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# Preparation and Intramolecular [2+2]-Photocycloaddition of 1,5-Dihydropyrrol-2-ones and 5,6-Dihydro-1*H*-pyridin-2-ones with C-, N-, and O-linked Alkenyl Side Chains at the 4-Position

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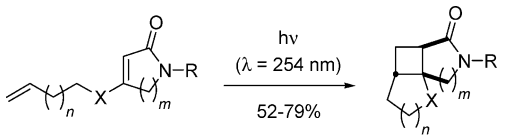


*n* = 1,2; *m* = 1,2; X = O, $CH_2$, $NCOOR^1$

The 1,5-dihydropyrrol-2-ones **2**, **6**, **9**, and **11** were prepared from methyl tetramates (**1a**−**c**), *N*-Boc-protected tetramic acid (**3**), or *N*-Boc-protected tetramic acid bromide (**7**) in short reaction sequences and in very good overall yields. The homologous 5,6-dihydro-1*H*-pyridin-2-ones **16**, **18**, **20**, **21**, **23**, and **27** were prepared along analogous routes starting from piperidin-2,4-dione (**19**) or from its *N*-*tert*-butyl derivative **15**. Optimized conditions for the [2+2]-photocycloaddition include the use of dichloromethane as the solvent and an irradiation with a mercury low-pressure lamp ($\lambda = 254$ nm). Upon applying these conditions at ambient temperature, the corresponding intramolecular photocycloaddition products **28**−**37** were obtained in good yields (52−79%) and with perfect diastereoselectivity. The constitution and configuration of the products was elucidated by NMR-spectroscopy. For the *O*-tethered substrates **2a** and **20**, a strong decrease of the photocycloaddition rate with temperature was observed. The effect was less pronounced for N- and C-tethered substrates **6**, **9**, **23**, and **27**. The use of a chiral complexing agent to achieve enantioselective reactions appears viable. Complexing agent (−)-**38**, however, is not suited because of its instability at $\lambda = 254$ nm.

## Introduction

The [2+2]-photocycloaddition reaction constitutes the easiest and most convenient access to cyclobutanes.[1] The key to a successful reaction is the activation of one of the olefin reaction partners by excitation with light. The α,β-unsaturated carbonyl group represents a commonly used chromophor, which exhibits a forbidden n$\pi$*-transition at relatively long wavelength. Intersystem crossing (ISC) is rapid and leads to a $\pi\pi$*-triplet state located mostly at the alkene part of the chromophor. Consecutive attack by another alkene moiety can occur either intra- or intermolecularly, leading to a 1,4-biradical, which yields the desired cyclobutane in a second C−C bond formation step.[2] To ensure a reasonable lifetime of the excited-state, cyclic five- or six-membered enones are preferred as substrates over noncyclic enones, which can undergo rapid energy dissipation by *E*/*Z*-isomerization. Due to their very general reactivity mode

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(2) For reviews of mechanistic studies on [2+2]-photocycloaddition reactions, see: (a) Schuster, D. I. In *CRC Handbook of Organic Photochemistry and Photobiology*, 2nd ed.; Horspool, W. M., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; pp 72.1−72.24. (b) Weedon, A. C. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, FL, 1995; pp 634−651. (c) Schuster, D. I. in *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song P.-S., Eds.; CRC Press: Boca Raton, FL, 1995; pp 652−669. (d) Mattay, J.; Conrads, R.; Hoffmann, R. In *Houben-Weyl Methods of Organic Chemistry*, 4th ed.; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, 1995; Vol. E 21c, pp 3085−3132. (e) Schuster, D. I.; Lem, G.; Kaprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3−22. (f) Gilbert, A.; Baggott, J. *Essentials of Molecular Photochemistry*; Blackwell Science Ltd: Oxford, 1991; pp 267−284.

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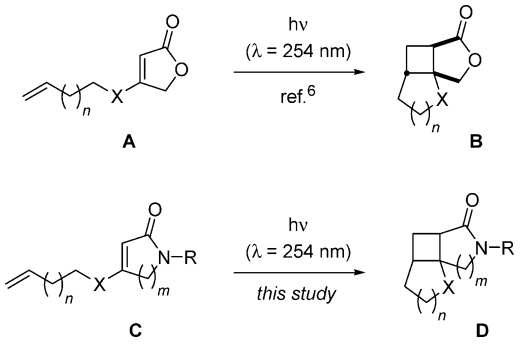
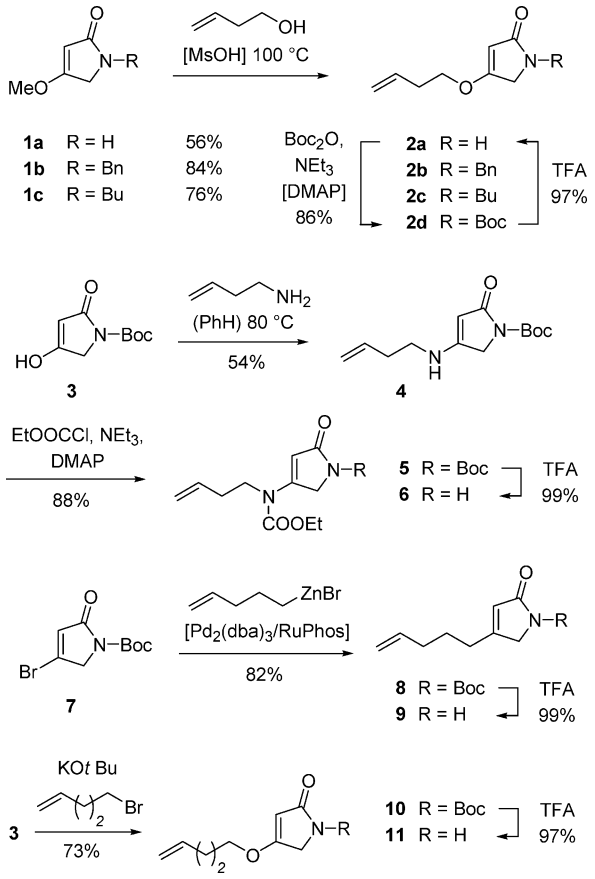
**SCHEME 1. Intramolecular [2+2]-Photocycloaddition of Tetronic Acid Derivatives A to Products B and of the Title Compounds C to the Products D**




and their high reliability, enone [2+2]-photocycloaddition reactions have been widely used in the synthesis of complex molecules.[3] If employed in the intramolecular mode, the reaction leads to annelated cyclobutanes, whereby the tether connecting the two reactive positions consists preferably of three or four atoms yielding five- or six-membered ring annelation products.

When replacing cyclic enones with α,β-unsaturated lactones or lactams as [2+2]-photocycloaddition substrates, one has to consider the shorter absorption wavelengths of the latter compound classes. Commonly, mercury low-pressure lamps are used as irradiation sources, which emit a sharp light band at $\lambda = 254$ nm. Provided that other functional groups in the starting materials and products are photochemically stable under these conditions, efficient [2+2]-photocycloaddition reactions of α,β-unsatured lactones or lactams are possible, and they can lead to valuable products.[4,5] In this context, we have discovered recently that *O*- and *N*-substituted 5*H*-furan-2-ones **A**, that is, the esters and amides of tetronic acids, undergo a clean and high yielding intramolecular [2+2]-photocycloaddition to the corresponding tricyclic racemic products **B** (Scheme 1).[6] Because the photocycloaddition proceeds with excellent simple diastereoselectivity and because the lactone ring is readily cleaved, compounds **B** represent attractive precursors for the stereoselective synthesis of 2-aza-bicyclo[3.2.0]heptanes ($n = 1$, X = NBoc) and 2-oxa-bicyclo[3.2.0]heptanes ($n = 1$, X = O). An application of this strategy to the synthesis of conformationally constrained β-amino acid derivatives has been described.[7] In addition, it has been shown that the regio- and diastereotopic discrimination of double bonds is possible in tetronate [2+2]-photocycloaddition reactions.[8]

**SCHEME 2. Synthesis of 1,5-Dihydropyrrol-2-ones 2, 6, 9, and 11 as [2+2]-Photocycloaddition Precursors**




In this paper, we describe an extension of our studies to tethered 1,5-dihydropyrrol-2-ones (**C**, $m = 1$, tetramic acid derivatives) and 5,6-dihydropyridin-2-ones (**C**, $m = 2$). In addition to variations previously performed with compounds **A**, the ring size *m* and the additional nitrogen substituent R were varied. The synthesis of the starting materials was elaborated, and optimized reaction conditions for the photocycloaddition were established. The relative configuration of products **D** was elucidated. Preliminary studies were conducted to evaluate the potential of free lactams (**C**, R = H) for enantioselective photochemical reactions in the presence of a chiral template.

## Results and Discussion

**Preparation of 1,5-Dihydropyrrol-2-ones.** The *N*-protected methyl tetramates **1** (Scheme 2) were prepared from methyl 4-bromo-3-methoxy-2-butenoate[9] and the corresponding amine. Although compounds **1a**[10] and **1b**[11] have been previously

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reported, the yet unknown *N*-butyl product **1c** was obtained in 70% yield. Transesterification to the photocycloaddition precursors **2a**−**c** was conducted at 100 °C in an excess of 3-buten-1-ol as the solvent employing methanesulfonic acid (MsOH) as the acidic catalyst. To provide alkenyl tetramate **1a** with a *N*-substituent that could be readily cleaved, we opted for a *tert*-butyloxycarbonyl (Boc) protection. The use of acetonitrile as solvent was decisive to obtain tetramate **2d** in high yields (86%).

Attempts to obtain alkenyl amides of tetramic acids (**C**, $m = 1$, X = N−R, Scheme 1) from methyl tetramates **1** by aminodemethoxylation failed. Although various procedures for the displacement of the methoxy group from methyl tetramates by nitrogen nucleophiles have been reported,[12] even the application of harsh conditions allowed no conversion to the desired products. Because tetronic acid bromide shows a strong propensity for nucleophilic substitution reactions by primary amines,[13] an access to the corresponding bromide of tetramic acid was desirable (*vide infra*). Attempts to adopt conditions reported for the conversion of 3-methoxy-2-cyclopentenone to its vinylogous bromide led to complete decomposition of methyl tetramates **1**.[14] Literature precedence for aminodehydroxylations of tetronic acids[15] and tetramic acids[16] encouraged us to choose the latter as precursors for the condensation with primary amines. Many examples for the hydrolysis of tetramic esters are reported.[17] Nevertheless, saponification of methyl tetramates **1** appeared to be problematic, due to the fact that numerous C-5 unsubstituted tetramic acids exhibit a strong tendency to self-dimerization.[16b,18] Therefore, the stable *N*-Boc-protected tetramic acid **3**[19] was selected as an easily accessible starting material for further transformations. The vinylogous amide **4** could be obtained by condensation of but-3-enyl amine[20] with acid **3** by refluxing in benzene for 4 h in a Dean−Stark apparatus. Acid-promoted aminodehydroxylation[21] and the application of microwave irradiation[22] led to more rapid transformations, but the product yields were lower. The necessity of a protecting group for the tether nitrogen atom in **4** was deduced from previous experience with photocycloaddition products of *N*-unprotected tetronic acid amides, which proved to be unstable and reacted further in a retro-Mannich reaction.[7,23] The choice of protecting group was guided by previous experience in our group.[7,24] Alkoxycarbonyl protecting groups such as *N*-*tert*-butyloxycarbonyl had turned out to be an excellent choice to allow for the otherwise impossible [2+2]-photocycloaddition reaction of enamines ($\lambda = 300-350$ nm).[25] The ethoxycarbonyl protecting group was chosen in this particular instance because of its high stability and its orthogonality to the Boc protecting group.[26] Amide **4** was easily protected using ethyl chloroformate in acetonitrile with an admixture of DMAP and $NEt_3$ furnishing protected amide **5** in 95% yield. Subsequent Boc-deprotection was performed with trifluoroacetic acid (TFA) at ambient temperature in dichloromethane in almost quantitative yield (99%).

