1H), 2.00–1.87 (m, 1H); ^{13}C NMR (1/1 methanol-d_4:$CDCl_3$) δ 163.5, 163.0, 149.1, 142.0, 136.6, 132.5, 131.9, 116.2, 106.8, 105.7, 67.9, 34.9, 29.1; IR (KBr) 3429, 1706, 1654, 1558, 1420, 1375, 1188, 1128, 1076, 900 cm^{-1}; MS (EI) 228 (M – H_2O, 52), 124 (53), 122 (100), 120 (92), 109 (91), 104 (53), 96 (57).

To a solution of 3-[3-(1,6-dihydro-6-oxo-2-pyridinyl)-1-hydroxypropyl]-2(1*H*)-pyridone (7a) (110 mg, 0.447 mmol) in methanol (30 mL) were added iodomethane (1.30 g, 9.16 mmol) and anhydrous potassium carbonate (1.30 g, 9.41 mmol). The mixture was stirred at rt for 36 h and then filtered through Celite. The filtrate was washed with saturated aqueous NaCl (100 mL), the aqueous layer was extracted with CH_2Cl_2 (100 mL), and the combined organics were dried with $MgSO_4$. Concentration and chromatography (0–5% gradient of methanol in CH_2Cl_2) gave 3-[3-(1,6-dihydro-1-methyl-6-oxo-2-pyridinyl)-1-hydroxypropyl]-1-methyl-2(1*H*)-pyridone (7c) (66 mg, 54%) as a pale yellow solid: R_f = 0.54 (1/9 methanol:CH_2Cl_2); mp 139–140 °C; ^{1}H NMR ($CDCl_3$) δ 7.29 (d, 1H, J = 2.5 Hz), 7.27 (t, 1H, J = 2.8 Hz), 7.22 (d, 1H, J = 2.1 Hz), 6.45 (d, 1H, J = 9.3 Hz), 6.08 (d, 1H, J = 6.7 Hz), 4.64 (d, 1H, J = 3.8 Hz), 4.61 (d, 1H, J = 3.7 Hz), 3.58 (s, 3H), 3.56 (s, 3H), 2.74 (m, 1H), 2.96 (m, 1H), 2.16 (m, 1H), 2.00

(m, 1H), 1.8 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 164.1, 162.6, 149.9, 138.7, 137.1, 135.2, 133.2, 117.3, 106.1, 106.0, 71.4, 37.4, 34.3, 31.0, 30.0; IR (KBr) 3354, 1649, 1567, 1408, 1079, 791, 773 cm^{-1}; MS (EI) 274 (0.4), 249 (1.2), 205 (1.9), 167 (5.1), 149 (31), 136 (100), 123 (40), 100 (28); HRMS (CI/NH_3) calcd for $C_{15}H_{19}N_2O_3$ 275.1396, found 275.1409.

