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RING-CLOSING OLEFIN METATHESIS FOR THE SYNTHESIS OF FUSED NITROGEN HETEROCYCLES

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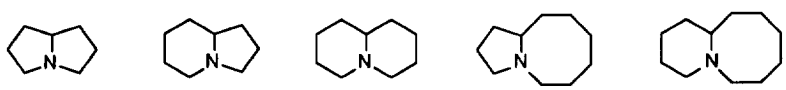
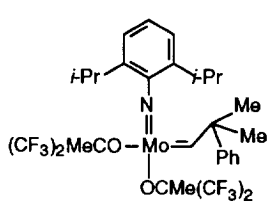
Abstract. A novel technique for the efficient synthesis of fused nitrogen heterocycles containing various combinations of five- and eight-membered rings has been developed. This method features the ring-closing metathesis (RCM), which is catalyzed by the molybdenum alkylidene complex **6**, of α,ω-dienes that have a nitrogen atom in the chain linking the two olefinic functional groups.

INTRODUCTION. Heterocyclic systems bearing a nitrogen atom at one of the ring fused positions constitute structural subunits that are common to a diverse array of alkaloid natural products. A number of biologically important alkaloids contain the pyrrolizidine, indolizidine, quinolizidine ring systems **1-3**, respectively.[1] The pyrrolidinoazocine and the piperidinoazocine ring systems **4** and **5** may either be found in alkaloids or serve as intermediates in their synthesis.[2] Consequently, the invention and development of general techniques for the construction of such systems represents a major challenge in the arena of alkaloid synthesis, and such problems have been the subject of extensive investigations in our laboratories for a number of years.



1 **2** **3** **4** **5**

We were recently attracted to several interesting reports by Grubbs,[3] who discovered that a series of heteroatom-linked α,ω-dienes underwent facile ring-closing olefin metatheses (RCM) to produce monocyclic unsaturated oxygen and nitrogen heterocycles having from five to seven members. These cyclizations were catalyzed by the molybdenum and ruthenium alkylidene complexes **6**[4] and **7**,[3c] respectively.[5,6] These reagents



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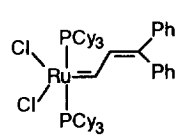

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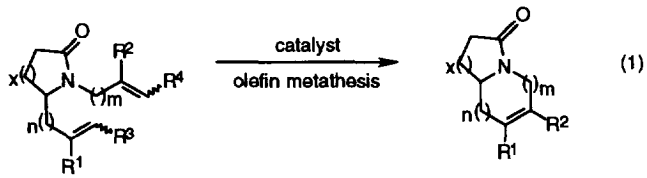
have been found to be more tolerant of other Lewis-basic functional groups than previously known metathesis catalysts. Based upon this finding, we were intrigued by the possible application of transition metal alkylidene-catalyzed ring-closing olefin metathesis to the general problem of constructing fused nitrogen heterocycles according to eq 1. The reduction of this idea to practice constitutes the substance of the present account.

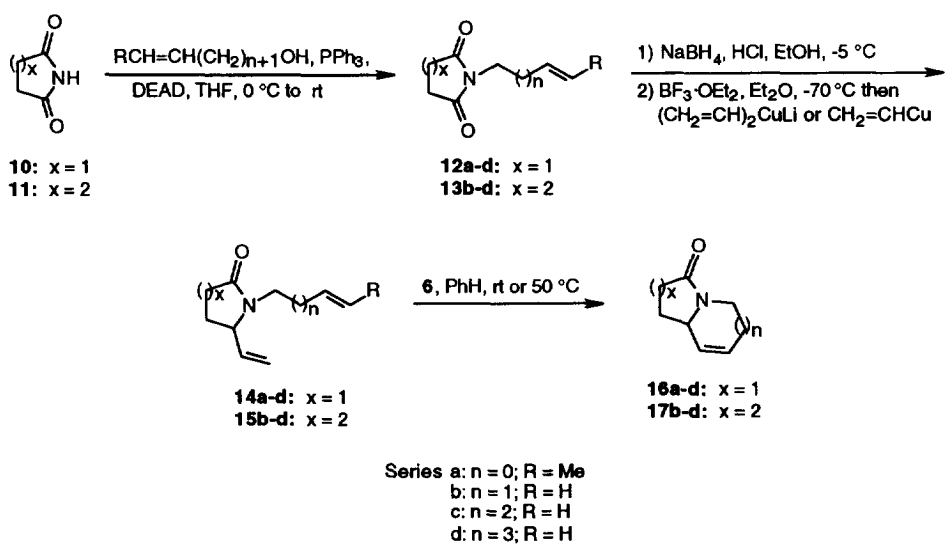


(1)

8 **9**

METHODOLOGICAL STUDIES. In order to explore the scope and limitations of the molybdenum alkylidene-catalyzed ring closing metathesis of α,ω-dienes in which the olefinic functions were linked via a nitrogen atom, a series of representative dienes were prepared from succinimide (**10**) and glutarimide (**11**) according to the sequences of reactions outlined in Schemes 1 and 2.[7] Thus, alkylation of **10** and **11** with a series of unsaturated alcohols under Mitsunobu conditions[8] furnished the corresponding imides **12a-d**, **13b-d**, **18** and **19** in 60-90% yields. Hydride reduction of these imides in absolute ethanol in the presence of acid gave the intermediate ethoxy amides.[9] These ethoxy amides were isolated and were treated under standard conditions with $BF_3{\cdot}Et_2O$ and lithium divinylcuprate, vinyl copper or allyl trimethylsilane to give the cyclization substrates **14a-d** and **15b-d**, and **20a-d** (38-87% unoptimized overall yields) *via* nucleophilic addition to the *N*-acyl iminium salts formed *in situ*.[10]