Tetramic acid **3** could be transformed into the vinylogous bromide **7** (*vide supra*) by treatment with preformed Vilsmeier reagent from oxalyl bromide and dimethylformamide (DMF) in dichloromethane.[27] The conventional procedure,[28] according to which DMF is added to a solution of $(COBr)_2$ and the substrate in dichloromethane, was not successful in our hands; nor could DMF be used in catalytic amounts. Negishi cross-coupling of **7** in DMA with pentenyl zinc bromide, prepared

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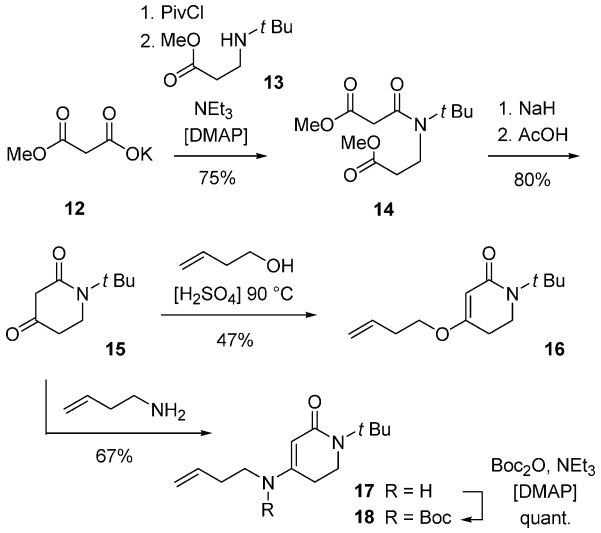
**SCHEME 3. Synthesis of *N*-*tert*-Butyl-protected 5,6-Dihydropyridin-2-ones 16 and 18 as [2+2]-Photocycloaddition Precursors**




from 5-bromo-1-pentene via reductive zincation,[29] proceeded at ambient temperature within 14 h in 82% yield using $Pd_2(dba)_3$ (5 mol %) as catalyst and 20 mol % RuPhos (2-dicyclohexylphosphino-2′,6′-diisopropoxy-1,1′-biphenyl)[30] as ligand. Treatment with TFA in dichloromethane gave the desired 4-substituted 1,5-dihydropyrrol-2-one **9** in 99% yield.

For the synthesis of 1,5-dihydropyrrol-2-ones with *O*-linked alkenyl side chains of varying lengths, acid **3** again turned out to be a valuable starting material. Tetramic acid derivatives are known to form methyl esters under Mitsunobu conditions[31] or by treatment with sulfuric acid dimethyl ester.[32] Other *O*-alkylations of tetramic acid derivatives by alkyl halides, except for allylations and benzylations,[33] have not been reported. For various tetronic acid derivatives, cesium fluoride (CsF)[34] or NaH[35] in DMF were shown to efficiently induce *O*-alkylation. We found potassium *tert*-butoxide (KO$^t$Bu) most suitable to generate ester **10** by *O*-alkylation of acid **3** with an appropriate alkyl bromide. Almost quantitative (97%) cleavage of the Boc-protecting group with TFA in dichloromethane furnished lactam **11**.

**Preparation of 5,6-Dihydropyridin-2-ones.** The 5,6-dihydropyridin-2-ones (**C**, $m = 2$, Scheme 1) were prepared to compare their behavior in the [2+2]-photocycloaddition reactions to the 1,5-dihydropyrrol-2-ones with identical side chains at the 4-position. The *N*-protected 5,6-dihydropyridin-2-ones **16**, **17**, and **18** (Scheme 3) were obtained from *N*-*tert*-butyl-piperidin-2,4-dione (**15**). Although syntheses of various *N*-protected piperidin-2,4-diones had been reported by Micovic et al.,[36] we decided to employ the yet unknown dione **15** as starting material.[37] The *tert*-butyl group appeared to be a suitable protecting group due to its possible cleavage under acidic conditions (*vide infra*).[38] Following Micovic's strategy, we started from commercially available potassium monomethyl malonate (**12**). The *in situ* generated mixed anhydride formed with pivaloyl chloride (PivCl) underwent smooth *N*-acylation of $\beta$-amino acid methyl ester **13**, which was prepared beforehand from *tert*-butyl amine and methyl acrylate by conjugate addition.[39] Amide **14** obtained in 75% yield was treated with sodium hydride in refluxing cyclohexane. The cyclization product was subjected to decarboxylation under reflux in aqueous acetic acid yielding *N*-*tert*-butyl-piperidin-2,4-dione (**15**). Attempts to perform an *O*-alkylation of this substrate under a variety of conditions were less successful than in the tetramate case, showing incomplete conversion and unsatisfactory chemoselectivity. A successful formation of the desired product **16** was eventually achieved by heating **15** in neat but-3-en-1-ol in the presence of $H_2SO_4$. For the preparation of amide **17**, we chose the conditions reported by Katzenellenbogen et al.[40] for the condensation of amines with dihydropyran-2,4-dione. Following Katzenellenbogen's procedure, the formation of vinylogous amide **17** succeeded in 67% yield by stirring compound **15** with excess but-3-enyl amine[20] at ambient temperature in DMF. Subsequent *N*-Boc-protection of the vinylogous amide **17** furnished the irradiation precursor **18** in quantitative yield.

Unfortunately, the desired *N*-deprotection of lactam **16** failed under acidic conditions. The *N*-unprotected 5,6-dihydro-1*H*-pyridin-2-ones, however, (Scheme 4) could be traced back to piperidin-2,4-dione **19**,[41] which was available in turn by acidic cleavage of the *tert*-butyl group from lactam **15**. Because attempts to isolate **19** were not fruitful, crude **19** was used for further transformations. Acid-catalyzed esterification (Dean−Stark trap) with but-3-en-1-ol transformed crude **19** into ester **20** in 90% yield over two steps. Subjecting pent-4-en-1-ol instead of but-3-en-1-ol to identical reaction conditions gave ester **21** in yields of 85% over two steps.

To establish the other alkenyl linkers at the 4-position of 5,6-dihydro-1*H*-pyridin-2-one, the corresponding 4-bromo precursor **22** stroke us as a suitable substrate. Vinylogous bromide **22** was accessible from $\beta$-ketolactam **15** within two steps with an overall yield of 83%.[27] Compound **22**, the structural homologue of bromide **7**, underwent a clean Negishi cross-coupling reaction with pentenyl zinc bromide to lactam **23** in 96% yield.

Attempts to deprotect the *tert*-butyl protected lactams **17** and **18** under acidic conditions led to complete decomposition of

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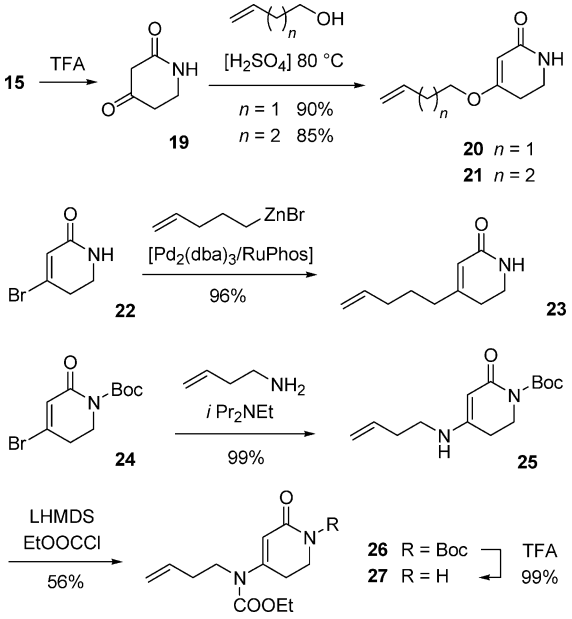
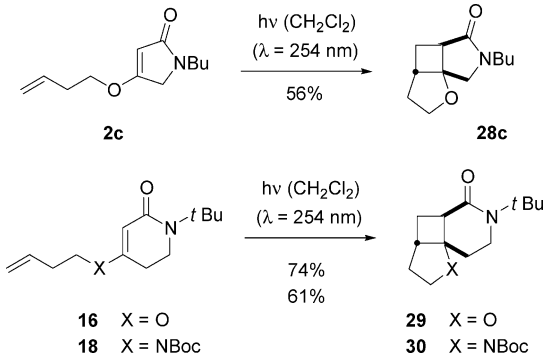
**SCHEME 4. Synthesis of 5,6-Dihydro-1*H*-pyridin-2-ones 20, 21, 23, and 27 as [2+2]-Photocycloaddition Precursors**



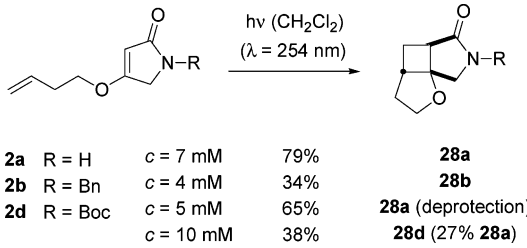

**SCHEME 5. Optimized Intramolecular [2+2]-Photocycloaddition Reactions of Substrates 2c, 16, and 18 at *c* = 5 mM in Dichloromethane**




the compounds. We circumvented this problem by employing bromide **22** as the precursor for the nucleophilic substitution by primary amines. Because substitution of bromide **22** with primary amines would have led to a compound bearing a *N*-unprotected lactam and a *N*-unprotected vinylogous amide, lactam **22** was Boc-protected beforehand under standard conditions with $Boc_2O$, DMAP, and Hünig's base in acetonitrile (75% yield). The subsequent substitution reaction to amide **25** proceeded in almost quantitative yield (99%). Installation of an alkyloxy carbonyl protecting group as *N*-protecting group was not trivial in the case of substrate **25** in contrast to its structural analogue **17**. A strong base such as LHMDS had to be applied, and compound **26** was obtained in only 56% yield. Application of amine bases or hydride bases did not show satisfying conversion to the desired product. Finally, cleavage of the Boc-protecting group from lactam **25** delivered [2+2]-photocycloaddition precursor **27** in 99% yield.

**Optimization of the Reaction Conditions and Proof of Relative Configuration.** Initial experiments to optimize the irradiation conditions were conducted with *N*-butyl-substituted tetramate **2c** (Scheme 5). To our surprise, they revealed that solvents previously employed in the tetronate photocycloaddition

**SCHEME 6. Intramolecular [2+2]-Photocycloaddition of Tetramates 2**




chemistry were not suitable for an irradiation of tetramates. At $\lambda = 254$ nm (irradiation source: Rayonet RPR-2537 Å), reactions in acetonitrile, *tert*-butanol, or diethyl ether led to significant decomposition, and the isolation of analytically pure products was difficult or not feasible at all. The best result was achieved in diethyl ether at a substrate concentration of 6 mM, in the case of which 20% of product **28c** (Scheme 5) was isolated. Addition of acetone as a sensitizer ($\lambda = 300$ nm) did not result in a significant improvement. A major breakthrough was achieved by employing dichloromethane as the solvent. At a substrate concentration of 5 mM, analytically pure product **28c** was isolated in 56% yield.

Similar reaction conditions were applied to the *N*-*tert*-butyl-substituted 5,6-dihydro-1*H*-pyridin-2-ones **16** and **18**, which reacted equally well yielding the tricyclic products **29** and **30**. Again, ideal substrate concentrations were in the range of 5 mM, and the time in which the reaction was completed varied from 1.25 h (**30**) to 3 h (**29**) to 7 h (**28c**). The extinction maximum for the longest wavelength absorption of compound **16** was shifted by 11 nm to a longer wavelength when replacing the solvent diethyl ether ($\lambda_{max} = 218$ nm) by dichloromethane ($\lambda_{max} = 229$ nm). This observation may indicate that the superiority of less polar dichloromethane as compared to the more polar solvents is due to a solvatochromic effect. Indeed, it was later shown that toluene and methylcyclohexane can also be employed as solvents for some reactions, although substrate solubility can become an issue (*vide infra*).

The different substituents at the nitrogen atom of tetramates **2** had a significant impact on the reaction course. The benzyl group (tetramate **2b**) proved to be unstable, and reaction yields were diminished by competing side reactions (Scheme 6). Similar observations were made in the reaction of *N*-Boc substituted substrate **2d**. Besides complete deprotection, observed at a substrate concentration of 5 mM, no other side reactions were observed, however, and product **28a** was obtained in 65% yield. The instability of the Boc group took us by surprise because neither in the above-mentioned reaction of substrate **18** nor in previous reactions with *N*-Boc protected tetronic acid amides[7] had there been an indication for a significant instability. The reaction velocity of the transformation **2d** → **28a** was high, presumably due to a rate acceleration by the electron withdrawing protecting group. Conversion was complete after 1 h. At higher substrate concentration ($c = 10$ mM), some *N*-Boc substituted product **28d** was obtained (38%) together with product **28a** (27%). This finding supports the hypothesis that deprotection occurs in the product **28d** rather than in the substrate **2d**. Indeed, *N*-unsubstituted tetramate **2a** reacted slowly (full conversion after 4 h at $c = 7$ mM) but cleanly, yielding product **28a** in a very good yield of 79% (Scheme 6).