3-[3-(1,6-Dihydro-1-methyl-6-oxo-2-pyridinyl)-1-((dimethyl(1,1-dimethylethyl)silyl)oxy)propyl]-1-methyl-2(1*H*)-pyridone (8c). To a solution of 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-propanol (**16**) (130 mg, 0.305 mmol) in acetonitrile (2 mL) were successively added *tert*-butyldimethylchlorosilane (230 mg, 1.52 mmol) and imidazole (206 mg, 3.02 mmol). After 3 h at rt, the solvent was removed on a rotary evaporator and the residue was purified by column chromatography (0–25% gradient of ether in hexanes). Concentration gave 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-((dimethyl(1,1-dimethylethyl)silyl)oxy)propane as a pale yellow waxy glass (148 mg, 90%): R_f = 0.75 (1/1 ether:hexanes); ^{1}H NMR ($CDCl_3$) δ 8.09 (dd, 1H, *J* = 5.0, 1.9 Hz), 7.83 (dd, 1H, *J* = 7.3, 1.7 Hz), 7.5–7.1 (m, 11H), 6.95 (dd, 1H, *J* = 7.3, 5.0 Hz), 6.65 (d, 1H, *J* = 7.5 Hz), 6.56 (d, 1H, *J* = 8.2 Hz), 5.44 (s, 2H), 5.32 (s, 2H), 5.19 (dd, 1H, *J* = 6.6, 4.2 Hz), 2.9–2.65 (m, 2H), 2.3–2.03 (m, 2H), 0.94 (s, 9H), 0.08 (s, 3H), –0.10 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 162.9, 159.7, 159.4, 144.9, 138.7, 138.6, 137.7, 137.6, 135.7, 128.4, 128.3, 128.1, 128.0, 127.6, 127.4, 117.1, 117.0, 115.2, 107.8, 67.9, 67.3, 67.2, 37.6, 33.4, 18.2, –4.7, –5.0; IR (neat) 3064, 3030, 2954, 2928, 2855, 1590, 1574, 1447, 1432, 1251, 1087, 1020 cm^{-1}; MS (CI/NH_3) 541 (9, MH^+), 402 (100), 344 (31), 91 (30); HRMS (CI/NH_3) calcd for $C_{33}H_{41}N_2O_3Si$ 541.2886, found 541.2877.

To a solution of 1-(3-(2-(benzyloxy)pyridyl))-3-(6-(2-(benzyloxy)pyridyl))-1-((dimethyl(1,1-dimethylethyl)silyl)oxy)propane (148 mg, 0.274 mmol) in ethanol:THF (1/1, 6 mL) was added 10% palladium on $CaCO_3$ (18 mg), and the mixture stirred under 1 atm of hydrogen for 3 h. Filtration through Celite and concentration gave 3-[3-(1,6-dihydro-6-oxo-2-pyridinyl)-1-((dimethyl(1,1-dimethylethyl)silyl)oxy)propyl]-2(1*H*)-pyridone (**8a**) (95 mg, 96%) as a nearly colorless glassy solid: R_f = 0.41 (1/9 methanol:CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 14.4 (bs, 1H), 13.3 (bs, 1H), 7.62 (d, 1H, *J* = 6.9, 1.6 Hz), 7.38 (dd, 1H, *J* = 9.0, 6.9 Hz), 7.31 (d, 1H, *J* = 5.7 Hz), 6.36 (d, 1H, *J* = 9.0 Hz), 6.28 (t, 1H, *J* = 6.7 Hz) , 6.11 (d, 1H, *J* = 6.8 Hz), 5.15 (dd, 1H, *J* = 8.8, 2.9 Hz), 2.92–2.78 (m, 1H), 2.75–2.62 (m, 1H), 2.35–2.22 (m, 1H), 1.84–1.71 (m, 1H), 0.96 (s, 9H), 0.12 (s, 3H), –0.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.2, 163.6, 150.6, 142.0, 136.6, 135.5, 133.0, 116.4, 106.6, 105.7, 68.1, 38.8, 26.0, 25.8, 18.2, –4.6, –5.1; IR (neat) 3272, 3127, 2948, 1645, 1612, 1561, 1455, 1162, 1068, 1007 cm^{-1}; MS (EI) 327 (3), 303 (8), 285 (81), 239 (47), 75 (100), 73 (72); HRMS (FAB) calcd for $C_{19}H_{29}N_2O_3Si$ 361.1947, found 361.1933.