Scheme 1



10: x = 1
11: x = 2

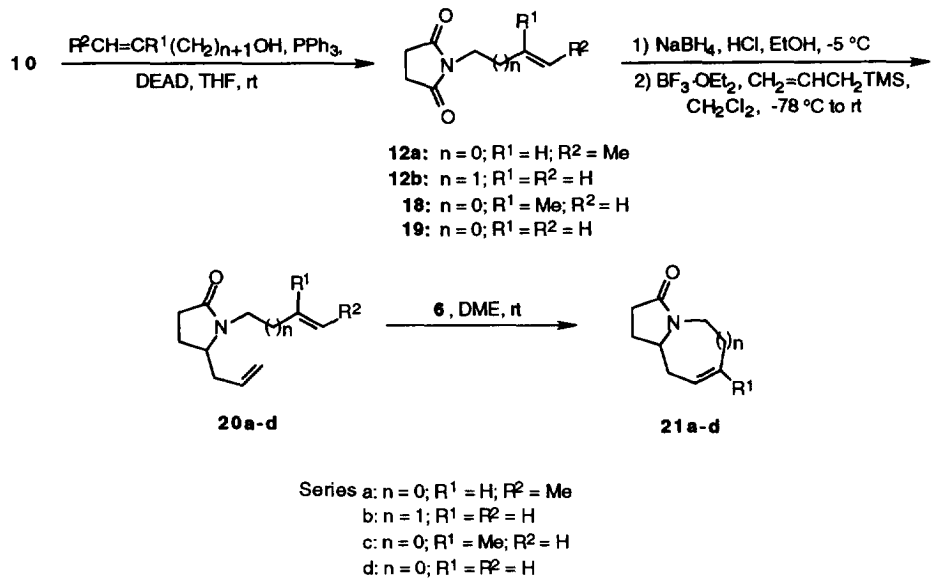
12a-d: x = 1
13b-d: x = 2

14a-d: x = 1
15b-d: x = 2

16a-d: x = 1
17b-d: x = 2

Series a: n = 0; R = Me
b: n = 1; R = H
c: n = 2; R = H
d: n = 3; R = H

Scheme 2

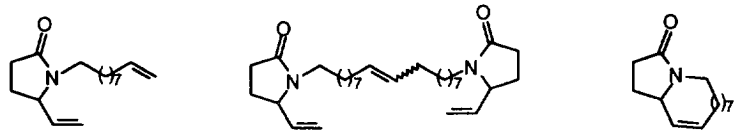


When the α,ω-dienes **14a-c**, **15b,c** and **20a-d** (0.01-0.02 M in either dry, degassed benzene or DME) were stirred with the molybdenum catalyst **6** (10-15 mol%) at room temperature, facile ring-closing metathesis ensued to give the corresponding bicyclics **16a-c**, **17b,c** and **21a-c** in 70-95% yields (unoptimized). The dienes **14d** and **15d** underwent cyclization to provide the medium ring products **16d** and **17d** in 50-60% yields (unoptimized), but these reactions required heating at 50 °C and frequently the addition of a second portion of **6** (10 mol%) after 3 h to effect completion of the reaction. The syntheses of the bicyclics **16d** and **17d** represent the first examples of forming eight-membered heterocycles by ring-closing olefin metathesis. Grubbs has recently extended this finding and has provided useful insights into some of the energetic requirements for the successful formation of medium sized rings by RCM.[11]

We made no effort to optimize the conditions for each of the RCM reactions, and observed starting material at the end of the reaction time in a number of cases; more catalyst could be added to effect completion. There appears to be an advantage to conducting these cyclizations in an inert atmosphere box. For example, when the cyclization of **20b** was executed on the bench-top under argon, **21b** was isolated in approximately 50% yield with nearly equal amounts of starting material being recovered. When the reaction was performed in a dry box using the same amount of catalyst, the bicyclic **21b** was isolated in 95% yield.

In the context of exploring the applicability of forming large rings, such as the 13-membered ring that is found in manzamine A (*vide infra*), the 1,13-diene **22** was prepared. However, even under highly dilute reaction conditions in which **22** (0.01 M in benzene) was slowly added to a solution of catalyst **6** (5 mL of 0.004 M in benzene) by a syringe pump, none of the desired cyclized product **24** was detected. Rather unreacted starting material together with an inseparable mixture of the dimers of the general structure **23** (*trans/cis* ≈ 2.3:1) was obtained. It should be noted that cyclizations of α,ω-dienes producing 13- and 14-membered rings by ring-closing

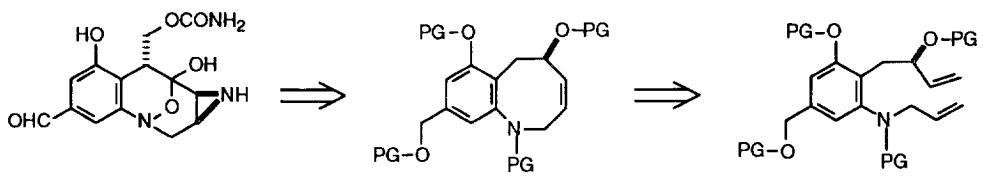
metathesis have recently been reported.[12-14] The scope and limitations of this useful tactic for ring formation clearly remain to be established, and we are currently exploring these issues.



22 **23** **24**

APPLICATIONS. Although we are presently examining the applicability of ring-closing metathesis reactions to a number of biologically active natural products, only two investigations will be presented herein. The first of these is the unusual antitumor antibiotic FR-900482 (**25**), which was isolated from *Streptomyces sandaensis* No. 6897 and appears to act by forming interstrand DNA-DNA and DNA-protein cross links.[15] One of the key structural features that distinguishes **25** from the structurally-related mitomycins is the unique hydroxylamine function whose hydroxyl group participates in a hemiketal array. There have been several reports of studies directed toward the synthesis of **25**, and an elegant total synthesis has recently been reported by Fukuyama.[16] Our effort to develop a novel approach to this important alkaloid incorporates ring-closing olefin metathesis as a key step to transform a substrate such as **27** to the highly substituted benzoazocine **26** (Scheme 3), which is related to a less highly functionalized intermediate in Fukuyama's synthesis of **25**. In order to establish the underlying feasibility of this plan, we examined such a RCM cyclization in a simple model system.[17,18]

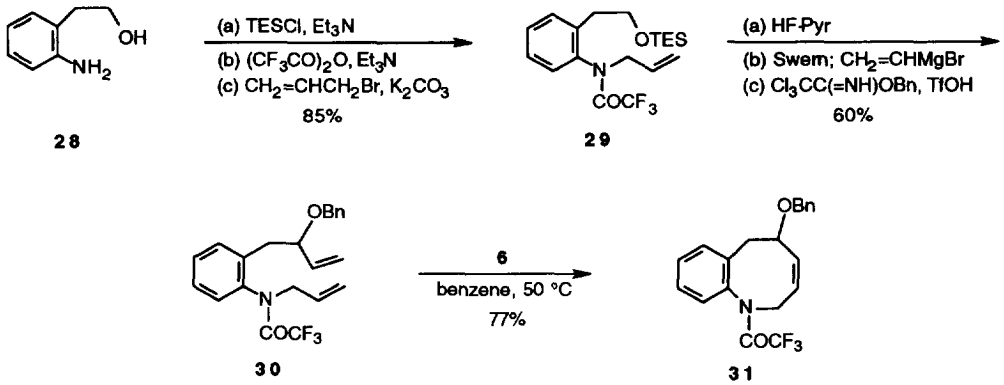
Scheme 3



25 **26** **27**

To test the key step in our approach to FR-900482, the α,ω-diene **30** was prepared in good overall yield from the commercially available amino alcohol **28** by a straightforward sequence of reactions (Scheme 4). Following protection of the primary alcohol in **28**, the requisite allyl group was introduced by *N*-allylation of the intermediate trifluoroacetamide to give **29** in 85% overall yield. Deprotection of the alcohol function in **29** followed by a one-pot oxidation and Grignard addition, and then protection of the allylic hydroxyl group gave the cyclization substrate **30** in about 60% overall yield for the three steps. Upon treatment with the molybdenum carbene complex **6** (15 mol%) in degassed benzene at 50 °C, **30** underwent facile ring-closing metathesis to give the benzoazocine **31** in 77% yield. The application of a related cyclization to the asymmetric, total synthesis of FR-900482 is in progress, and the results of these investigations will be reported in due course.