The excellent result achieved with *N*-unprotected substrate **2a** is testimony to the fact that electron-deficient nitrogen atoms,

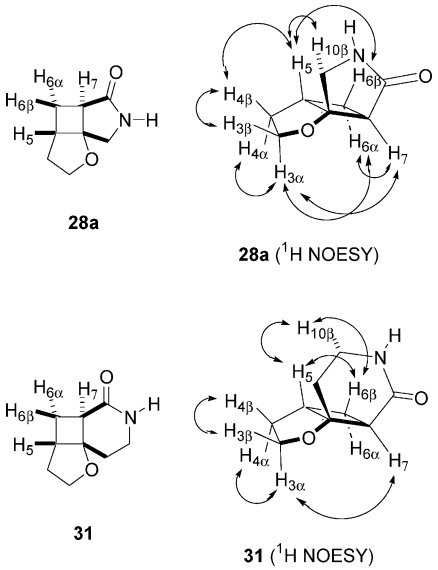


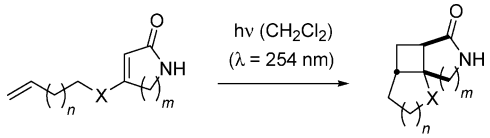

**FIGURE 1.** $^1$H NMR spectroscopic determination of the regioselectivity and simple diastereoselectivity in the [2+2]-photocycloaddition of 1,5-dihydropyrrol-2-ones exemplified by product **28a** and of 5,6-dihydro-1*H*-pyridin-2-ones exemplified by product **31**.

for example, in amides and lactams, frequently do not require protecting groups in photochemical reactions. The statement is supported by further reactions conducted both with 1,5-dihydropyrrol-2-ones and with 5,6-dihydro-1*H*-pyridin-2-ones. Nonetheless, it should be mentioned that the *tert*-butyl group in product **29** could be removed by treatment with neat trifluoroacetic acid under reflux yielding product **31** (Figure 1) in 66% yield.

All [2+2]-photocycloaddition reactions mentioned so far proceeded with perfect regio- and simple diastereoselectivity. The products shown were not contaminated with another regio- nor with another diastereoisomer. Spectra of crude material did not indicate formation of side products, either. The regioselective formation of the straight vs the crossed photocycloaddition product was unequivocally established by the NMR coupling pattern in the individual products. The observations are illustrated in Figure 1 for the 9-aza-2-oxa-tricyclo[5.3.0.0$^{1,5}$]-decan-8-one skeleton generated by [2+2]-photocycloaddition of butenyloxy-substituted tetramates **2**. Product **28a** serves as a prototypical example. The proton in α-position to the carbonyl group, which becomes proton H-7 in product **28a**, resonates at $\delta = 2.81$. A single doublet (d) was to be expected had the photocycloaddition occurred in a crossed fashion. It exhibits, however, a dd coupling pattern with two $^3J$ coupling constants of 10.0 and 4.0 Hz, indicating the formation of the straight photocycloaddition product. The result is confirmed by looking at proton H-6$\beta$, which derives from one of the former protons at the terminal alkene carbon atom. If the connectivity is straight, a ddd structure is expected originating from the $^2J$ coupling to H-6α and two $^3J$ couplings to H-5 and H-7, which is indeed observed. NOE contacts (Figure 1) prove the relative configuration, which is in line with the expectations based on the diastereoselectivity in the photocycloaddition reactions of tetronates (Scheme 1)[6] and which was further corroborated by X-ray crystallographic evidence.

The arguments provided above for the 9-aza-2-oxa-tricyclo-[5.3.0.0$^{1,5}$]decan-8-one skeleton apply similarly to the 9-aza-2-oxa-tricyclo[5.4.0.0$^{1,5}$]undecan-8-one skeleton generated by photocycloaddition of 5,6-dihydro-1*H*-pyridin-2-ones. Compound **31** represents one member of this compound class, which exhibits the diagnostic dd $^1$H NMR pattern for proton H-7 ($^3J = 11.1$ Hz, $^3J = 7.1$ Hz) and NOE data, which compare well with the data obtained for products **28a**.

**TABLE 1. Diastereoselective [2+2]-Photocycloaddition of Various N-Unsubstituted 1,5-Dihydropyrrol-2-ones ($m = 1$) and 5,6-Dihydro-1*H*-pyridin-2-ones ($m = 2$)**



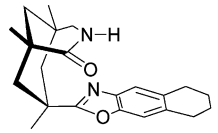

**2a**, **6**, **9**, **11**, **20**, **21**, **23**, **27** → **28a**, **31**-**37**

| entry | substrate | m | X[a] | n | *t* (h) | product | yield (%)[b] |
|---|---|---|---|---|---|---|---|
| 1 | **2a** | 1 | O | 1 | 2.5 | **28a** | 79 |
| 2 | **20** | 2 | O | 1 | 0.5 | **31** | 60 |
| 3 | **11** | 1 | O | 2 | 0.5 | **32** | 70 |
| 4 | **21** | 2 | O | 2 | 9 | **33** | 55 |
| 5 | **6** | 1 | NCOOEt | 1 | 1 | **34** | 72 |
| 6 | **27** | 2 | NCOOEt | 1 | 1 | **35** | 58 |
| 7 | **9** | 1 | $CH_2$ | 1 | 1 | **36** | 61 |
| 8 | **23** | 2 | $CH_2$ | 1 | 1 | **37** | 52 |

[a] All reactions were conducted at a substrate concentration of $5 \times 10^{-3}$ mol $L^{-1}$ in dichloromethane as the solvent at ambient temperature using Rayonet RPR-2537 Å lamps as irradiation source. [b] Yield of isolated product.

**Variation of Substituent X and Tether Length *n*.** In a subsequent series of irradiation experiments, we investigated the efficiency of the cycloaddition depending on the substitution pattern at the 4-position of *N*-unsubstituted 1,5-dihydropyrrol-2-ones and 5,6-dihydro-1*H*-pyridin-2-ones. The [2+2]-photocycloaddition precursors were subjected to optimized irradiation conditions (*vide supra*) and the results are summarized in Table 1. In comparison to butenyloxy-substituted precursors **2a** and **20** (entries 1, 2), pentenyloxy-substituted lactams **11** and **21** (entries 3, 4) performed the respective photocycloaddition reactions with slightly lower yields of 70 and 55%. Interestingly, the side chain elongation of **2a** vs **20** resulted in shorter reaction times, whereas extension of the side chain of **11** vs **21** led to a decrease of the reaction rate. Amides **6** and **27** with *N*-linked alkenyl side chains showed smooth formation of photoproducts **34** and **35** after 1 h irradiation time in yields of 72 and 58% (entries 5, 6). Irradiation of lactams **9** and **23**, bearing a non-heteroatom-linked alkene tether attached to carbon atom C-4, delivered the cycloaddition products **36** and **37** possessing the all-carbon [3.2.0]bicycloheptane backbone in yields of 61 and 52% (entries 7, 8). In all cases, the simple diastereoselectivity was high and only one diastereoisomer was detected. Applying optimal reaction conditions delivered crude products of high purity, and subsequent flash chromatography afforded analytically pure products. In general, it is apparent from the obtained yields that 5,6-dihydro-1*H*-pyridin-2-ones ($m = 2$) are slightly inferior to their structural homologous 1,5-dihydropyrrol-2-ones ($m = 1$). In all cases, the use of anhydrous and degassed dichloromethane was of decisive importance for the success of the [2+2]-photocycloaddition reactions. In oxygen-containing solvents, lower yields were observed due to decomposition reactions, which were visible by coloration of the reaction mixture and by formation of a precipitate, for example, when irradiating amide **27**.

The [2+2]-photocycloaddition reaction gives access to new ring systems, which are difficult to prepare by other methods.




(–)-**38**

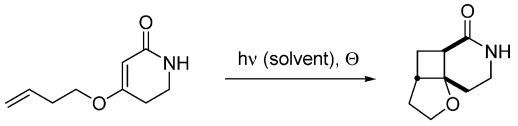
**FIGURE 2.** Structure of the chiral complexing agent (-)-**38**.

In addition, the heteroatoms in products **28a**, **31**−**37** invite ring opening reactions that can lead to bicyclic products incorporating a strained cyclobutane. Lactam ring opening, for example, gives access to bicyclo[3.2.0]heptane or bicyclo[4.2.0]octanes with a heteroatom (O for **28a**, **31**, **32**, **33** or N for **34**, **35**) in the 2-position. Cleavage of the carbon−oxygen or carbon−nitrogen bond of the linker produces a 3-azabicyclo[3.2.0]heptane skeleton. In addition, one can consider ring opening reactions occurring at the cyclobutane[3b,c,42] ring, which makes various spiro compounds accessible in a highly diastereoselective fashion.

**Solvent and Temperature Variation, Enantioselectivity.** A possible approach to conduct enantioselective photochemical reactions in solution is based on the stoichiometric use of the chiral complexing agent (−)-**38** (Figure 2), which transfers its chiral information to a corresponding substrate bound by noncovalent interactions.[43] The sterically demanding tetrahydronaphthalene backbone of **38** shields one of the enantiotopic faces of a bound substrate. So far, this principle has been successfully employed in Norrish-Yang cyclizations,[44] photochemically induced Diels−Alder reactions,[45] [6$\pi$]-cyclizations,[46] [4+4]-photocycloaddition reactions,[47] radical cyclizations,[48] and in intra- and intermolecular [2+2]-photocycloaddition reactions.[49] Enantioselectivities up to 95% *ee* were observed in specific cases.

Based on this precedence, *N*-unsubstituted lactams **C** (Scheme 1) appeared to us as possible substrates for enantioselective [2+2]-photocycloaddition experiments. Facial stereocontrol increases with an increasing amount of complexing agent (−)-**38**, lower temperatures, and less polar solvents because these parameters favor the formation of the template-substrate complex. Different solvents and temperatures were consequently tested in preliminary work for enantioselective [2+2]-photocycloaddition reactions.

**TABLE 2. Variation of Solvent and Temperature Θ in the [2+2]-Photocycloaddition 20 → 31 and Observed Progress in Conversion**




**20** **31**

| entry | solvent[a] | Θ (°C) | *t* (h) | conversion (%)[b] |
|---|---|---|---|---|
| 1 | $CH_2Cl_2$ | −60 | 3.0 | 5 |
| 2 | toluene | −60 | 3.0 | 6 |
| 3 | MCH[c] | −60 | 3.0 | 0.5 |
| 4 | $CH_2Cl_2$ | +30 | 0.5 | 100 |
| 5 | MCH | +30 | 2.0 | 100 |
| 6 | toluene | +30 | 3.0 | 100 |
| 7 | toluene | 0 | 1.0 | 7 |
| 8 | toluene | −20 | 1.0 | 6 |

[a] All reactions were conducted at a substrate concentration of $7 \times 10^{-3}$ mol $L^{-1}$ using Rayonet RPR-2537 Å as the irradiation source. [b] Conversions determined by GC-analysis. [c] MCH = methylcyclohexane.

**TABLE 3. Enantioselective [2+2]-Photocycloaddition 20 → (+)-31 in the Presence of Chiral Template (−)-38**

| entry | *t* (h) | conversion (%)[b] | *ee* [%][c] |
|---|---|---|---|
| 1 | 3.0 | 6 | 75 |
| 2 | 6.0 | 14 | 69 |
| 3 | 8.5 | 22 | 67 |
| 4 | 18.5 | 35 | 65 |
| 5 | 29.0 | 45 | 59 |

[a] All reactions were conducted at a substrate concentration of $7 \times 10^{-3}$ mol $L^{-1}$ using Rayonet RPR-2537 Å as the irradiation source in toluene at −60 °C. [b] Conversions determined by GC-analysis. [c] The *ee* values were calculated from the enantiomeric ratios, which were determined by GC analysis.

Due to its easy accessibility, 5,6-dihydro-1*H*-pyridin-2-one **20** was selected for optimizing reaction conditions. At ambient temperature (Table 2, entries 4−6), completion of the [2+2]-photocycloaddition reactions required only 30 min (in dichloromethane) or a few hours in the case of less-polar solvents like methylcyclohexane and toluene. Cooling down the reaction mixture dramatically decreased the reaction rate. At −60 °C, the standard temperature applied in many [2+2]-photocycloaddition reactions,[49] the reaction proceeded sluggishly with poor conversions (0.5−6%) after 3 h (entries 1−3).

A possible reason why the reaction progress in methylcyclohexane is literally nearly frozen might be the high viscosity of the solvent at −60 °C. Unfortunately, in toluene, the most appropriate solvent for applications of complexing agent (−)-**38** in highly enantioselective [2+2]-photocycloaddition reactions,[49] an impressively drop of the reaction rate was already observed by lowering the reaction temperature from 30 to 0 °C (entries 7 and 8).