To a solution of 3-[3-(1,6-dihydro-6-oxo-2-pyridinyl)-1-((dimethyl(1,1-dimethylethyl)silyl)oxy)propyl]-2(1*H*)-pyridone (**8a**) (815 mg, 2.26 mmol) in methanol (150 mL) were added successively anhydrous K_2CO_3 (6.42 g, 45.2 mmol) and iodomethane (6.25 g, 45.2 mmol). After 36 h of stirring at rt, the volatiles were removed on a rotary evaporator and the residue was taken up in three 100-mL portions of hexane:ether (1/1) and filtered. The combined filtrates were concentrated and then purified by radial chromatography (2–16% gradient of methanol in CH_2Cl_2) to yield **8c** as a colorless solid (501 mg, 57%): R_f = 0.53 (1/9 methanol:CH_2Cl_2); mp 133–134 °C; ^{1}H NMR ($CDCl_3$) δ 7.52 (d, 1H, *J* = 6.6 Hz), 7.26–7.16 (m, 2H), 6.41 (d, 1H, *J* = 9.0 Hz), 6.22 (t, 1H, *J* = 6.6 Hz), 5.05 (dd, 1H, *J* = 6.1, 2.6 Hz), 3.55 (s, 3H), 3.50 (s, 3H), 2.76–2.57 (m, 2H), 2.14–1.99 (m, 1H), 1.95–1.81 (m, 1H), 0.93 (s, 9H), 0.06 (s, 3H), –0.07 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 163.9, 161.1, 150.1, 138.4, 136.5, 134.8, 134.6, 117.0, 105.4, 105.3, 68.4, 37.2, 35.0, 30.6, 29.1, 25.7, 18.0, –4.8, –5.2; IR (KBr) 3074, 2953, 2927, 2854, 1651, 1601, 1580, 1560, 1251, 1092, 981 cm^{-1}; MS (CI/NH_3) 389 (36, MH^+), 257 (100), 136 (13), 124 (13); HRMS (CI/NH_3) calcd for $C_{21}H_{33}N_2O_3Si$ 389.2260, found 389.2249.

Photocycloaddition of 6c. A stream of dry nitrogen was bubbled through a solution of bis(2-pyridone) **6c** (140.2 mg, 0.54 mmol) in methanol (10 mL, 0.05 M) in a Pyrex test tube for several minutes and the tube was then affixed with a septum and a nitrogen balloon. This solution was irradiated for 8 h, concentrated in vacuo, and chromatographed (1/19 methanol:ethyl acetate) to give two [4 + 4] products.

9c-t: 79.6 mg, 57%; R_f = 0.21 (1/19 methanol:ethyl acetate); mp 162.5–163.5 °C; ^{1}H NMR ($CDCl_3$) δ 6.52 (dd, 1 H, *J* = 6.8, 8.3 Hz), 6.15 (m, 2H), 5.84 (dd, 1H, *J* = 1.2, 8.3 Hz), 3.93 (ddd, 1H, *J* = 1.2, 6.8, 9.9 Hz), 3.56 (ddd, 1H, *J* = 1.9, 6.8, 9.9 Hz), 2.83 (s, 3H), 2.82 (s, 3H), 2.76–2.81 (m, 1H), 2.24–2.33 (m, 1H), 1.79–2.04 (m, 3H), 1.43–1.52 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 175.3, 174.9, 143.2, 136.8, 134.0, 127.6, 74.5, 65.0, 57.8, 50.1, 36.9, 36.2, 35.4, 31.1, 26.2; IR (KBr) 3452, 2954, 2882, 2360, 1652, 1457, 1396, 1381, 1256, 1207, 1070, 1049, 983, 924, 869, 803 cm^{-1}; MS (EI) 258 (M^+, 9), 136 (100), 123 (16), 122 (6); UV 214 nm (ε = 2600), 230 nm (ε = 16 500); HRMS (CI/NH_3) calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1360. Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.85. Found; C, 69.41; H, 7.13; N, 10.63.