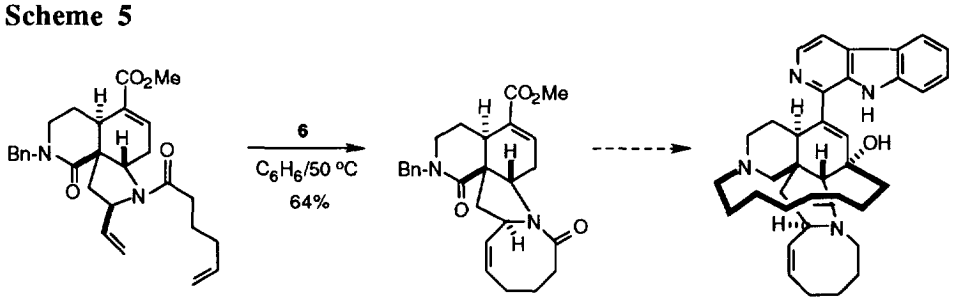
Scheme 4



28 29 30 31

We have also explored the feasibility of using olefin metathesis as a key transformation in the total synthesis of the complex anti-cancer alkaloid manzamine A (**34**).[19-21] Namely, we discovered that the molybdenum carbene complex **6** may be exploited to catalyze the ring closing metathesis of the highly functionalized substrate **32** to deliver the tetracyclic pyrrolidinoazocine **33**, which is an advanced intermediate in our novel approach to manzamine A (Scheme 5).[20] In the preliminary model study involving the attempted cyclization of **22**, we had hoped to establish the feasibility of using a ring-closing metathesis reaction for the elaboration of a 13-membered ring. Although **22** did not cyclize, Pandit has recently shown that ring forming metathesis may be used to construct the 13-membered ring of manzamine A in a more conformationally restricted model system.[14]

Scheme 5



32 33 34

CONCLUDING REMARKS. We have established the feasibility of forming pyrrolizidines, indolizidines, quinolizidines, pyrrolidinoazocines, and piperidinoazocines *via* the facile ring-closing metathesis of α,ω-diolefins catalyzed by the molybdenum reagent **6**. Such reactions are now being employed in the syntheses of a variety of alkaloids. In other studies we are examining substrates bearing vinyl halide substituents to ascertain whether more highly functionalized products may be prepared. These efforts, coupled with those of others in the field, seem likely to further the use of RCM in the synthesis of complex natural products. Perhaps the principal problem that lies on the horizon is the development of more active catalysts that are more readily available, more easily manipulated, and have greater functional group tolerance.

Acknowledgment. We thank the National Institutes of Health and The Robert A. Welch Foundation for their generous support of this research and the Stipendium-Fonds des Verbandes der Chemischen Industrie for a Liebig-Stipendium (to MP). We also thank Prof. R. H. Grubbs (California Institute of Technology) and D. R. Hamm (Catalytica Fine Chemicals) for providing generous quantities of the molybdenum catalyst **6**.

EXPERIMENTAL SECTION

Representative Procedure for Preparation of *N*-Alkyl Imides. Synthesis of *N*-(2-Butene-1-yl)-succinimide (12a). A solution of vacuum-dried succinimide (**10**) (4.00 g, 40.4 mmol), vacuum-dried PPh_3 (13.77 g, 52.5 mmol), and 2-buten-1-ol (3.49 g, 48.5 mmol) in THF (150 mL) was treated dropwise at 0-25 °C with diethyl azodicarboxylate (9.13 g, 52.5 mmol). The reaction mixture was stirred at rt for 24 h. The reaction mixture was concentrated under reduced pressure, and Et_2O (150 mL) was added. The organic solution was concentrated under reduced pressure to approximately 40-50 mL at which point a significant quantity of solid (Ph_3PO) was visible. The solid was removed by filtration, and the filtrate was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with hexanes/EtOAc (3:1) to give 4.91 g (79%) of **12a**. ^1H NMR ($CDCl_3$) δ 5.64-5.57 (m, 1 H), 5.36-5.30 (m, 1 H), 3.92 (td, J = 6.0, 0.5 Hz, 2 H), 2.60 (s, 4 H), 1.55 (dq, J = 6.5, 1.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.7, 130.2, 123.5, 40.2, 28.0, 17.4; IR ($CDCl_3$) 1775, 1676 cm^{-1}; mass spectrum (C/I) *m/z* 154.0864 [$C_8H_{12}NO_2$ (M+1) requires 154.0868].

***N*-(3-Buten-1-yl)-succinimide (12b).** Prepared as a yellow oil in 95% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.70 (ddt, J = 17.0, 10.2, 6.9 Hz, 1 H), 5.07-4.99 (comp, 2 H), 3.57 (t, J = 7.1 Hz, 2 H), 2.67 (s, 4 H), 2.32 (q, J = 7.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 176.0, 134.1, 117.1, 37.6, 31.6, 27.8; IR (neat) 1773, 1690, 1640, 1438, 1402 cm^{-1}; mass spectrum (CI) *m/z* 154.0870 [$C_8H_{12}NO_2$ (M+1) requires 154.0868].

***N*-(4-Penten-1-yl)-succinimide (12c).** Prepared as a yellow oil in 51% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.75 (ddt, J = 17.0, 6.7, 6.6 Hz, 1 H), 5.05-4.90 (m, 2 H), 3.48 (t, J = 7.4 Hz, 2 H), 2.66 (s, 4 H), 2.03 (q, J = 6.7 Hz, 2 H), 1.64 (p, J = 7.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 177.2, 137.2, 115.2, 38.4, 30.9, 28.1, 26.6; IR (neat) 1825, 1774, 1728, 1640, 1440 cm^{-1}; mass spectrum (CI) *m/z* 168.1024 [$C_9H_{14}NO_2$ (M+1) requires 168.1025], 138, 126, 112.

***N*-(5-Hexen-1-yl)-succinimide (12d).** Prepared as a colorless oil in 86% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.77 (ddt, J = 17.0, 10.3, 6.7 Hz, 1 H), 5.06-4.90 (m, 2 H), 3.51 (t, J = 7.1 Hz, 2 H), 2.70 (s, 4 H), 2.07 (q, J = 7.1 Hz, 2 H), 1.63-1.45 (m, 2 H), 1.43-1.23 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 177.0, 138.0, 114.6, 38.4, 33.0, 27.9, 26.9, 25.8; IR (neat) 1772, 1695 cm^{-1}; mass spectrum (CI) *m/z* 182.1169 [$C_{10}H_{16}NO_2$ (M+1) requires 182.1181], 182, 180, 100.