Although [2+2]-photocycloaddition precursor **20** revealed only slow formation of product **31** by [2+2]-photocycloaddition at −60 °C, we applied chiral template (−)-**38** in 2.5 equiv to investigate a potential induction of chirality. To our delight, the addition of (−)-**38** did not lead to a further decrease of the reaction rate and afforded (+)-**31** with 75% *ee* after 3 h of irradiation and 6% conversion (Table 3). Upon continued irradiation of the reaction mixture, the *ee* of product (+)-**31**

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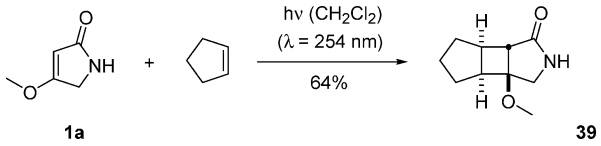
**SCHEME 7. Intermolecular [2+2]-Photocycloaddition of Tetronate 1a and Cyclopentene**




decreased, which is likely due to the fact that chiral template (−)-**38** decomposes significantly at an irradiation wavelength of $\lambda = 254$ nm. The recovery yield was low (<50%).

With the decomposition of template (−)-**38** being a significant drawback, further enantioselective experiments with the substrates **2a**, **6**, **9**, **11**, **21**, **23**, and **27** were not extensively pursued. In general, substrates with an oxygen atom in the tether showed a strong rate decrease at lower reaction temperature. The substrates **9** and **23** with an all-carbon tether exhibited the best performance regarding their reaction rate but the achieved enantioselectivities were not satisfactory. As a typical example, substrate **23** furnished lactam (+)-**37** in 80% yield and 34% *ee* upon irradiation for 6 h in the presence of template (−)-**38**.

## Conclusion

In summary, we could show that the title compounds undergo a clean and diastereoselective intramolecular [2+2]-photocycloaddition. An extension to intermolecular [2+2]-photocycloaddition seems feasible. Upon irradiation of tetramate **1a** in the presence of cyclopentene (20 equiv) for 9 h at ambient temperature, product **39** (exo/endo = 4.6/1) was isolated in 64% (Scheme 7).

All starting materials for the intramolecular reactions were readily accessible from *N*-protected or unprotected $\beta$-ketolactams, that is, from compounds **3**, **15**, and **19**. Attempts to conduct the intramolecular [2+2]-photocycloaddition enantioselectively were met with moderate success mostly because of the insufficient stability of the chiral template (−)-**38** under the reactions conditions.

## Experimental Section

**Preparation of Starting Materials.** 4-Methoxy-pyrrolin-2-one (**1a**),[10] 1-benzyl-4-hydroxy-1,5-dihydro-pyrrol-2-one (**1b**),[11] $\beta$-amino acid methyl ester **13**,[39] the chiral complexing agent (−)-**38**,[50] and but-3-enyl amine[20] were synthesized according to reported procedures. 5-Bromo-1-pentene and 3-buten-1-ol are commercially available.

**1-Butyl-4-methoxy-1,5-dihydro-pyrrol-2-one (1c).** At 0 °C, 2.13 g (10.2 mmol) of 4-bromo-3-methoxy-2-butenoate[9] was added via syringe pump over 1 h to 4.94 mL (3.66 g, 50.0 mmol) of *n*-butyl amine. The mixture was stirred for another 30 min at 0 °C and then at rt for an additional 18 h. The mixture was poured into a separatory funnel, and 50 mL of EtOAc was added. This solution was washed with saturated aqueous solution $NH_4Cl$ (2 × 50 mL) and brine (50 mL). The organic layer was dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (EtOAc 100%) to afford 1.21 g (7.15 mmol, 70%) 1-butyl-4-methoxy-1,5-dihydro-pyrrol-2-one (**1c**) as a pale-yellow oil. $R_f$ = 0.16 (EtOAc 100%); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.04 (s, 1 H), 3.81 (s, 2 H), 3.77 (s, 3 H), 3.36 (t, $^3J$ = 7.3 Hz, 2 H), 1.47−1.55 (m, 2 H), 1.27−1.37 (m, 2 H), 0.92 (t, $^3J$ = 7.3 Hz, 3 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 172.9 (C), 171.9 (C), 94.6 (CH), 58.0 ($CH_3$), 50.3 (C), 41.1 ($CH_2$), 30.6 ($CH_2$), 20.0 ($CH_2$), 13.7 ($CH_3$); IR (film) $\nu_{max}$ 3103 (w, $CH_{olef}$), 2956 (s, CH), 2926 (s, CH), 2870 (s, CH), 1680 (s, C=O), 1626 (s, C=C), 1454 (s), 1409 (s), 1354 (s), 1230 (s), 1173 (m), 1139 (m), 1067 (m), 999 (s), 915 (s), 802 (s), 744 (w), 629 (m) cm$^{-1}$; MS (EI, *m/z*, %) 169 (38) [$M^+$], 154 (2) [$(M - CH_3)^+$], 140 (3) [$(M - C_2H_5)^+$], 126 (100) [$(M - C_3H_7)^+$], 113 (12) [$(M - C_4H_8)^+$], 99 (3), 94 (18), 83 (9), 69 (9), 53 (9), 43 (14) [$C_3H_7^+$]; HRMS (EI) calcd for $C_9H_{15}NO_2$ 169.1103, found: 169.1103.

**4-But-3-enyloxy-1,5-dihydro-pyrrol-2-one (2a).** A total of 339 mg (3.00 mmol) of 4-methoxy-pyrrolin-2-one (**1a**)[10] was dissolved in 2.10 mL (1.73 g, 24.0 mmol) of 3-buten-1-ol at rt; 29.0 mg (0.33 mmol) of methanesulfonic acid was added, and the mixture was stirred at 100 °C in an open flask for 1 h. The reaction was cooled to rt and concentrated under reduced pressure. The resulting oil was dissolved in EtOAc (40 mL), and the organic layer was washed with $H_2O$ (40 mL), saturated aqueous $NaHCO_3$, and brine (40 mL). The organic layer was dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (EtOAc/MeOH = 19/1) to afford 256 mg (1.67 mmol, 56%) of 4-but-3-enyloxy-1,5-dihydro-pyrrol-2-one (**2a**) as colorless crystals. $R_f$ = 0.22 (EtOAc/MeOH = 95/5); mp 123 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 6.11 (br. s, 1 H), 5.81 (ddt, $^3J$ = 17.1, $^3J$ = 10.3, $^3J$ = 6.7 Hz, 1 H), 5.10−5.18 (m, 2 H), 5.06 (s, 1 H), 4.00 (t, $^3J$ = 6.7 Hz, 2 H), 3.93 (s, 2 H), 2.51 (virt. qt, $^3J \approx 6.7$, $^4J \approx 1.3$ Hz, 2 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 175.7 (C), 175.2 (C), 133.4 (CH), 118.0 ($CH_2$), 94.5 (CH), 70.8 ($CH_2$), 47.0 ($CH_2$), 33.0 ($CH_2$); Anal. Calcd for $C_8H_{11}NO_2$ (153.18): C, 62.73; H, 7.24; N, 9.14. Found: C, 62.45; H, 7.28; N, 9.07; IR (film) $\nu_{max}$ 3208 (s, NH), 3102 (m, $CH_{olef}$), 2922 (s, CH), 2853 (s, CH), 1682 (s, C=O), 1614 (s, C=C), 1464 (s), 1428 (m), 1405 (m), 1376 (s), 1225 (s), 1090 (m), 1058 (m), 1010 (w), 984 (m), 935 (m), 911 (m), 866 (m), 822 (m), 729 (m) cm$^{-1}$; MS (EI, *m/z*, %) 153 (38) [$M^+$], 125 (2), 122 (4), 110 (3), 99 (21) [$(M - C_4H_6)^+$], 82 (5), 69 (15), 55 (100) [$C_4H_7^+$], 43 (8), 39 (26); HRMS (EI) calcd for $C_8H_{11}NO_2$ 153.0790, found: 153.0789.

**1-Benzyl-4-but-3-enyloxy-1,5-dihydro-pyrrol-2-one (2b).** A total of 610 mg (3.00 mmol) of 1-benzyl-4-methoxy-1,5-dihydro-pyrrol-2-one (**1b**)[11] was dissolved in 5.17 mL (4.33 g, 60.0 mmol) of 3-buten-1-ol at rt; 32.0 mg (0.33 mmol) of methanesulfonic acid was added, and the mixture was stirred at 100 °C in an open flask for 1 h. The reaction was cooled to rt and concentrated under reduced pressure. The resulting oil was dissolved in EtOAc (40 mL), and the organic layer was washed with $H_2O$ (40 mL), saturated aqueous $NaHCO_3$, and brine (40 mL). The organic layer was dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (P/EtOAc = 1/2) to afford 616 mg (2.53 mmol, 84%) 1-benzyl-4-but-3-enyloxy-1,5-dihydro-pyrrol-2-one (**2b**) as colorless crystals. $R_f$ = 0.35 (P/EtOAc = 1/4); mp 39−41 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 7.21−7.35 (m, 5 H), 5.78 (ddt, $^3J$ = 17.1, $^3J$ = 10.3, $^3J$ = 6.7 Hz, 1 H), 5.06−5.84 (m, 3 H), 4.57 (s, 2 H), 3.96 (t, $^3J$ = 6.7 Hz, 2 H), 3.72 (s, 2 H), 2.48 (virt. q, $^3J \approx$ 6.7 Hz, 2 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 172.3 (C), 172.2 (C), 137.4 (C), 133.3 (CH), 128.7 (CH), 128.0 (CH), 127.5 (CH), 117.7 ($CH_2$), 94.4 (CH), 70.2 ($CH_2$), 50.1 ($CH_2$), 45.4 ($CH_2$), 32.8 ($CH_2$); IR (film) $\nu_{max}$ 3100 (w, $CH_{ar}$), 3064 (w, $CH_{olef}$), 3030 (w, $CH_{ar}$), 2916 (s, CH), 2852 (s, CH), 1666 (s, C=O), 1614 (s, C=C), 1494 (w), 1463 (s), 1407 (m), 1372 (s), 1216 (s), 1068 (w), 1028 (w), 989 (w), 923 (m), 823 (m), 739 (w), 695 (s) cm$^{-1}$; MS (EI, *m/z*, %) 243 (100) [$M^+$], 215 (5), 189 (25) [$(M - C_4H_6)^+$], 188 (80) [$(M - C_4H_7)^+$], 153 (4), 146 (7), 139 (7), 120 (10), 110 (20), 106 (20), 91 (90) [$C_7H_7^+$], 85 (31), 69 (14), 55 (55) [$C_4H_7^+$], 43 (12); HRMS (EI) calcd for $C_{15}H_{17}NO_2$ 243.1259, found: 243.1258.

**4-But-3-enyloxy-1-butyl-1,5-dihydro-pyrrol-2-one (2c).** A total of 728 mg (4.30 mmol) of 1-butyl-4-methoxy-1,5-dihydro-pyrrol-2-one (**1c**) was dissolved in 5.00 mL (4.19 g, 58.1 mmol) of 3-buten-1-ol at rt; 41.0 mg (0.43 mmol) of methanesulfonic acid was added, and the mixture was stirred at 100 °C in an open flask for 1 h. The reaction was cooled to rt and concentrated under reduced pressure. The resulting oil was dissolved in EtOAc (40

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mL), and the organic layer was washed with $H_2O$ (40 mL), saturated aqueous $NaHCO_3$, and brine (40 mL). The organic layer was dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (P/EtOAc = 1/3) to afford 686 mg (3.28 mmol, 76%) of 4-but-3-enyloxy-1-butyl-1,5-dihydro-pyrrol-2-one (**2c**) as a pale-yellow oil. $R_f = 0.36$ (P/EtOAc = 1/4); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.80 (ddt, $^3J = 17.1$, $^3J = 10.3$, $^3J = 6.7$ Hz, 1 H), 5.03−5.17 (m, 3 H), 3.95 (t, $^3J = 6.6$ Hz, 2 H), 3.81 (s, 2 H), 3.36 (t, $^3J = 7.0$ Hz, 2 H), 2.43−2.55 (m, 2 H), 1.44−1.56 (m, 2 H), 1.24−1.38 (m, 2 H), 0.91 (t, $^3J = 7.3$ Hz, 3 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 172.1 (C), 171.9 (C), 133.3 (CH), 117.7 ($CH_2$), 94.7 (CH), 70.2 ($CH_2$), 50.5 ($CH_2$), 41.1 ($CH_2$), 32.8 ($CH_2$), 30.6 ($CH_2$), 19.9 ($CH_2$), 13.7 ($CH_3$); IR (film) $\nu_{max}$ 3077 (w, $CH_{olef}$), 2955 (s, CH), 2929 (s, CH), 2870 (m, CH), 1681 (vs, C=O), 1624 (vs, C=C), 1458 (s), 1401 (m), 1345 (s), 1217 (s), 1137 (w), 1067 (w), 987 (m), 916 (m), 802 (m) cm$^{-1}$; MS (EI, *m/z*, %) 209 (29) [$M^+$], 194 (9) [$(M - CH_3)^+$], 180 (6) [$(M - C_2H_5)^+$], 166 (100) [$(M - C_3H_7)^+$], 155 (17) [$(M - C_4H_6)^+$], 138 (4), 126 (9), 112 (59) [$(166 - C_4H_6)^+$], 99 (9), 84 (33), 69 (7), 55 (23) [$C_4H_7^+$], 42 (9); HRMS (EI) calcd for $C_{12}H_{19}NO_2$ 209.1416, found: 209.1416.