9c-c: 38.3 mg, 27%; R_f = 0.32 (1/19 methanol:ethyl acetate); mp 90.0–91.0 °C; ^{1}H NMR ($CDCl_3$) δ 6.06–6.15 (m, 2H), 5.89–5.93 (m, 2H), 4.09 (ddd, 1 H, *J* = 1.5, 6.8, 10.0 Hz), 3.61 (ddd, 1H, *J* = 1.6, 7.1, 10.0 Hz), 2.96 (s, 3H), 2.89 (s, 3H), 2.65–2.73 (m, 1H), 2.36–2.43 (m, 1H), 1.66–2.03 (m, 3H), 1.23–1.55 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 174.2, 174.0, 141.7, 140.0, 132.1, 130.2, 77.2, 66.5, 60.5, 51.5, 37.3, 35.3, 34.6, 28.4, 26.1; IR (KBr) 3515–3510, 2965, 2924, 1643, 1469, 1436, 1418, 1398, 1382, 1360, 1293, 1251, 1219, 1128, 1073, 1055, 1015, 980, 950, 903, 874, 848, 807 cm^{-1}; UV 210 nm (ε = 4410), 248 nm (ε = 1170); MS (20 eV, EI) 258 (M^+, 8), 207 (2), 136 (100), 123 (11); HRMS (20 eV, EI) calcd for $C_{15}6H_{19}N_2O_3$ 258.1368, found 258.1371.

Photocycloaddition of 7b. A stream of dry nitrogen was bubbled through a solution of bis(2-pyridone) **7b** (95.6 mg, 0.367 mmol) in methanol (20 mL, 0.02 M) in a Pyrex test tube for 20 min and the tube was then affixed with a septum and a nitrogen balloon. The tube was taped to the side of the quartz cooling jacket and irradiated for 5 h. By TLC the clear and colorless solution was found to contain no starting material. The mixture was concentrated *in vacuo* and purified by flash chromatography (1.5– × 17-cm column, eluting with 7/93 (v/v) methanol/CH_2Cl_2). Collection gave four compounds:

10b-cs: 3.7 mg, 4%; R_f = 0.53 (1/9 methanol:CH_2Cl_2); ^{1}H NMR (methanol-d_4) δ 6.28 (d, 1H, *J* = 8.2 Hz), 6.25 (d, 1H, *J* = 8.2 Hz), 6.13 (dd, 1H, *J* = 8.2, 1.4 Hz), 6.06 (dd, 1H, *J* = 8.2, 1.5 Hz), 4.29 (ddd, 1 H, *J* = 10.1, 6.8, 1.4 Hz), 4.1 (m, 1H), 3.45 (ddd, 1 H, *J* = 10.1, 7.0, 1.5 Hz), 3.34 (s, 3H), 1.55 (m, 2H), 1.90 (m, 2H); ^{13}C NMR (methanol-d_4) δ 177.9, 177.8, 140.8, 140.4, 133.7, 133.3, 81.5, 72.3, 67.2, 61.1, 51.9, 35.5, 34.0, 33.6; MS (CI/NH_3) 261 (100, MH^+), 243 (93), 152 (24), 122 (24); HRMS (CI/NH_3) calcd for $C_{14}H_{17}N_2O_3$ 261.1239, found 261.1253.

10b-ts: 5.8 mg, 6%; R_f = 0.49 (1/9 methanol:CH_2Cl_2); solid, mp 188–189 °C dec; ^{1}H NMR (DMSO-d_6) δ 7.9 (bs, 1H), 6.60 (t, 1H, *J* = 7.5 Hz), 6.27 (d, 1H, *J* = 8.0 Hz), 6.15 (t, 1H, *J* = 7.5 Hz), 5.89 (d, 1 H, *J* = 8.8 Hz), 5.71 (d, 1H, *J* = 8.1 Hz), 4.15 (dd, 1H, *J* = 6.7, 9.7 Hz), 3.96 (m, 1H), 3.3 (m, 1H), 2.67 (s, 3H), 2.0–1.6 (m, 3H); ^{13}C NMR (DMSO-d_6) δ 176.7, 176.0, 142.0, 137.2, 134.7, 128.3, 79.3, 67.6, 63.6, 57.5, 50.3, 34.8, 33.5, 32.7; IR (KBr) 3503, 3190, 3058, 1671, 1623, 1438, 1400, 1251, 1093, 1036, 795, 674 cm^{-1}; MS (EI) 242 (M^+ – 18, 0.8), 187 (1), 152 (9), 139 (30), 138 (21), 134 (20), 123 (17), 122 (100), 110 (16).