***N*-(3-Buten-1-yl)-glutarimide (13b).** Prepared as a colorless oil in 90% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.71 (ddt, J = 17.1, 10.0, 7.1 Hz, 1 H), 5.03-4.94 (m, 2 H), 3.81 (t, J = 6.5 Hz, 4 H), 2.60 (, J = 6.5 Hz, 4 H), 2.24 (q, J = 7.3 Hz, 2 H), 1.88 (p, J = 6.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 172.4, 135.1, 116.7, 38.5, 32.8, 32.4, 17.1; IR (neat) 1724, 1680, 1436 cm^{-1}; mass spectrum (CI) *m/z* 167.0939 [$C_9H_{13}NO_2$ (M+1) requires 167.0946], 138, 126, 114, 108.

***N*-(4-Penten-1-yl)-glutarimide (13c).** Prepared as a colorless oil in 66% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.81 (ddt, J = 17.0, 10.3, 6.5 Hz, 1 H), 5.03 (dd, J = 17.0, 1.4 Hz, 1 H), 4.96 (dd, J = 10.3, 1.4 Hz, 1 H), 3.76 (t, J = 7.5 Hz, 2 H), 2.64 (t, J = 6.6 Hz, 4 H), 2.10-1.89 (m, 2 H), 1.93 (t, J = 6.6 Hz, 2 H), 1.61 (p, J = 7.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 172.3, 137.6, 114.7, 39.1, 32.7, 31.0, 26.9, 17.1; IR (neat) 1725, 1673 cm^{-1}; mass spectrum (CI) *m/z* 182.1185 [$C_{10}H_{16}NO_2$ (M+1) requires 182.1181], 182 (base), 180, 167.

***N*-(5-Hexen-1-yl)-glutarimide (13d).** Prepared as a yellow oil in 88% yield according to the procedure described above for **12a**. ^1H NMR ($CDCl_3$) δ 5.77 (ddt, J = 10.3, 17.0, 6.9 Hz, 1 H), 5.03-4.88 (m, 2 H), 3.73 (t, J

= 7.4 Hz, 2 H), 2.62 (t, *J* = 6.6 Hz, 2 H), 2.05 (q, *J* = 6.9 Hz, 2 H), 1.90 (p, *J* = 6.6 Hz, 2 H), 1.54-1.20 (comp, 4 H); ^{13}C NMR ($CDCl_3$) δ 172.4, 138.5, 114.7, 39.5, 33.4, 32.9, 27.5, 26.2, 17.2; IR ($CDCl_3$) 1724, 1670, 1359 cm^{-1}; mass spectrum (CI) *m/z* 196.1337 [$C_{11}H_{18}NO_2$ (M+1) requires 196.1338].

***N*-(2-Methyl-2-propen-1-yl)-succinimide (18).** Prepared as a white crystalline solid in 68% yield according to the procedure described above for **12a**. mp 38-39 °C; ^{1}H NMR ($CDCl_3$) δ 4.83 (p, *J* = 1.5 Hz, 1 H), 4.69 (t, *J* = 0.9 Hz, 1 H), 4.00 (s, 2 H), 2.71 (s, 4 H), 1.69 (d, *J* = 0.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.8, 138.5, 112.1, 43.9, 28.1, 20.4; IR ($CHCl_3$) 1778, 1707, 1427, 1394 cm^{-1}; mass spectrum (C/I) *m/z* 154.0860 [$C_8H_{12}NO_2$ (M+1) requires 154.0868].

***N*-(2-Propen-1-yl)-succinimide (19).** Prepared as a pale yellow oil in 75% yield according to the procedure described for **12a.** ^{1}H NMR ($CDCl_3$) δ 5.75 (tdd, *J* = 17.2, 10.1, 5.9 Hz, 1 H), 5.20 (dq, *J* = 17.2, 1.3 Hz, 1 H), 5.16 (dq, *J* = 10.1, 1.3 Hz, 1 H), 4.09 (dt, *J* = 5.9, 1.2 Hz, 2 H), 2.71 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 176.7, 130.7, 118.4, 40.9, 28.2; IR ($CDCl_3$) 1775, 1705, 1646, 1432 cm^{-1}; mass spectrum (C/I) *m/z* 128.0713 [$C_7H_9NO_2$ (M + 1) requires 128.0712].

Representative Procedure for Preparation of Amide *N,O*-Acetals. Synthesis of 1-(2'-Butene-1'-yl)-5-ethoxy-2-pyrrolidinone. To a mixture of **12a** (4.91 g, 32.1 mmol) and bromocresol green indicator (10 drops) in EtOH (120 mL) containing $NaBH_4$ (4.85 g, 128.2 mmol) at -10 to 0 °C was *slowly* added ten drops of HCl (2 M in EtOH) every 10 min for a period of 2 h. The reaction mixture was brought to pH 3 – 5 by the addition of HCl (6 M in EtOH) and was diluted with H_2O (50 mL). The mixture was extracted with CH_2Cl_2 (3 x 50 mL), and the combined organic layers were washed with saturated aq. $NaHCO_3$ (25 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with hexanes/EtOAc (3:1) to give 3.95 g (55%) of product as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.60-5.54 (m, 1 H), 5.54-5.28 (m, 1 H), 4.85 (dd, *J* = 6.3, 1.3 Hz, 1 H), 4.12 (ddt, *J* = 15.0, 5.0, 1.5 Hz, 1 H), 3.44 (ddd, *J* = 8.0, 7.1, 0.5 Hz, 1 H), 3.38 (q, *J* = 7.1 Hz, 2 H), 2.45 (p, *J* = 9.0 Hz, 1 H), 2.23 (ddd, *J* = 10.0, 7.1, 3.1 Hz, 1 H), 2.12-2.02 (m, 1 H), 1.92-1.86 (m, 1 H), 1.61 (dd, *J* = 6.4, 0.6 Hz, 3 H), 1.31 (t, 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.3, 129.2, 125.2, 88.2, 61.5, 42.0, 29.0, 24.8, 17.5, 15.2; IR 1689 cm^{-1}; mass spectrum (C/I) *m/z* 184.1335 [$C_{10}H_{18}NO_2$ (M + 1) requires 184.1338].