**4-But-3-enylamino-2-oxo-2,5-dihydro-pyrrole-1-carboxylic Acid *tert*-Butyl Ester (4).** A solution of 5.00 g (25.1 mmol) of 2-oxo-4-pent-4-enyloxy-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**3**) and 3.57 g (50.2 mmol) of but-3-enyl amine[20] in 20 mL dry benzene was refluxed using Dean−Stark water separator for 4 h. Solvent and unreacted but-3-enyl amine were removed under reduced pressure. After purification by flash chromatography (cyclohexane/EtOAc = 1/9), 3.42 g (13.6 mmol, 54%) of 4-but-3-enylamino-2-oxo-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**4**) was obtained as colorless crystals. $R_f = 0.62$ (EtOAc/MeOH = 9/1); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.80−5.69 (m, 2 H), 5.11−5.06 (m, 2 H), 4.67 (s, 1 H), 4.20 (s, 2 H), 3.15 (virt. q, $^3J \approx 6.4$ Hz, 2 H), 2.33 (virt. q, $^3J \approx 6.9$ Hz, 2 H), 1.49 (s, 9 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 171.2 (C), 162.0 (C), 149.8 (C), 134.8 (CH), 117.7 ($CH_2$), 88.0 (CH), 81.7 (C), 49.3 ($CH_2$), 43.7 ($CH_2$), 32.9 ($CH_2$), 28.3 ($CH_3$); Anal. Calcd for $C_{13}H_{20}N_2O_3$ (252.15) C, 61.88; H, 7.99; N, 11.10. Found: C, 62.23; H, 7.73; N, 10.80; IR (film) $\nu_{max}$ 3247 (m, NH), 2978 (w, $CH_{olef}$), 2931 (w, CH), 1774 (s, C=O), 1598 (s, C=C), 1532 (w), 1438 (w), 1377 (m), 1365 (m), 1252 (w), 1164 (m), 1083 (m), 998 (w), 906 (w), 775 (w), 733 (w) cm$^{-1}$; MS (EI, *m/z*, %) 252 (11) [$M^+$], 179 (20) [$(M - OC_4H_9)^+$], 152 (58) [$(M - C_4H_8 - CO_2)^+$], 111 (100), 57 (53) [$C_4H_9^+$], 41 (23); HRMS (EI) calcd for $C_{13}H_{20}N_2O_3$ 252.1474, found: 252.1470.

**4-(But-3-enyl-ethoxycarbonyl-amino)-2-oxo-2,5-dihydro-pyrrole-1-carboxylic Acid *tert*-Butyl Ester (5).** One gram (3.96 mmol) of 4-but-3-enylamino-2-oxo-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**4**) was dissolved in 10 mL of dry acetonitrile. At 0 °C, 575 mg (4.75 mmol) of 4-dimethylaminopyridine, 830 $\mu$L (5.94 mmol) of anhydrous $NEt_3$, and 930 $\mu$L (11.88 mmol) of ethyl chloroformate were added, and the solution was stirred at 0 °C for 30 min and then at rt for 16 h. The solvent was evaporated at reduced pressure, and the resulting crude product was purified by flash column chromatography (P/EtOAc = 9/1) to give 1.22 g (3.76 mmol, 95%) of 4-(but-3-enyl-ethoxycarbonyl-amino)-2-oxo-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**5**) as a colorless oil. $R_f = 0.30$ (P/EtOAc = 9/1); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.74−5.62 (m, 1 H), 5.29 (s, 1 H), 5.04−4.99 (m, 2 H), 4.71 (s, 2 H), 4.22 (q, $^3J = 7.1$ Hz, 2 H), 3.65 (t, $^3J = 7.5$ Hz, 2 H), 2.33−2.27 (m, 2 H), 1.48 (s, 9 H), 1.29 (t, $^3J = 7.1$ Hz, 3 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 168.6 (C), 156.6 (C), 152.8 (C), 149.2 (C), 133.6 (CH), 117.8 ($CH_2$), 102.6 (CH), 82.5 (C), 63.4 ($CH_2$), 51.7 ($CH_2$), 47.1 ($CH_2$), 31.2 ($CH_2$), 28.1 ($CH_3$), 14.2 ($CH_3$); IR (film) $\nu_{max}$ 2977 (w, $CH_{olef}$), 2928 (w, CH), 1776 (m, C=O), 1722 (vs, C=O), 1601 (s, C=C), 1437 (w), 1394 (m), 1332 (s), 1293 (m), 1228 (m), 1158 (m), 1099 (m), 1075 (m), 1038 (w) cm$^{-1}$; MS (EI, *m/z*, %) 324 (4) [$M^+$], 251 (31) [$(M - OC_4H_9)^+$], 224 (100) [$(M - C_4H_8 - CO_2)^+$], 206 (58), 111 (65), 57 (95) [$C_4H_9^+$]; HRMS (EI) calcd for $C_{16}H_{24}N_2O_5$ 324.1685, found: 324.1683.

**2-Oxo-4-pent-4-enyloxy-2,5-dihydro-pyrrole-1-carboxylic Acid *tert*-Butyl Ester (10).** To a solution of 500 mg (2.51 mmol) of 4-hydroxy-2-oxo-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**3**) in 40 mL of dry DMF were added 310 mg (2.76 mmol) of potassium *tert*-butoxide and 326 $\mu$L (2.76 mmol) of 5-bromo-1-pentene at 0 °C. After the reaction mixture was stirred at rt for 14 h, the solvent was removed under reduced pressure. After purification by flash chromatography (cyclohexane/EtOAc = 1/1), 489 mg (1.83 mmol, 73%) of 2-oxo-4-pent-4-enyloxy-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**10**) was obtained as colorless crystals. $R_f = 0.40$ (P/EtOAc = 1/1); mp 64 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.79 (ddt, $^3J = 16.9$, 10.2, 6.7 Hz, 1 H), 5.08−5.01 (m, 3 H), 4.17 (s, 2 H), 3.98 (t, $^3J = 6.4$ Hz, 2 H), 2.18 (virt. q, $^3J \cong 7.0$ Hz, 2 H), 1.90−1.82 (m, 2 H), 1.53 (s, 9 H); $^{13}$C NMR (63 MHz, $CDCl_3$) $\delta$ 173.8 (C), 169.4 (C), 149.5 (C), 136.9 (CH), 116.0 ($CH_2$), 95.2 (CH), 82.6 (C), 71.1 ($CH_2$), 49.5 ($CH_2$), 29.8 ($CH_2$), 28.2 ($CH_3$), 27.6 ($CH_2$); Anal. Calcd for $C_{14}H_{21}NO_4$ (267.32): C, 62.90; H, 7.92; N, 5.24. Found: C, 62.91; H, 8.09; N, 5.25; IR (film) $\nu_{max}$ 3019 (w, $CH_{olef}$), 2985 (w, CH), 1738 (s, C=O), 1681 (s, C=O), 1631 (s, C=C), 1467 (w), 1454 (w), 1371 (m), 1332 (s), 1309 (s), 1244 (m), 1144 (m), 1088 (m), 978 (m), 921 (w), 852 (w), 820 (w), 772 (w), 701 (w), 675 (w) cm$^{-1}$; MS (EI, *m/z*, %) 252 (2) [$(M - CH_3)^+$], 212 (8) [$(M - C_4H_7)^+$], 194 (30) [$(M - OC_4H_9)^+$], 167 (54) [$(M - C_4H_8 - CO_2)^+$], 149 (26), 69 (61), 57 (100) [$C_4H_9^+$], 41 (82); HRMS (EI) calcd for $C_{14}H_{21}NO_4 - C_4H_7$ 212.0923, found: 212.0921.

***N*-*tert*-Butyl-*N*-(2-methoxycarbonyl-ethyl)-malonamic Acid Methyl Ester (14).** To a solution of 9.38 g (60.1 mmol) of monomethyl malonate potassium salt in 120 mL of anhydrous $Et_2O$ was added 6.83 mL (6.69 g, 55.5 mmol) of pivaloyl chloride at 0 °C. After the mixture was stirred at this temperature for 4 h, successively 7.73 mL (5.64 g, 55.7 mmol) of $NEt_3$, 0.81 g (6.63 mmol) of DMAP, and 8.02 g (50.4 mmol) of $\beta$-amino acid methyl ester[39] (**13**) were added. The mixture was stirred at rt for 18 h and washed with saturated aqueous $NaHCO_3$ (3 × 100 mL) and brine (100 mL). The organic layer was dried over $Na_2SO_4$, filtered, and concentrated. Flash column chromatography (P/EtOAc = 7/3) afforded 9.84 g (37.9 mmol, 75%) of *N*-*tert*-butyl-*N*-(2-methoxycarbonyl-ethyl)-malonamic acid methyl ester (**14**) as colorless oil. $R_f = 0.31$ (P/EtOAc = 7/3); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 3.72 (s, 3 H), 3.68 (s, 3 H), 3.57−3.61 (m, 2 H), 3.46 (s, 2 H,), 2.56−2.60 (m, 2 H), 1.43 (s, 9 H); $^{13}$C NMR (90.6 MHz, $CDCl_3$) $\delta$ 171.1 (C), 168.4 (C), 166.7 (C), 57.9 (C), 52.3 ($CH_3$), 51.9 ($CH_3$), 43.5 ($CH_2$), 41.5 ($CH_2$), 36.1 ($CH_2$), 28.8 ($CH_3$); IR (film) $\nu_{max}$ 2957 (m, CH), 1738 (s, C=O), 1652 (s, C=O), 1436 (s), 1399 (s), 1367 (s), 1324 (s), 1262 (s), 1200 (s), 1061 (m), 1023 (m), 899 (w), 840 (w) cm$^{-1}$; MS (EI, *m/z*, %) 259 (6) [$M^+$], 244 (10) [$(M - CH_3)^+$], 228 (3) [$(M - OCH_3)^+$], 204 (21), 186 (5) [$(M - C_3H_5O_2)^+$], 172 (31) [$(M - C_4H_7O_2)^+$], 158 (7) [$(M - C_4H_5O_3)^+$], 144 (100) [$C_7H_{14}NO_2^+$], 130 (26), 112 (13) [$(M - CH_4O)^+$], 102 (33) [$C_4H_8NO_2^+$], 70 (23), 57 (44) [$C_4H_9^+$], 40 (21); HRMS (EI) calcd $C_{12}H_{21}NO_5$ 259.1420, found: 259.1416.

***N*-*tert*-Butyl-piperidine-2,4-dione (15).** A suspension of 3.10 g of NaH (60%; 77.5 mmol) in 120 mL of dry cyclohexane was heated to reflux and a solution of 9.84 g of *N*-*tert*-butyl-*N*-(2-methoxycarbonyl-ethyl)-malonamic acid methyl ester (**14**) (37.9 mmol) in 10 mL of anhydrous toluene was added dropwise over 1 h. Stirring and heating was continued for 2 h during which time hydrogen was evolved and a pale-yellow precipitate was formed. The mixture was cooled to rt and filtered. The precipitate was washed with cyclohexane, dried under vacuum, and transferred to a flask with 150 mL of 10% aq AcOH. The mixture was stirred at reflux for 3 h until $CO_2$ evolution ceased. After cooling to rt, the mixture was neutralized with saturated aqueous $NaHCO_3$ and extracted with $CH_2Cl_2$ (3 × 50 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated. Purification by flash chromatography (P/EtOAc = 1/1) yielded 5.13 g (30.3 mmol, 80%) of *N*-*tert*-butyl-piperidine-2,4-dione (**15**) as colorless crystals. $R_f = 0.24$ (P/EtOAc = 1/1); mp 92−96 °C; $^1$H NMR (360 MHz,

$CDCl_3$) $\delta$ 3.65 (t, $^3J$ = 6.0 Hz, 2 H), 3.34 (s, 2 H), 2.50 (t, $^3J$ = 6.0 Hz, 2 H), 1.47 (s, 9 H); $^{13}$C NMR (90.6 MHz, $CDCl_3$) $\delta$ 204.7 (C), 166.8 (C), 57.9 (C), 52.2 ($CH_2$), 39.7 ($CH_2$), 39.5 ($CH_2$), 28.7 ($CH_3$); Anal. Calcd for $C_9H_{15}NO_2$ (169.2209): C, 63.88; H, 8.93; N, 8.28. Found: C, 63.76; H, 9.17; N, 8.23; IR (film) $\nu_{max}$ 2922 (s, CH), 2853 (s, CH), 1650 (w, C═O), 1614 (m, C═O), 1556 (s), 1463 (s), 1430 (s), 1357 (s), 1319 (s), 1280 (m), 1227 (s), 1190 (s), 994 (w), 835 (m), 689 (w) cm$^{-1}$; MS (EI, *m/z*, %) 169 (77) [$M^+$], 154 (77) [$(M - CH_3)^+$], 141 (3), 126 (19) [$C_6H_8NO_2^+$], 114 (66), 112 (26) [$(M - C_4H_9)^+$], 84 (11) [(112 - CO)$^+$], 70 (100), 57 (47) [$C_4H_9^+$], 41 (34); HRMS (EI) calcd $C_9H_{15}NO_2$ 169.1103, found: 169.1104.