10b-ca: 13.6 mg, 14%; R_f = 0.36 (1/9 methanol:CH_2Cl_2); solid, mp 205 °C dec; ^{1}H NMR (methanol-d_4) δ 6.50 (dd, 1H, *J* = 8.5, 1.5 Hz), 6.20 (m, 2H), 6.08 (dd, 1 H, *J* = 8.2, 1.5 Hz), 4.73 (dd, 1H, *J* = 6.3, 4.8 Hz), 4.28 (ddd, 1H, *J* = 10.0, 6.8, 1.5 Hz), 3.43 (ddd, 1H, *J* = 10.0, 6.8, 1.5 Hz), 2.95 (s, 3H), 2.1 (m, 2H), 1.8 (m, 2H); MS (CI/NH_3) 261 (64, MH^+), 243 (100), 110 (70); HRMS (CI/NH_3) calcd for $C_{14}H_{17}N_2O_3$ 261.1239, found 261.1250.

10b-ta: 65.7 mg, 69%; R_f = 0.31 (1/9 methanol/CH_2Cl_2); solid, mp 202–204 °C; ^{1}H NMR (DMSO-d_6) δ 7.9 (bs, 1H), 6.52 (t, 1H, *J* = 8 Hz), 6.20 (d, 1H, *J* = 7.8 Hz), 6.1 (m, 2H), 4.96 (d, 1H, *J* = 4.8 Hz), 4.6 (m, 1H), 4.08 (dd, 1H, *J* = 6.7, 9.7 Hz), 3.3 (m, 1H), 2.64 (s, 3H), 1.9–1.6 (m, 3H); ^{13}C NMR (DMSO-d_6) 176.3, 174.5, 142.0, 132.8, 132.5, 128.1, 71.5, 68.3, 67.0, 57.4, 50.7, 35.3, 34.1, 32.8; IR (KBr) 3300, 3230, 1660, 1630, 1480, 1395, 1120, 1060 cm^{-1}; MS (EI) 242 (M^+ – 18, 1.1), 152 (11), 139 (44), 138 (30), 136 (17), 134 (28), 123 (22), 122 (100). Anal. Calcd for $C_{14}H_{16}H_2O_3$: C, 64.60; H, 6.20; N, 10.76. Found: C, 64.77; H, 6.13; N, 10.69.

Photocycloaddition of 7c. As described for **7b**, irradiation of **7c** gave four isomers of **10c**:

10c-cs: R_f = 0.50 (6/94 methanol:CH_2Cl_2); mp 137.5–138.5 °C; ^{1}H NMR (methanol-d_4) δ 6.22 (m, 2H), 6.04 (m, 2H), 4.30 (ddd, 1H, *J* = 9.0, 6.6, 0.9 Hz), 4.18 (t, 1H, *J* = 4.8 Hz), 3.62 (ddd, 1H,

J = 9.0, 6.9, 1.7 Hz), 2.93 (s, 3H), 2.92 (s, 3H), 1.99 (m, 2H), 1.88 (m, 2H); IR (KBr) 3450, 2960, 1660, 1630, 1400, 800, 606 cm^{-1}; MS (DEI) 275 (9), 257 (5), 152 (10), 136 (100); HRMS (DEI) calcd for $C_{15}H_{19}N_2O_3$ 275.1396, found 275.1404.