1-(3'-Buten-1'-yl)-5-ethoxy-2-pyrrolidinone. Prepared as a colorless oil from **12b** in 40% yield according to the procedure described above. ^{1}H NMR ($CDCl_3$) δ 5.76 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.10-4.95 (m, 3 H), 3.58 (dt, *J* = 13.7, 7.5 Hz, 1 H), 3.44 (q, *J* = 6.9 Hz, 2 H), 3.13 (p, *J* = 7.0 Hz, 1 H), 2.57-1.88 (comp, 8 H); ^{13}C NMR ($CDCl_3$) δ 174.4, 134.9, 116.2, 88.7, 60.9, 39.3, 31.6, 28.5, 24.3, 14.8; IR (neat) 1696, 1449 cm^{-1}; mass spectrum (CI) *m/z* 184.1337 [$C_{10}H_{18}NO_2$ (M+1) requires 184.1338], 166, 138.

5-Ethoxy-1-(4'-penten-1'-yl)-2-pyrrolidinone. Prepared as a colorless oil from **12c** in 51% yield according to the procedure described above. ^{1}H NMR ($CDCl_3$) δ 5.81 (ddt, *J* = 17.0, 10.3, 6.6 Hz, 1 H), 5.06-5.00 (comp, 3 H), 3.50 (q, *J* = 7.0 Hz, 2 H), 3.16-3.07 (m, 1 H), 2.58-2.46 (m, 1 H), 2.35-2.21 (m, 1 H), 2.10-1.94 (comp, 4 H), 1.76-1.59 (comp, 4 H), 1.23 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.1, 137.8, 114.6, 89.0, 63.2, 45.3, 32.2, 31.0, 27.0, 26.9, 15.7, 15.2; IR (neat) 1653 cm^{-1}; mass spectrum (CI) *m/z* 212.1646 [$C_{12}H_{22}NO_2$ (M+1) requires 212.1651], 184, 177, 166, 128, 105.

5-Ethoxy-1-(5'-hexen-1'-yl)-2-pyrrolidinone. Prepared as a colorless oil from **12d** in 66% yield according to the procedure described above. ^{1}H NMR ($CDCl_3$) δ 5.78 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1 H), 5.02-4.92 (comp, 3 H), 3.47 (app. q, *J* = 7.0 Hz, 1 H), 3.10 (ddd, *J* = 14.0, 8.1, 5.9 Hz, 1 H), 2.56-2.44 (m, 1 H), 2.34-1.93 (comp, 5 H), 1.63-1.51 (m, 2 H), 1.48-1.35 (m, 2 H), 1.22 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.3, 137.9, 114.2, 88.6, 60.9, 39.8, 32.9, 28.6, 26.6, 25.8, 24.4, 14.9; IR (neat) 1697, 1640 cm^{-1}; mass spectrum (CI) *m/z* 212.1651 [$C_{12}H_{22}NO_2$ (M+1) requires 212.1639], 212 (base), 210, 202, 156, 137, 133, 117, 113, 103.

1-(3'-Buten-1'-yl)-5-ethoxy-2-piperidone. Prepared as a pale yellow oil from **13b** in 87% yield according to the procedure described above. ^{1}H NMR ($CDCl_3$) δ 5.74 (ddt, *J* = 17.1, 10.1, 6.9 Hz, 1 H), 5.05-4.92 (m, 2 H), 4.53 (t, *J* = 2.8 Hz, 1 H), 3.78-3.62 (m, 1 H), 3.54-3.35 (m, 2 H), 3.13-3.01 (m, 1 H), 2.45-2.17 (comp, 4 H), 2.05-1.84 (m, 2 H), 1.68-1.57 (m, 2 H), 1.18 (t, *J* = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.3, 135.7, 116.4, 86.8, 63.2,

45.3, 32.4, 32.2, 27.0, 15.8, 15.3; IR ($CDCl_3$) 1636, 1473 cm^{-1}; mass spectrum (CI) *m/z* 198.1499 [$C_{11}H_{20}NO_2$ (M+1) requires 198.1494], 164, 132.

5-Ethoxy-1-(4'-penten-1'-yl)-2-piperidone. Prepared as a colorless oil from **13c** in 50% yield according to the procedure described above. ^1H NMR ($CDCl_3$) δ 5.81 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1 H), 5.03 (dd, *J* = 16.9, 1.5 Hz, 1 H), 4.97 (d, *J* = 10.2 Hz, 1 H), 4.58 (t, *J* = 2.9 Hz, 1 H), 3.73-3.61 (m, 1 H), 3.50 (q, *J* = 7.0 Hz, 2 H), 3.16-3.06 (m, 1 H), 2.49-2.41 (m, 1 H), 2.35-2.23 (m, 1 H), 2.10-1.94 (comp, 4 H), 1.76-1.59 (comp, 4 H), 1.23 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.1, 137.8, 115.0, 86.5, 63.2, 45.3, 32.2, 31.0, 27.0, 26.9, 15.7, 15.2; IR (neat) 1653 cm^{-1}; mass spectrum (CI) *m/z* 212.1646 [$C_{12}H_{22}NO_2$ (M+1) requires 212.1651], 184, 177, 166, 128.

5-Ethoxy-1-(5'-hexen-1'-yl)-2-piperidone. Prepared as a yellow oil from **13d** in 79% yield according to the procedure described above. ^1H NMR ($CDCl_3$) δ 5.77 (ddt, *J* = 17.0, 10.2, 6.6 Hz, 1 H), 5.01-4.89 (m, 2 H), 4.54 (t, *J* = 3.1 Hz, 1 H), 3.73-3.59 (m, 1 H), 3.53-3.36 (m, 2 H), 3.10-2.99 (m, 1 H), 2.47-2.38 (m, 1 H), 2.32-2.19 (m, 1 H), 2.08-1.89 (m, 4 H), 1.69-1.49 (comp, 4 H), 1.37 (q, *J* = 7.2 Hz, 2 H), 1.20 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 170.1, 138.5, 114.4, 86.4, 63.2, 45.5, 33.4, 32.2, 27.3, 27.1, 26.2, 15.8, 15.2; IR ($CDCl_3$) 2930, 1637, 14.73, 1080 cm^{-1}; mass spectrum (CI) *m/z* 226.1810 [$C_{13}H_{24}NO_2$ (M+1) requires 226.1807], 180, 154, 136, 110.

5-Ethoxy-1-(2'-methyl-2'-propen-1'-yl)-2-pyrrolidinone. Prepared as a yellow oil from **18** in 74% yield according to the procedure described above. ^1H NMR ($CDCl_3$) δ 4.86-4.76 (m, 2 H), 4.77 (p, *J* = 0.8 Hz, 1 H), 4.20 (d, *J* = 15.0 Hz, 1 H), 3.48 (s, 1 H), 3.45 (t, *J* = 3.5 Hz, 1 H), 3.43 (q, *J* = 3.5 Hz, 1 H), 2.54 (p, *J* = 8.6 Hz, 1 H), 2.33 (ddd, *J* = 3.0, 7.0, 10.0 Hz, 1 H), 2.15-2.08 (m, 1 H), 1.99-1.96 (m, 1 H), 1.65 (d, *J* = 0.5 Hz, 3 H), 1.72 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.8, 140.2, 112.6, 88.3, 62.1, 45.8, 28.9, 25.1, 20.1, 15.3; IR ($CDCl_3$) 1694 cm^{-1}; mass spectrum (C/I) *m/z* 184.1339 [$C_{10}H_{18}NO_2$ (M+1) requires 184.1338].