**4-But-3-enyloxy-1-*tert*-butyl-5,6-dihydro-1*H*-pyridin-2-one (16).** To a solution of 507 mg (3.00 mmol) of *N*-*tert*-butyl-piperidine-2,4-dione (**15**) in 1.29 mL (1.08 g, 15.0 mmol) of 3-buten-1-ol was added two drops of concentrated $H_2SO_4$. The reaction mixture was stirred at 90 °C for 5 h and cooled to rt After 3-buten-1-ol was removed under reduced pressure, the resulting crude product was subjected to column chromatography to afford 312 mg (1.40 mmol, 47%) of 4-but-3-enyloxy-1-*tert*-butyl-5,6-dihydro-1*H*-pyridin-2-one (**16**) as colorless crystals. $R_f$ = 0.28 (P/EtOAc = 3/1); mp 51 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.80 (ddt, $^3J$ = 17.1, $^3J$ = 10.3, $^3J$ = 6.7 Hz, 1 H), 5.06−5.15 (m, 2 H), 4.98 (s, 1 H), 3.83 (t, $^3J$ = 6.7 Hz, 2 H), 3.39 (t, $^3J$ = 6.9 Hz, 2 H), 2.45 (virt. qt, $^3J \approx$ 6.7, $^4J \approx$ 1.2 Hz, 2 H), 2.34 (t, $^3J$ = 6.9 Hz, 2 H), 1.43 (s, 9 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 168.7 (C), 167.2 (C), 133.9 (CH), 117.2 ($CH_2$), 97.3 (CH), 67.3 ($CH_2$), 56.2 (C), 41.0 ($CH_2$), 32.9 ($CH_2$), 28.9 ($CH_2$), 28.8 ($CH_3$); IR (film) $\nu_{max}$ 3078 (w, $CH_{olef}$), 2957 (s, CH), 2914 (s, CH), 1654 (s, C═O), 1627 (s, C═C), 1466 (m), 1412 (s), 1370 (s), 1322 (s), 1293 (w), 1188 (s), 1030 (m), 996 (m), 947 (w), 918 (w), 830 (m), 804 (w) cm$^{-1}$; MS (EI, *m/z*, %) 223 (41) [$M^+$], 208 (75) [$(M - CH_3)^+$], 180 (18), 167 (16) [$(208 - C_3H_5)^+$], 154 (15) [$(208 - C_4H_6)^+$], 139 (24), 124 (11), 112 (21), 97 (11), 84 (20), 70 (58), 55 (100) [$C_4H_7^+$], 40 (19); HRMS (EI) calcd for $C_{13}H_{21}NO_2$ 223.1572, found: 223.1571.

**4-But-3-enylamino-1-*tert*-butyl-5,6-dihydro-1*H*-pyridin-2-one (17).** To a solution of 169 mg (1.00 mmol) of *N*-*tert*-butyl-piperidine-2,4-dione (**15**) in 3 mL of dry DMF 213 mg (3.00 mmol) was added but-3-enyl amine[20] at rt. After the reaction mixture was stirred at rt for 18 h, the reaction was quenched with 75 mL $H_2O$. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (P/EtOAc = 1/1) to afford 149 mg (0.67 mmol, 67%) of 4-but-3-enylamino-1-*tert*-butyl-5,6-dihydro-1*H*-pyridin-2-one (**17**) as a pale-yellow oil. $R_f$ = 0.23 (P/EtOAc = 1/1); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.75 (ddt, $^3J$ = 17.1, $^3J$ = 10.2, $^3J$ = 6.6 Hz, 1 H), 5.08−5.13 (m, 2 H), 4.68 (s, 1 H), 3.71 (br. s, 1 H), 3.36 (t, $^3J$ = 6.6 Hz, 2 H), 3.07 (virt. q, $^3J \approx$ 6.6 Hz, 2 H), 2.33 (virt. q, $^3J \approx$ 6.6 Hz, 2 H), 2.25 (t, $^3J$ = 6.6 Hz, 2 H), 1.43 (s, 9 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 170.2 (C), 154.1 (C), 135.1 (CH), 117.3 ($CH_2$), 91.3 (CH), 55.8 (C), 41.7 ($CH_2$), 41.1 ($CH_2$), 32.7 ($CH_2$), 30.0 ($CH_2$), 28.9 ($CH_3$); IR (film) $\nu_{max}$ 3218 (s, NH), 3031 (s, C═C), 2922 (s, CH), 2860 (s, CH), 1629 (s, C═O), 1588 (s), 1454 (s), 1360 (s), 1321 (s), 1242 (s), 1204 (s), 1150 (m), 1099 (w), 994 (m), 919 (m), 806 (m), 790 (m), 690 (m) cm$^{-1}$; MS (EI, *m/z*, %) 222 (49) [$M^+$], 207 (54) [$(M - CH_3)^+$], 194 (18), 166 (50) [$(M - C_4H_8)^+$], 151 (28), 137 (18), 125 (100) [$(166 - C_3H_5)^+$], 108 (26), 95 (33), 70 (79) [$C_4H_8N^+$], 57 (38) [$C_4H_9^+$]; HRMS (EI) calcd for $C_{13}H_{22}N_2O$ 222.1732, found: 222.1731.

**4-But-3-enyloxy-5,6-dihydro-1*H*-pyridin-2-one (20).** A solution of 1.67 g (10.0 mmol) of *N*-*tert*-butyl-piperidine-2,4-dione (**15**) in 20 mL triflouroacetic acid was refluxed for 1 h. After removal of the solvent, the crude product was dissolved in 20 mL of dry benzene; 2.60 mL (30.0 mmol) of 3-buten-1-ol and 2 drops of concd $H_2SO_4$ were added before the reaction mixture was refluxed using a Dean−Stark water separator for 2 h. Solvent and 3-buten-1-ol were removed under reduced pressure. After purification by flash chromatography (EtOAc/MeOH = 95/5), 1.50 g (9.0 mmol, 90%) of 4-but-3-enyloxy-5,6-dihydro-1*H*-pyridin-2-one (**20**) was obtained as colorless crystals. $R_f$ = 0.30 (EtOAc/MeOH = 95/5); mp 66 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.81 (ddt, $^3J$ = 17.1, $^3J$ = 10.3, $^3J$ = 6.8 Hz, 1 H), 5.68 (br. s, 1 H), 5.08−5.16 (m, 2 H), 5.04 (s, 1 H), 3.88 (t, $^3J$ = 6.6 Hz, 2 H), 3.40 (virt. td, $^3J \approx$ 7.2, $^3J \approx$ 2.5 Hz, 2 H), 2.42−2.51 (m, 4 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 169.7 (C), 169.4 (C), 133.7 (CH), 117.4 ($CH_2$), 94.1 (CH), 67.4 ($CH_2$), 38.7 ($CH_2$), 32.8 ($CH_2$), 27.9 ($CH_2$); IR (film) $\nu_{max}$ 3193 (m, NH), 3074 (m, $CH_{olef}$), 2954 (m, CH), 2922 (s, CH), 2856 (s, CH), 1694 (s, C═O), 1610 (s, C═C), 1463 (s), 1427 (m), 1366 (s), 1344 (s), 1223 (s), 1187 (s), 1129 (w), 1056 (m), 996 (m), 907 (m), 810 (s), 718 (w), 690 (w) cm$^{-1}$; MS (EI, *m/z*, %) 167 (25) [$M^+$], 152 (3) [$(M - CH_3)^+$], 139 (6), 111 (10) [$(152 - C_3H_5)^+$], 96 (31), 85 (13), 69 (13), 55 (100) [$C_4H_7^+$], 43 (26); HRMS (EI) calcd for $C_9H_{13}NO_2$ 167.0946, found: 167.0946.

**4-But-3-enylamino-6-oxo-3,6-dihydro-2H-pyridine-1-carboxylic acid *tert*-butyl ester (25).** A total of 786 mg (2.85 mmol) of 4-bromo-6-oxo-3,6-dihydro-2H-pyridine-1-carboxylic acid *tert*-butyl ester (**24**) was dissolved in 2 mL of dry tetrahydrofuran, and 404 mg (5.69 mmol) of but-3-enyl amine[20] and 975 $\mu$L (5.69 mmol) of anhydrous diisopropyl ethylamine were added. The reaction mixture was stirred at rt for 60 h and filtered. The filtrate was evaporated to dryness, and the crude product was purified by column chromatography (EtOAc = 100%) to give 753 mg (2.83 mmol, 99%) of 4-but-3-enylamino-6-oxo-3,6-dihydro-2H-pyridine-1-carboxylic acid *tert*-butyl ester (**25**) as pale-yellow crystals. $R_f$ = 0.34 (EtOAc 100%); mp 104−106 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 5.79−5.68 (m, 1 H), 5.14−5.09 (m, 2 H), 4.77 (s, 1 H), 4.42 (br. s, 1 H), 3.82 (t, $^3J$ = 6.4 Hz, 2 H), 3.15 (virt. q, $^3J \approx$ 6.2 Hz, 2 H), 2.39−2.31 (m, 4 H), 1.51 (s, 9 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 167.0 (C), 159.4 (C), 152.5 (C), 134.8 (CH), 117.1 ($CH_2$), 87.6 (CH), 81.5 (C), 42.8 ($CH_2$), 42.0 ($CH_2$), 32.3 ($CH_2$), 28.6 ($CH_2$), 28.1 ($CH_3$); Anal. Calcd for $C_{14}H_{22}N_2O_3$ (266.16): C, 63.13; H, 8.33; N, 10.52. Found: C, 63.05; H, 8.46; N, 10.33; IR (film) $\nu_{max}$ 3279 (vs, NH), 3085 (w, $CH_{olef}$), 2933 (w, CH), 1700 (s), 1634 (s, C═O), 1595 (s), 1551 (vs, C═C), 1474 (m), 1365 (m), 1319 (m), 1307 (m), 1225 (m), 1208 (m), 1142 (s), 1056 (w), 921 (w), 854 (w) cm$^{-1}$; MS (EI, *m/z*, %) 266 (24) [$M^+$], 193 (21) [$(M - OC_4H_9)^+$], 166 (100) [$(M - C_4H_8 - CO_2)^+$], 125 (100), 57 (74) [$C_4H_9^+$]; HRMS (EI) calcd for $C_{14}H_{22}N_2O_3$ 266.1631, found: 266.1635.

**General Procedure for the [2+2]-Photocycloaddition Reactions.** In a quartz vessel, a solution of the respective tetramic acid derivate or its six-membered ring homologue in anhydrous, degassed (argon purge under ultrasound for 20 min) dichloromethane was irradiated at rt and 254 nm until GC and TLC analysis indicated complete conversion (light source: Rayonet RPR-2537 Å). The solvent was then evaporated under reduced pressure, and the remaining residue was purified by column chromatography to give the desired compound.