10c-ts: R_f = 0.44 (6/94 methanol:CH_2Cl_2); ^1H NMR (methanol-d_4) δ 6.61 (dd, 1H, J = 8.2, 6.8 Hz), 6.29 (m, 2H), 6.10 (dd, 1H, J = 8.3, 1.2 Hz), 4.16 (ddd, 1H, J = 10.0, 6.8, 1.3 Hz), 4.07 (dd, 1H, J = 10.0, 5.4 Hz), 3.57 (m, 1H), 2.83 (s, 3H), 2.80 (s, 3H), 2.36 (m, 1H), 2.23 (m, 1H), 2.10 (m, 1H), 1.90 (ddd, 1H, J = 12.7, 5.5, 2.7 Hz); IR (KBr) 3401, 2966, 1655, 1628, 1437, 1055, 1002, 814, 709, 615 cm^{-1}; MS (CI/NH_3) 275 (100, MH^+), 259 (12), 136 (46); HRMS (CI/NH_3) calcd for $C_{15}H_{19}N_2O_3$ 275.1396, found 275.1409.

10c-ca: R_f = 0.31 (6/94 methanol:CH_2Cl_2); mp 183 °C dec; ^1H NMR (methanol-d_4) δ 6.5 (dd, 1H, J = 8.5, 1.5 Hz), 6.20 (m, 2H), 6.02 (dd, 1H, J = 8.3, 1.7 Hz), 4.75 (dd, 1H, J = 7.6, 4.8 Hz), 4.29 (ddd, 1H, J = 10.1, 6.7, 1.5 Hz), 3.60 (ddd, 1H , J = 10.1, 7.0, 1.6 Hz), 2.92 (s, 3H), 2.86 (s, 3H), 2.37 (m, 1H), 2.13 (m, 1H), 1.97 (m, 1H), 1.77 (m, 1H).

10c-ta: R_f = 0.26 (6/94 methanol:CH_2Cl_2); mp 189–190 °C; ^1H NMR (methanol-d_4) δ 6.56 (dd, 1H, J = 8.5, 6.7 Hz), 6.38 (dd, 1H, J = 8.5, 1.4 Hz), 6.22 (m, 2H), 4.61 (t, 1H, J = 3.6 Hz), 4.12 (ddd, 1 H, J = 9.8, 6.7, 1.4 Hz), 3.55 (ddd, 1H, J = 9.8, 6.2, 2.4 Hz), 2.82 (s, 3H), 2.78 (s, 3H), 2.58 (m, 1H), 2.17 (m, 1H), 1.92 (m, 1H), 1.77 (m, 1H); IR (KBr) 3356, 2921, 1654, 1631, 1483, 1374, 1111, 1065, 1042, 808, 711 cm^{-1}; MS (CI/NH_3) 275 (30, MH^+), 257 (11), 152 (12), 136 (100); HRMS (CI/NH_3) calcd for $C_{15}H_{19}N_2O_3$ 275.1396, found 275.1399.

Photocycloaddition of 8c. A solution of **8c** (97.0 mg, 0.250 mmol) in methanol (12 mL, 0.02 M) was irradiated for 4 h. Preparative TLC (1/19 methanol:ethyl acetate) gave **11c-ta** (56.7 mg, 58%), **11c-ca** (28.6 mg, 29%), and a third compound tentatively identified as a syn isomer (1.4 mg, 1%). Irradiation of **8c** (112 mg, 0.288 mmol) in CH_2Cl_2 (13 mL, 0.02 M) for 5 h gave **11c-ta** (69 mg, 62%) and **11c-ca** (26.4 mg, 24%) as a mixture with **23**.