5-Ethoxy-1-(2'-propen-1'-yl)-2-pyrrolidinone. Prepared as a colorless oil in 50% yield from **19** as described in the procedure above. ^1H NMR ($CDCl_3$) δ 5.80-5.66 (m, 1 H), 5.19 (dq, *J* = 5.9, 1.5 Hz, 1 H), 5.21 - 5.14 (m, 1 H), 4.91 (dd, *J* = 6.3, 1.4 Hz, 1 H), 4.25 (dd, *J* = 15.3, 4.3 Hz, 1 H), 3.57 (dd, *J* = 7.0, 15.0 Hz, 1 H), 3.45 (q, *J* = 7.1 Hz, 2 H), 1.9-2.6 (comp, 4 H), 1.16 (t, *J* = 7.1 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.6, 132.6, 117.7, 88.4, 61.7, 42.7, 28.9, 24.9, 15.2; IR ($CDCl_3$) 1680, 1452 cm^{-1}; mass spectrum (C/I) *m/z* 170.1183 [$C_9H_{15}NO_2$ (M+1) requires 170.1181].

Representative Procedure for Substitutions of Amide *N,O*-Acetals (Method A). Synthesis of 1-(2'-Buten-1-yl)-5-ethenyl-2-pyrrolidinone (14a). A 1 M solution of vinylmagnesium bromide in THF (60 mL, 60.0 mmol) was added slowly to a suspension of $CuBr{\bullet}SMe_2$ (30.0 mmol) in Me_2S (50 mL) and THF (200 mL) at -50 °C. The reaction was stirred at -50 °C for 1 h, and then cooled to -78 °C, whereupon $BF_3{\bullet}Et_2O$ (4.23 g, 30.0 mmol) and 1-(2'-butene-1'-yl)-5-ethoxy-2-pyrrolidinone (1.83 g, 10.0 mmol) in THF (5 mL) were added sequentially. The reaction was allowed to warm to rt, and saturated aq. NH_4Cl/NH_4OH (10 mL, v/v = 1:1) was added. The blue reaction mixture was stirred for 1 h, and Et_2O (10 mL) was added. The layers were separated, and the organic layer was washed with H_2O (3 x 5 mL). The combined aq. layers were back-extracted with Et_2O (3 x 10 mL), and the combined organic layers were concentrated under reduced pressure until approximately 10 mL of solvent remained. This solution was stirred at rt with HCl (0.5 N, 5 mL) for 2 h to hydrolyze any remaining starting material. The organic layer was separated and washed with saturated aq. $NaHCO_3$ (10 mL) and H_2O (2 x 5 mL). The combined aq. layers were extracted with Et_2O (2 x 10 mL), and the organic layers were combined, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with EtOAc/hexanes (2:1) to give **14a** in 59% yield. ^1H NMR ($CDCl_3$) δ 5.70-5.49 (comp, 2 H), 5.37-5.26 (comp, 1 H), 5.21 (s, 1 H), 5.15 (d, *J* = 5.2 Hz, 1 H), 4.21 (dd, *J* = 14.9, 5.0 Hz, 1 H), 3.31 (dd, *J* = 14.9, 7.7 Hz, 1 H), 2.47-2.13 (comp, 3 H), 1.80-1.70 (m, 1 H), 1.66 (d, *J* = 6.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.2, 136.8, 128.0, 124.3, 116.6, 59.4, 41.2, 28.9, 24.3, 16.6; IR 1682, 1419 cm^{-1}; mass spectrum (CI) *m/z* 165.1150 [$C_{10}H_{15}NO$ (M+1) requires 165.1154], 163, 162.

Representative Procedure for Substitutions of Amide *N,O*-Acetals (Method B). Synthesis of 1-(3'-Buten-1'-yl)-5-ethenyl-2-pyrrolidinone (14b). Vinylmagnesium bromide (4 mL of 1 N in THF, 4 mmol) was added dropwise to a mixture of $CuBr{\bullet}SMe_2$ (826 mg, 4 mmol) in Me_2S (6 mL) and Et_2O (7 mL) at -40 °C. The

resulting mixture was stirred for 2 h, then cooled to -78 °C, whereupon BF_3•Et_2O (0.5 mL, 4 mmol) was added. After stirring for 5 min, a solution of 5-ethoxy-1-(2'-propen-1'-yl)-2-pyrrolidinone (245 mg, 1.3 mmol) in Et_2O (10 mL) was added. The solution was stirred at -78 °C for 30 min and then at rt for 30 min, and saturated aq. NH_4Cl/NH_4OH (10 mL, v/v = 1:1) was added. The blue reaction mixture was worked-up as in the previous experiment, and the residue was purified by flash chromatography on silica gel eluting with EtOAc to give **14b** in 71% yield. ^1H NMR ($CDCl_3$) δ 5.80-5.56 (comp, 2 H), 5.25-5.16 (comp, 2 H), 5.07-4.96 (comp, 2 H), 4.02 (q, *J* = 7.9 Hz, 1 H), 3.63 (td, *J* = 13.7, 7.7 Hz, 1 H), 2.91 (qd, *J* = 7.7, 5.9 Hz, 1 H), 2.46-2.10 (comp, 4 H), 1.76-1.63 (comp, 2 H); ^{13}C NMR ($CDCl_3$) δ 174.7, 137.6, 135.1, 117.6, 116.5, 61.1, 39.6, 31.6, 29.8, 25.3; IR (neat) 1682 cm^{-1}; mass spectrum (CI) *m/z* 166.1227 [$C_{10}H_{16}NO$ (M+1) requires 166.1232], 166 (base), 152, 138, 124.

5-Ethenyl-1-(4'-penten-1'-yl)-2-pyrrolidinone (14c). Prepared from **12c** as a colorless oil in 71% yield according to Method A. ^1H NMR ($CDCl_3$) δ 5.86-5.61 (comp, 2 H), 5.24 (d, *J* = 17.0 Hz, 1 H), 5.21 (d, *J* = 10.1 Hz, 1 H), 5.05-4.95 (comp, 2 H), 4.04 (td, *J* = 7.8, 5.8 Hz, 1 H), 3.55 (ddd, *J* = 13.6, 8.8, 7.1 Hz, 1 H), 2.91 (ddd, *J* = 13.6, 8.8, 5.4 Hz, 1 H), 2.48-2.20 (comp, 3 H), 2.09-1.98 (m, 2 H), 1.80-1.70 (m, 1 H), 1.67-1.49 (comp, 2 H); ^{13}C NMR ($CDCl_3$) δ 174.7, 137.8, 137.7, 117.8, 114.9, 61.3, 40.1, 31.0, 30.0, 26.4, 25.5; IR (neat) 1689 cm^{-1}; mass spectrum (CI) *m/z* 180.1391 [$C_{11}H_{17}NO$ (M+1) requires 180.1388], 180 (base), 179, 178, 152, 124.