**Hexahydro-1-oxa-6-aza-cyclobuta[1,2:1,4]dicyclopenten-5-one (28a).** The compound was prepared from 77.0 mg (0.50 mmol) of 4-but-3-enyloxy-1,5-dihydro-pyrrol-2-one (**2a**) in 72 mL of anhydrous dichloromethane by irradiation for 4 h. Column chromatography (EtOAc/MeOH = 19/1) yielded 61.0 mg (0.40 mmol, 79%) of the desired product as colorless crystals. $R_f$ = 0.20 (EtOAc/MeOH = 95/5); mp 138 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 6.76 (br. s, 1 H), 4.23 (virt. t, $^2J \approx {}^3J \approx$ 8.7 Hz, 1 H), 3.98 (ddd, $^3J$ = 11.5, $^2J$ = 8.7, $^3J$ = 5.3 Hz, 1 H), 3.53 (d, $^2J$ = 10.3 Hz, 1 H), 3.45 (d, $^2J$ = 10.3 Hz, 1 H), 2.90−2.96 (m, 1 H), 2.81 (dd, $^3J$ = 10.0, $^3J$ = 4.0 Hz, 1 H), 2.22 (ddd, $^2J$ = 12.9, $^3J$ = 8.6, $^3J$ = 4.0 Hz, 1 H), 1.88−2.00 (m, 2 H), 1.73 (dd, $^2J$ = 12.6, $^3J$ = 5.3 Hz, 1 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 179.0 (C), 86.8 (C), 68.5 ($CH_2$), 49.5 ($CH_2$), 42.8 (CH), 42.5 (CH), 31.8 ($CH_2$), 25.9 ($CH_2$); IR (film) $\nu_{max}$ 3188 (br. m, NH), 2922 (s, CH), 2853 (s, CH), 1679 (s, C═O), 1481 (m), 1456 (m), 1375 (m), 1316 (m), 1238 (m), 1190 (m), 1070 (m), 990 (m), 954 (w), 898 (w), 803 (m), 713 (w), 670 (m), 636 (m) cm$^{-1}$; MS (EI, *m/z*, %) 153 (49) [$M^+$], 122 (25), 99 (45),

98 (43) [(M − $C_3H_3O$)$^+$], 79 (17), 69 (31), 55 (100) [$C_3H_3O^+$], 51 (22); HRMS (EI) calcd for $C_8H_{11}NO_2$ 153.0790, found: 153.0792.

**6-Benzyl-hexahydro-1-oxa-6-aza-cyclobuta[1,2:1,4]dicyclopenten-5-one (28b).** The compound was prepared from 41.0 mg (0.17 mmol) of 1-benzyl-4-but-3-enyloxy-1,5-dihydro-pyrrol-2-one (**2b**) in 48 mL of anhydrous dichloromethane by irradiation for 4 h. Column chromatography (EtOAc 100%) yielded 14.0 mg (0.06 mmol, 34%) of the desired product as a pale-yellow oil. $R_f$ = 0.33 (EtOAc 100%); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 7.24−7.36 (m, 5 H), 4.58 (d, $^2J$ = 14.8 Hz, 1 H), 4.46 (d, $^2J$ = 14.8 Hz, 1 H), 4.20 (virt. t, $^2J \approx {}^3J \approx$ 8.7 Hz, 1 H), 3.96 (ddd, $^3J$ = 11.4, $^2J$ = 8.7, $^3J$ = 5.4 Hz, 1 H), 3.43 (d, $^2J$ = 10.4 Hz, 1 H), 3.27 (d, $^2J$ = 10.4 Hz, 1 H), 2.94 (dd, $^3J$ = 10.0, $^3J$ = 4.1 Hz, 1 H), 2.76−2.83 (m, 1 H), 2.23 (ddd, $^2J$ = 13.0, $^3J$ = 8.6, $^3J$ = 4.1 Hz, 1 H), 1.84−1.98 (m, 2 H), 1.72 (dd, $^2J$ = 12.6, $^3J$ = 5.4 Hz, 1 H); $^{13}$C NMR (90 MHz, $CDCl_3$): $\delta$ = 175.3 (C), 136.1 (C), 128.8 (CH), 128.0 (CH), 127.6 (CH), 83.8 (C), 68.4 ($CH_2$), 53.7 ($CH_2$), 46.4 ($CH_2$), 44.0 (CH), 42.5 (CH), 31.9 ($CH_2$), 26.2 ($CH_2$); IR (film) $\nu_{max}$ 2942 (m, CH), 2861 (m, CH), 1682 (s, C═O), 1483 (m), 1446 (m), 1420 (m), 1355 (w), 1316 (m), 1243 (w), 1183 (w), 1116 (w), 1081 (m), 990 (w), 953 (w), 909 (w), 700 (m) cm$^{-1}$; MS (EI, *m/z*, %) 243 (100) [M$^+$], 215 (8), 188 (53) [(M − $C_3H_3O$)$^+$], 152 (9), 139 (8), 106 (25), 91 (81) [$C_7H_7^+$], 84 (16), 69 (11), 55 (63) [$C_3H_3O^+$], 40 (35); HRMS (EI) calcd for $C_{15}H_{17}NO_2$ 243.1259, found: 243.1258.

**6-Butyl-hexahydro-1-oxa-6-aza-cyclobuta[1,2:1,4]dicyclopenten-5-one (28c).** The compound was prepared from 70.0 mg (0.33 mmol) of 4-but-3-enyloxy-1-butyl-1,5-dihydro-pyrrol-2-one (**2c**) in 72 mL of anhydrous dichloromethane by irradiation for 7 h. Column chromatography (EtOAc 100%) yielded 39.0 mg (0.19 mmol, 56%) of the desired product as a pale-yellow oil. $R_f$ = 0.29 (EtOAc 100%); $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 4.22 (virt. t, $^2J \approx {}^3J \approx$ 8.8 Hz, 1 H), 3.96 (ddd, $^3J$ = 11.5, $^2J$ = 8.8, $^3J$ = 5.3 Hz, 1 H), 3.54 (d, $^2J$ = 10.2 Hz, 1 H), 3.26−3.39 (m, 3 H), 2.80−2.88 (m, 2 H), 2.15 (ddd, $^2J$ = 12.9, $^3J$ = 8.5, $^3J$ = 4.3 Hz, 1 H), 1.85−2.00 (m, 2 H), 1.72 (dd, $^2J$ = 12.6, $^3J$ = 5.3 Hz, 1 H), 1.52 (virt. quint., $^3J \approx$ 7.4 Hz, 2 H), 1.33 (virt. sext., $^3J \approx$ 7.4 Hz, 2 H), 0.93 (t, $^3J$ = 7.4 Hz, 3 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 175.1 (C), 83.8 (C), 68.4 ($CH_2$), 54.2 ($CH_2$), 44.1 (CH), 42.5 (CH), 42.1 ($CH_2$), 32.0 ($CH_2$), 29.1 ($CH_2$), 26.2 ($CH_2$), 20.0 ($CH_2$), 13.7 ($CH_3$); IR (film) $\nu_{max}$ 2957 (s, CH), 2863 (s, CH), 1682 (s, C═O), 1485 (m), 1428 (m), 1312 (s), 1242 (w), 1179 (w), 1080 (m), 991 (m), 954 (w), 911 (w) cm$^{-1}$; MS (EI, *m/z*, %) 209 (64) [M$^+$], 194 (16) [(M − $CH_3$)$^+$], 180 (9) [(M− $C_2H_5$)$^+$], 166 (100) [(M − $C_3H_7$)$^+$], 154 (39) [(M − $C_3H_3O$)$^+$], 138 (11), 126 (9), 112 (39), 98 (17), 84 (25), 69 (10), 55 (69) [$C_3H_3O^+$], 40 (21); HRMS (EI) calcd for $C_{12}H_{19}NO_2$ 209.1416, found: 209.1415.

**5-Oxo-hexahydro-1-oxa-6-aza-cyclobuta[1,2:1,4]dicyclopentene-6-carboxylic Acid *tert*-Butyl Ester (28d).** The compound was prepared from 168 mg (0.66 mmol) of 4-but-3-enyloxy-2-oxo-2,5-dihydro-pyrrole-1-carboxylic acid *tert*-butyl ester (**2d**) in 67 mL of anhydrous dichloromethane by irradiation for 1.5 h. Column chromatography (P/EtOAc = 1/1 → EtOAc/MeOH = 19/1 as eluent) afforded 45.0 mg (0.18 mmol, 27%) of the desired product **28d** as colorless crystals and 38.0 mg (0.25 mmol, 38%) of compound **28a**. $R_f$ = 0.20 (EtOAc/MeOH = 95/5); mp 86 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.24 (virt. t, $^2J \approx {}^3J \approx$ 8.8 Hz, 1 H), 3.96 (ddd, $^3J$ = 11.2, $^2J$ = 8.8, $^3J$ = 5.3 Hz, 1 H), 3.84 (d, $^2J$ = 11.7 Hz, 1 H), 1.54 (s, 9 H), 3.80 (d, $^2J$ = 11.7 Hz, 1 H), 2.97 (dd, $^3J$ = 10.2, $^3J$ = 4.1 Hz, 1 H), 2.89−2.93 (m, 1 H), 2.25 (ddd, $^2J$ = 13.1, $^3J$ = 8.6, $^3J$ = 4.1 Hz, 1 H), 1.93−2.01 (m, 2 H), 1.75 (dd, $^2J$ = 12.7, $^3J$ = 5.3 Hz, 1 H). $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 175.0 (C), 150.0 (C), 83.2 (C), 81.9 (C), 68.4 ($CH_2$), 53.4 ($CH_2$), 45.1 (CH), 42.3 (CH), 31.9 ($CH_2$), 28.0 ($CH_3$), 25.7 ($CH_2$); IR (film) $\nu_{max}$ 2977 (m, CH), 1782 (s, C═O), 1744 (s, C═O), 1716 (s, C═O), 1477 (w), 1368 (s), 1296 (s), 1258 (m), 1158 (s), 1110 (m), 1045 (w), 989 (w), 907 (w), 853 (w), 780 (w), 731 (w) cm$^{-1}$; MS (EI, *m/z*, %) 238 (<1) [(M − $CH_3$)$^+$], 197 (5) [(M− $C_4H_8$)$^+$], 180 (15), 153 (100) [(197 − $CO_2$)$^+$], 135 (82), 122 (23), 98 (71) [(153 − $C_3H_3O$)$^+$], 69 (18), 57 (43) [$C_4H_9^+$], 55 (89) [$C_3H_3O^+$]; HRMS (EI) calcd for $C_{13}H_{19}NO_4$ − $CH_3$ 238.1079, found: 238.1082.

**6-tert-Butyl-hexahydro-1-oxa-6-aza-cyclopenta$^{1,4}$cyclobuta$^{1,2}$-benzen-5-one (29).** The compound was prepared from 56.4 mg (0.25 mmol) of 4-but-3-enyloxy-1-*tert*-butyl-5,6-dihydro-1*H*-pyridin-2-one (**16**) in 36 mL of anhydrous dichloromethane by irradiation for 2.5 h. Column chromatography (P/EtOAc = 2/1) afforded 42.0 mg (0.19 mmol, 74%) of the desired product as colorless crystals. $R_f$ = 0.23 (P/EtOAc = 2/1); mp 59 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 4.13−4.17 (m, 1 H), 1.44 (s, 9 H), 3.96 (ddd, $^3J$ = 11.2, $^2J$ = 9.3, $^3J$ = 5.5 Hz, 1 H), 3.61 (ddd, $^2J$ = 13.3, $^3J$ = 5.9, $^3J$ = 4.0 Hz, 1 H), 3.38 (ddd, $^2J$ = 13.3, $^3J$ = 9.7, $^3J$ = 3.3 Hz, 1 H), 1.70 (dd, $^2J$ = 12.6, $^3J$ = 5.5 Hz, 1 H), 2.94 (ddd, $^3J$ = 11.0, $^3J$ = 7.1, $^4J$ = 1.0 Hz, 1 H), 2.60 (virt. td, $^3J$ = 8.7, $^3J$ = 4.4 Hz, 1 H), 1.81−2.02 (m, 5 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 173.3 (C), 84.7 (C), 67.2 ($CH_2$), 57.6 (C), 45.4 (CH), 41.2 ($CH_2$), 39.1 (CH), 32.3 ($CH_2$), 32.0 ($CH_2$), 28.6 ($CH_3$), 24.9 ($CH_2$); NOE-contacts H-3α/H-4α, H-3α/H-6α, H-3α/H-7, H-3*β*/H-4*β*, H-5/H-4*β*, H-5/H-6*β*, H-5/H-10*β*, H-7/H-6α; IR (film) $\nu_{max}$ 2922 (s, CH), 2853 (s, CH), 1655 (s, C═O), 1458 (s), 1376 (s), 1323 (s), 1204 (m), 1104 (w), 1061 (w), 1022 (w), 938 (w), 722 (m) cm$^{-1}$; MS (EI, *m/z*, %) 223 (38) [M$^+$], 208 (29) [(M − $CH_3$)$^+$], 180 (18), 166 (15) [(M − $C_4H_9$)$^+$], 139 (18), 124 (9), 110 (25), 84 (38), 70 (62), 57 (57) [$C_4H_9^+$], 55 (100) [$C_3H_3O^+$]; HRMS (EI) calcd for $C_{13}H_{21}NO_2$ 223.1572, found: 223.1571.