11c-ca: R_f = 0.39 (1/19 methanol:ethyl acetate); ^1H NMR ($CDCl_3$) δ 6.51 (dd, 1H, J = 8.5, 1.1 Hz), 6.17–6.09 (m, 2H), 5.91 (dd, J = 8.2, 1.4 Hz), 4.83 (dd, 1H, J = 5.7, 5.0 Hz), 4.11 (ddd, 1H, J = 9.9, 6.8, 1.4 Hz), 3.63 (t, 1H, J = 8.5), 2.98 (s, 3H), 2.91 (s, 3H), 2.37–2.27 (m, 1H), 2.21–2.11 (m, 1H), 1.98–1.89 (m, 1H), 1.80–1.71 (m, 1H), 0.88 (s, 9H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C ($CDCl_3$) δ 174.5, 173.4, 140.0, 136.1, 132.1, 128.9, 73.4, 69.5, 60.3, 51.4, 34.4, 32.3, 29.9, 28.6, 25.8, –4.7, –4.8; IR (KBr) 2952, 2926, 2855, 1666, 1655, 1463, 1251, 1447, 1112, 838 cm^{-1}.

11c-ta: R_f = 0.30 (1/19 methanol:ethyl acetate); mp 184–185 °C; ^1H NMR ($CDCl_3$) δ 6.56 (dd, 1H, J = 8.5, 6.7 Hz), 6.29 (dd, 1H, J = 7.5, 1.1 Hz), 6.18–6.13 (2H, m), 4.67 (1H, t, J = 2.4 Hz), 3.93 (ddd, 1H, J = 9.8, 6.7, 1.1 Hz), 3.59–3.52 (m, 1H), 2.83 (s, 3H), 2.80 (s, 3H), 1.88 (ddt, 1H, 12.6, 5.8, 1.8), 1.72 (ddd, 1H, J = 12.6, 5.8, 1.8 Hz), 0.91 (s, 9H), 0.12 (s, 3H), 0.05 (s, 3H); ^{13}C ($CDCl_3$) δ 175.0, 174.6, 143.0, 133.2, 131.5, 127.8, 73.8 (two resonances), 68.9, 58.3, 50.2, 35.9, 34.3, 32.8, 30.7, 25.8, 18.0, –4.7, –5.0; IR (KBr) 2953, 2926, 2882, 2855, 1648, 1251, 1045, 834; MS (CI/NH_3) 389 (100, MH^+), 257 (60), 136 (44), 124 (59), 110 (40); HRMS (CI/NH_3) calcd for $C_{21}H_{33}N_2O_3Si$ 389.2260, found 389.2243.

Cyclobutane 23: R_f = 0.50 (1/19 methanol:ethyl acetate); ^1H NMR ($CDCl_3$) δ 6.17 (dd, 1H, J = 9.9, 4.6 Hz), 5.94 (m, 2H), 5.07 (dd, 1H, J = 10.0, 6.8 Hz), 4.73 (dd, 1H, J = 8.0, 4.6 Hz), 3.54 (dd, 1H, J = 9.2, 4.3 Hz), 3.25 (dd, 1H, J = 9.2, 4.3 Hz), 3.00 (s, 3H), 2.88 (s, 3H), 2.35–2.27 (m, 1H), 2.21–2.12 (m, 1H), 1.98–1.89 (m, 1H), 1.64–1.57 (m, 1H), 0.83 (s, 9H), 0.04 (s, 3H), –0.06 (s, 3H); ^{13}C ($CDCl_3$) δ 177.0, 163.1, 136.1, 130.5, 123.6, 102.5, 72.8, 60.4, 43.4, 35.2, 34.1, 33.9, 31.2, 29.9, 25.7, 24.5, 17.9, –4.9, –5.0; IR (neat) 2921, 2850, 1731, 1648, 1470, 1396, 1084, 836 cm^{-1}; MS (CI/NH_3) 389 (25, MH^+), 331 (68), 257 (67), 253 (100), 208 (28), 136 (83); HRMS (CI/NH_3) calcd for $C_{21}H_{33}N_2O_3Si$ 389.2260, found 389.2254.

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Supplementary Material Available: Proton NMR spectra for **6c**, **7a-c**, **8a**, **8c**, **13-16**, isomers of **9c**, **10b**, **10c**, and **11c** and intermediates (29 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.