5-Ethenyl-1-(5'-hexen-1'-yl)-2-pyrrolidinone (14d). Prepared as a colorless oil in 55% yield from 5-ethoxy-1-(5'-hexen-1'-yl)-2-pyrrolidinone according to Method A. ^1H NMR ($CDCl_3$) δ 5.84-5.60 (comp, 2 H), 5.24 (d, *J* = 17.0 Hz, 1 H), 5.21 (d, *J* = 10.1 Hz, 1 H), 5.03-4.93 (comp, 2 H), 4.04 (td, *J* = 7.9, 5.8 Hz, 1 H), 3.55 (ddd, *J* = 10.0, 8.5, 6.8 Hz, 1 H), 2.88 (ddd, *J* = 13.7, 8.2, 5.5 Hz, 1 H), 2.46-2.02 (comp, 5 H), 1.80-1.69 (m, 1 H), 1.56-1.34 (comp, 4 H); ^{13}C NMR ($CDCl_3$) δ 174.7, 138.4, 137.8, 117.7, 114.6, 61.3, 40.3, 33.3, 30.1, 26.6, 26.0, 25.5; IR (neat) 1693, 1641 cm^{-1}; mass spectrum (CI) *m/z* 194.1547 [$C_{12}H_{20}NO$ (M+1) requires 194.1545], 194 (base), 182, 172, 154, 136, 124.

1-(3'-Buten-1'-yl)-5-ethenyl-2-piperidone (15b). Prepared as a colorless oil in 43% yield from 1-(3'-buten-1'-yl)-5-ethoxy-2-piperidone according to Method B. ^1H NMR ($CDCl_3$) δ 5.84-5.68 (comp, 2 H), 5.22 (d, *J* = 10.3 Hz, 1 H), 5.12 (d, *J* = 17.7 Hz, 1 H), 5.06 (d, *J* = 19.1 Hz, 1 H), 5.01 (d, *J* = 9.8 Hz, 1 H), 4.02-3.93 (comp, 2 H), 2.77 (ddd, *J* = 13.3, 8.0, 6.8 Hz, 1 H), 2.38-2.26 (comp, 4 H), 1.91-1.62 (comp, 4 H); ^{13}C NMR ($CDCl_3$) δ 169.8, 137.6, 135.3, 116.3, 116.1, 59.4, 44.6, 31.8, 31.7, 28.4, 17.0; IR (CCl_4) 1646 cm^{-1}; mass spectrum (CI) *m/z* 180.1388 [$C_{11}H_{18}NO$ (M+1) requires 180.1388], 180 (base), 166, 138.

5-Ethenyl-1-(4'-penten-1'-yl)-2-piperidone (15c). Prepared as a colorless oil in 50% yield from 5-ethoxy-1-(4'-penten-1'-yl)-2-piperidone according to Method A. ^1H NMR ($CDCl_3$) δ 5.87-5.68 (comp, 2 H), 5.23-4.94 (comp, 4 H), 3.98-3.82 (comp, 2 H), 2.80-2.70 (m, 1 H), 2.44-2.22 (m, 2 H), 2.10-2.00 (comp, 3 H), 1.98-1.56 (comp, 5 H); ^{13}C NMR ($CDCl_3$) δ 170.0, 138.0, 137.9, 116.6, 114.7, 59.5, 45.1 32.1, 31.1, 28.8, 26.5, 17.3; IR (neat) 1644 cm^{-1}; mass spectrum (CI) *m/z* 194.1537 [$C_{12}H_{20}NO$ (M+1) requires 194.1545], 194 (base), 166, 138.

5-Ethenyl-1-(5'-hexen-1'-yl)-2-piperidone (15d). Prepared as a colorless oil in 30% yield from 5-ethoxy-1-(5'-hexen-1'-yl)-2-piperidone according to Method B. ^1H NMR ($CDCl_3$) δ 5.84-5.66 (comp, 2 H), 5.20 (d, *J* = 10.3 Hz, 1 H), 5.10 (d, *J* = 17.0 Hz, 1 H), 5.01-4.91 (comp, 2 H), 3.96-3.91 (m, 1 H), 3.89-3.82 (m, 1 H), 2.76-2.66 (m, 1 H), 2.38-2.33 (comp, 2 H), 2.08-2.01 (comp, 2 H), 1.90-1.61 (comp, 4 H), 1.58-1.47 (comp, 2 H), 1.40-1.31 (comp, 2 H); ^{13}C NMR ($CDCl_3$) δ 169.7, 138.3, 137.7, 116.3, 114.2, 59.1, 45.0, 33.2, 31.8, 28.6, 26.5, 25.9, 17.1; IR (neat) 1643 cm^{-1}; mass spectrum (CI) *m/z* 208.1710 [$C_{13}H_{22}NO$ (M+1) requires 208.1701], 207 (base), 137.

Representative Procedure for Substitutions of Amide *N,O*-Acetals (Method C). Synthesis of 1-(2'-Buten-1'-yl)-5-(2''-propen-1''-yl)-2-pyrrolidinone (20a). A solution of 1-(2'-butene-1'-yl)-5-ethoxy-2-pyrrolidinone (865 mg, 4.7 mmol) in CH_2Cl_2 (28 mL) was cooled to -78 °C, and allyl trimethylsilane (3.5 mL, 22 mmol) and BF_3•Et_2O (2.0 mL, 16.5 mmol) were added. After 2 h at -78 °C, the reaction was warmed to rt and stirred overnight. The reaction mixture was washed with H_2O (2 x 10 mL) and brine (1 x 10 mL). The organic layer was then dried ($MgSO_4$) and concentrated under reduced pressure, and the crude product was purified by flash chromatography on silica gel eluting with EtOAc/hexanes (1:10) to give **20a** as a clear oil in 75% yield. ^1H NMR ($CDCl_3$) δ 5.71-5.52 (comp, 2 H), 5.36-5.24 (m, 1 H), 5.11-5.08 (m, 1 H), 5.04 (d, *J* = 1.1 Hz, 1 H), 4.25-

4.16 (m, 1 H) 3.62 (sept, J = 4.0 Hz, 1 H), 3.38 (dd, J = 15.1, 7.6 Hz, 1 H), 2.43-2.26 (comp, 3 H), 2.21-1.95 (comp, 2 H), 1.76-1.66 (m, 1 H), 1.62 (d, J = 5.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 174.8, 132.7, 129.2, 125.2, 118.6, 56.5, 42.3, 37.1, 30.0, 23.0, 17.5; IR ($CHCl_3$) 1668, 1449, 1423, 1246 cm^{-1}; mass spectrum (C/I) *m/z* 180.1391 [$C_{11}H_{18}NO$ (M+1) requires 180.1388].