**6-*tert*-Butyl-5-oxo-octahydro-1,6-diaza-cyclopenta$^{1,4}$cyclobuta$^{1,2}$-benzene-1-carboxylic Acid *tert*-Butyl Ester (30).** The compound was prepared from 38.0 mg (0.12 mmol) of but-3-enyl-(1-*tert*-butyl-6-oxo-1,2,3,6-tetrahydro-pyridin-4-yl)-carbamic acid *tert*-butyl ester (**18**) in 24 mL of anhydrous dichloromethane by irradiation for 1.75 h. Column chromatography (P/EtOAc = 1/1) afforded 23.0 mg (0.07 mmol, 61%) of the desired product as colorless crystals. $R_f$ = 0.27 (P/EtOAc = 1/1); mp 64−67 °C; $^1$H NMR (500 MHz, DMSO-$d_6$, 353 K) $\delta$ 3.62−3.69 (m, 2 H), 3.29−3.39 (m, 2 H), 2.69−2.78 (m, 1 H), 2.66 (dd, $^3J$ = 10.2, $^3J$ = 6.1 Hz, 1 H), 2.29 (virt. td, $^2J \approx {}^3J \approx$ 12.4, $^3J$ = 4.3 Hz, 1 H), 1.99−2.05 (m, 2 H), 1.89−1.95 (m, 1 H), 1.66−1.72 (m, 1 H), 1.49−1.56 (m, 1 H), 1.40 (s, 9 H), 1.39 (s, 9 H); $^{13}$C NMR (90 MHz, DMSO-$d_6$, 353 K) $\delta$ 171.8 (C), 152.7 (C), 78.3 (C), 63.8 (C), 55.9 (C), 47.3 ($CH_2$), 43.9 (CH), 39.8 ($CH_2$), 39.1 (CH), 29.8 ($CH_2$), 29.0 ($CH_2$), 27.8 ($CH_3$), 27.6 ($CH_3$), 25.9 ($CH_2$); IR (film) $\nu_{max}$ 2971 (s, CH), 2872 (m, CH), 1694 (s, C═O), 1644 (s, C═O), 1480 (m), 1454 (s), 1392 (s), 1326 (s), 1250 (m), 1172 (s), 1094 (m), 938 (w), 773 (w) cm$^{-1}$; MS (EI, *m/z*, %) 322 (15) [M$^+$], 307 (2) [(M − $CH_3$)$^+$], 266 (10) [(M − $C_4H_8$)$^+$], 249 (4), 237 (6), 222 (9) [(266 − $CO_2$)$^+$], 210 (11), 193 (5), 166 (19), 137 (11), 122 (13), 108 (11), 95 (36), 84 (28), 57 (100) [$C_4H_9^+$]; HRMS (EI) calcd for $C_{18}H_{30}N_2O_3$ 322.2257, found: 322.2251.

**Hexahydro-1-oxa-6-aza-cyclopenta$^{1,4}$cyclobuta$^{1,2}$benzen-5-one (31).** The compound was prepared from 28.0 mg (0.17 mmol) of 4-but-3-enyloxy-5,6-dihydro-1*H*-pyridin-2-one (**20**) in 26 mL of anhydrous dichloromethane by irradiation for 3.5 h. Column chromatography ($CH_2Cl_2$/MeOH = 95/5) afforded 22.0 mg (0.13 mmol, 79%) of the desired product as colorless crystals. $R_f$ = 0.16 ($CH_2Cl_2$/MeOH = 95/5); mp 91 °C; $^1$H NMR (360 MHz, $CDCl_3$) $\delta$ 6.72 (br. s, 1 H), 4.18 (virt. t, $^2J \approx {}^3J \approx$ 9.0 Hz, 1 H), 4.00 (ddd, $^3J$ = 10.8, $^2J$ = 9.0, $^3J$ = 5.4 Hz, 1 H,), 3.38−3.45 (m, 2 H), 2.88 (dd, $^3J$ = 11.1, $^3J$ = 7.1 Hz, 1 H), 2.71 (virt. td, $^3J \approx$ 8.7, $^3J$ = 4.7 Hz, 1 H), 2.08 (ddd, $^2J$ = 13.2, $^3J$ = 8.7, $^3J$ = 7.1 Hz, 1 H), 1.90−1.99 (m, 3 H), 1.80 (virt. dt, $^2J$ = 13.5, $^3J \approx$ 4.0 Hz, 1 H), 1.73 (dd, $^2J$ = 12.6, $^3J$ = 5.4 Hz, 1 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 174.8 (C), 85.0 (C), 67.2 ($CH_2$), 43.1 (CH), 39.6 (CH), 39.2 ($CH_2$), 32.0 ($CH_2$), 30.4 ($CH_2$), 25.1 ($CH_2$); NOE-contacts H-3α/H-4α, H-3α/H-7, H-3*β*/H-4*β*, H-5/H-6*β*, H-5/H-10*β*, H-5/H-11*β*, H-6*β*/H-10*β*, H-10/NH; IR (film) $\nu_{max}$ 3192 (m, NH), 2949 (s, CH), 2872 (s, CH), 1682 (s, C═O), 1464 (s), 1448 (s), 1410 (m), 1352 (s), 1237 (w), 1188 (w), 1103 (m), 1042 (m), 997 (m), 929 (w), 819 (m), 757 (w), 681 (m) cm$^{-1}$; MS (EI, *m/z*, %) 167 (32) [M$^+$], 152 (2) [(M − $CH_3$)$^+$], 138 (5), 122 (4), 111 (17), 96 (66), 84 (15), 72

(15), 55 (100) [$C_3H_3O^+$]; HRMS (EI) calcd for $C_9H_{13}NO_2$ 167.0946, found: 167.0947.

**5-Oxo-octahydro-1,6-diaza-cyclobuta[1,2:1,4]dicyclopentene-1-carboxylic Acid Ethyl Ester (34).** The compound was prepared from 20.0 mg (0.09 mmol) of but-3-enyl-(5-oxo-2,5-dihydro-1*H*-pyrrol-3-yl)-carbamic acid ethyl ester (**6**) in 18 mL of anhydrous dichloromethane by irradiation for 1 h. Column chromatography (EtOAc/MeOH = 19/1) yielded 14.5 mg (0.06 mmol, 72%) of the desired product as colorless crystals. $R_f$ = 0.45 (EtOAc/MeOH = 9/1); mp 118−120 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 7.04 (br. s, 1 H), 4.12 (q, $^3J$ = 6.9 Hz, 2 H), 3.96 (br. s, 1 H), 3.70 (br. s, 1 H), 3.15 (br. s, 1 H), 2.98−2.94 (m, 1 H), 2.79 (br. s, 1 H), 2.31−2.26 (m, 2 H), 2.07−2.00 (m, 2H), 1.78−1.72 (m, 1 H), 1.22 (t, $^3J$ = 6.9 Hz, 3 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 179.2 (C), 155.2 (C), 67.6 (C), 61.4 ($CH_2$), 48.9 ($CH_2$), 47.2 (CH), 44.0 ($CH_2$), 40.4 (CH), 28.3 ($CH_2$), 26.0 ($CH_2$), 14.7 ($CH_3$); IR (film) $\nu_{max}$ 3195 (m, NH), 2965 (m, CH), 1690 (vs, C═O), 1664 (s, C═O), 1461 (w), 1396 (w), 1376 (w), 1360 (w), 1339 (w), 1309 (w), 1221 (w), 1169 (w), 1122 (w), 1097 (w), 1052 (w), 1009 (w), 894 (w), 832 (w), 805 (w), 775 (w), 748 (w), 727 (w), 708 (w), 692 (w), 673 (w) cm$^{-1}$; MS (EI, *m/z*, %) 224 (100) [$M^+$], 196 (5) [$(M - C_2H_4)^+$], 169 (70), 123 (18), 97 (36); HRMS (EI) calcd for $C_{11}H_{16}N_2O_3$ 224.1161, found: 224.1153.

**Octahydro-6-aza-cyclopenta[1,4]cyclobuta[1,2]benzen-5-one (37).** The compound was prepared from 16.0 mg (0.10 mmol) of 4-pent-4-enyl-5,6-dihydro-1*H*-pyridin-2-one (**23**) in 20 mL of anhydrous dichloromethane by irradiation for 1 h. Column chromatography (EtOAc/MeOH = 19/1) yielded 8.5 mg (0.05 mmol, 52%) of the desired product as colorless crystals. $R_f$ = 0.30 (EtOAc/MeOH = 9/1); mp 97−99 °C; $^1$H NMR (500 MHz, $CDCl_3$) $\delta$ 6.04 (br. s, 1 H), 3.56 (dt, $^3J$ = 12.8, $^3J$ = 1.8 Hz, 2 H), 3.40−3.35 (m, 1 H), 2.54 (dd, $^3J$ = 10.7, $^3J$ = 6.8 Hz, 1 H), 2.42 (br. s, 1 H), 2.15−2.09 (m, 1 H), 1.96−1.83 (m, 3 H), 1.74−1.68 (virt. dt, $^3J \approx$ 13.4, $^3J \approx$ 4.6 Hz, 1 H), 1.64−1.57 (m, 4 H), 1.35 (dt, $^3J$ = 12.6, $^3J$ = 6.7 Hz, 1 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 176.4 (C), 47.8 (C), 40.9 (CH), 40.6 ($CH_2$), 39.7 ($CH_2$), 38.6 (CH), 33.0 ($CH_2$), 31.7 ($CH_2$), 27.8 ($CH_2$), 24.9 ($CH_2$); IR (film) $\nu_{max}$ 3177 (w, NH), 2923 (s, CH), 2854 (m, CH), 1659 (vs, C═O), 1489 (w), 1443 (w), 1409 (w), 1340 (w), 1318 (w), 1260 (w), 1215 (w), 1144 (w), 1124 (w), 1068 (w), 1025 (w), 932 (w), 820 (w) cm$^{-1}$; MS (EI, *m/z*, %) 165 (100) [$M^+$], 150 (14), 136 (29), 122 (31), 109 (78), 82 (58), 55 (42); HRMS (EI) calcd for $C_{10}H_{15}NO$ 165.1154, found: 165.1153.

**3a-Methoxy-octahydro-cyclopenta[3,4]cyclobuta[1,2-c]pyrrol-1-one (39).** The compound was prepared from 100 mg (0.75 mmol) of 1,5-dihydro-4-methoxy-2*H*-pyrrol-2-one (**1a**) and 1.37 mL (15.0 mmol) of cyclopentene in 150 mL of anhydrous dichloromethane by irradiation for 9 h. Column chromatography (EtOAc/MeOH = 19/1) afforded 87.0 mg (0.48 mmol, 64%) of the major diastereoisomer **39** (exo/endo selectivity = 4.6/1) as colorless crystals. $R_f$ = 0.36 (EtOAc/MeOH = 95/5); mp 92−94 °C; $^1$H NMR (250 MHz, $CDCl_3$) $\delta$ 5.98 (br. s, 1 H), 3.65 (d, $^3J$ = 10.8 Hz, 1 H), 3.42 (d, $^3J$ = 10.7 Hz, 1 H), 3.17 (s, 3 H), 2.75 (virt. t, $^3J \approx$ 7.3 Hz, 1 H), 2.62−2.54 (m, 1 H), 2.37 (d, $^3J$ = 4.0 Hz, 1 H), 2.07−1.99 (m, 1 H), 1.87−1.75 (m, 2 H), 1.70−1.57 (m, 2 H), 1.50−1.40 (m, 1 H); $^{13}$C NMR (90 MHz, $CDCl_3$) $\delta$ 179.0 (C), 77.3 (C), 52.4 ($CH_2$), 50.6 ($CH_3$), 48.3 (CH), 46.9 (CH), 38.7 (CH), 33.5 ($CH_2$), 27.0 ($CH_2$), 24.4 ($CH_2$); Anal. Calcd for $C_{10}H_{15}NO_2$ (181.23): C, 66.27; H, 8.34; N, 7.73. Found: C, 66.10; H, 8.23; N, 7.55; IR (film) $\nu_{max}$ 3202 (m, NH), 2939 (m, CH), 1671 (vs, C═O), 1495 (w), 1438 (w), 1369 (w), 1331 (w), 1304 (w), 1291 (w), 1261 (w), 1240 (w), 1207 (w), 1131 (w), 1079 (w), 1058 (w), 1038 (w), 1002 (w), 762 (w), 691 (w), 674 (w), 652 (w) cm$^{-1}$; MS (EI, *m/z*, %) 181 (1) [$M^+$], 166 (1) [$(M - CH_3)^+$], 114 (100), 82 (28).

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**Supporting Information Available:** Complete experimental and analytical data of compounds **2d**, **6**−**9**, **11**, **18**, **21**−**27**, **32**, **33**, **35**, and **36**. This material is available free of charge via the Internet at http://pubs.acs.org.

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