1-(3'-Buten-1'-yl)-5-(2''-propen-1''-yl)-2-pyrrolidinone (20b). Prepared as a colorless oil in 59% yield from 1-(3'-butene-1'-yl)-5-ethoxy-2-pyrrolidinone according to Method C. ^{1}H NMR ($CDCl_3$) δ 5.85-5.61 (comp, 2 H), 5.20-5.00 (comp, 4 H), 3.80-3.65 (comp, 2 H), 3.00-2.89 (comp, 1 H), 2.45-1.65 (comp, 8 H); ^{13}C NMR ($CDCl_3$) δ 175.1, 135.2, 132.8, 118.7, 116.8, 56.8, 39.5, 37.5, 31.8 30.1, 23.4; IR ($CDCl_3$) 1671, 1459, 1424 cm^{-1}; mass spectrum (C/I) *m/z* 180.1397 [$C_{11}H_{18}NO$ (M+1) requires 180.1388].

1-(2'-Methyl-2'-propen-1'-yl)-5-(2''-propen-1''-yl)-2-pyrrolidinone (20c). Prepared as a yellow oil in 70% yield from 5-ethoxy-1-(2'-methyl-2'-propen-1'-yl)-2-pyrrolidinone according to Method C. ^{1}H NMR ($CDCl_3$) δ 5.67 (ddt, J = 20.2, 9.1, 7.1 Hz, 1 H), 5.15-5.13 (m, 1 H), 5.08 (s, 1 H), 4.84 (d, J = 19.5 Hz, 2 H), 3.63 (m, 1 H), 3.41 (d, J = 15.3 Hz, 1 H), 2.43-2.29 (comp, 3 H), 2.21-2.00 (comp, 2 H), 1.82-1.68 (m, 1 H), 1.65 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.1, 140.2, 132.9, 118.6, 112.9, 56.5, 46.3, 37.1, 30.0, 23.3, 20.0; IR ($CHCl_3$) 1673, 1447, 1423 cm^{-1}; mass spectrum (C/I) *m/z* 180.1394 [$C_{11}H_{18}NO$ (M+1) requires 180.1388].

1-(2'-Propen-1'-yl)-5-(2''-propen-1''-yl)-2-pyrrolidinone (20d). Prepared as a clear oil in 70% yield from 5-ethoxy-1-(2'-propen-1'-yl)-2-pyrrolidinone according to Method C. ^{1}H NMR ($CDCl_3$) δ 5.67 (ddt, J = 20.2, 9.1, 7.1 Hz, 1 H), 5.15-5.13 (m, 1 H), 5.08 (s, 1 H), 4.84 (d, J = 19.5 Hz, 2 H), 3.63 (m, 1 H), 3.41 (d, J = 15.3 Hz, 1 H), 2.43-2.29 (comp, 3 H), 2.21-2.00 (comp, 2 H), 1.82-1.68 (m, 1 H), 1.65 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ ;174.8, 132.7, 132.7, 118.7, 117.7, 56.6, 43.1, 37.3, 30.0, 23.3; IR ($CHCl_3$) 3012, 1729, 1662, 1447 cm^{-1}; mass spectrum (C/I) *m/z* 166.1230 [$C_{10}H_{16}NO$ (M+1) requires 166.1232].

Representative Procedure for Ring-Closing Metathesis (RCM) (Method A). Synthesis of 1-Azabicyclo[3.3.0]oct-3-ene-8-one (16a). A yellow solution of molybdenum catalyst **6** (25 mg, 0.03 mmol) and **14a** (53 mg, 0.33 mmol) in anhydrous, degassed benzene (11 mL) was stirred under argon at 50 °C for 2 h. This reaction was conducted on a bench-top. This mixture was exposed to air for 30 min, whereupon the solvent was removed under reduced pressure. The green residue was triturated with pentane (3 x 5 mL) and filtered. The filtrate was concentrated, and the residue was purified by flash chromatography eluting with CH_2Cl_2/acetone (9:1) to give **16a** in 68% yield. ^{1}H NMR ($CDCl_3$) δ 5.92-5.82 (comp, 2 H), 4.70-4.60 (m, 1 H), 4.39 (dd, J = 15.9, 3.9 Hz, 1 H), 3.66 (dd, J = 15.9, 4.3 Hz, 1 H), 2.80-2.65 (m, 1 H), 2.46-2.28 (m, 2 H), 1.90-1.72 (comp, 3 H); ^{13}C NMR ($CDCl_3$) δ 178.0, 130.6, 128.1, 67.4, 49.7, 34.0, 29.6; IR 1732, 1682 cm^{-1}; mass spectrum (CI) *m/z* 124.0762 [$C_7H_{10}NO$ (M+1) requires 124.0762].

1-Azabicyclo[4.3.0]non-4-ene-9-one (16b). The RCM of **14b** was conducted at rt for 1 h according to Method A to give **16b** as a pale yellow oil in 92% yield. ^{1}H NMR ($CDCl_3$) δ 5.78 (m, 1 H), 5.69 (ddt, J = 10.3, 2.9, 1.5 Hz, 1 H), 4.19 (dd, J = 13.1, 6.8 Hz, 1 H), 4.16-4.13 (m, 1 H), 2.89-2.82 (m, 1 H), 2.49-2.37 (comp, 2 H), 2.29-2.23 (comp, 2 H), 2.17-2.05 (m, 1 H), 1.64-1.56 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 172.9, 128.1, 124.8, 54.7 36.0, 31.5, 26.1, 24.3; IR (CCl_4) 1644 cm^{-1}; mass spectrum (CI) *m/z* 138.0918 [$C_8H_{12}NO$ (M+1) requires 138.0919], 138 (base).

1-Azabicyclo[5.3.0]dec-5-ene-10-one (16c). The RCM of **14c** was conducted for 3 h at rt according to Method A to give **16c** as a colorless oil in 81% yield. ^{1}H NMR ($CDCl_3$) δ 5.75 (dtd, J = 11.4, 5.4, 2.5 Hz, 1 H), 5.50 (ddd, J = 11.4, 3.8, 1.9 Hz, 1 H), 4.35-4.30 (m, 1 H), 4.09 (ddd, J = 13.6, 8.8, 5.0 Hz, 1 H), 3.00 (dt, J = 13.6, 5.0 Hz, 1 H), 2.43 (q, J = 8.3 Hz, 1 H), 2.35-2.20 (comp, 4 H), 1.92-1.76 (comp, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.5, 132.0, 131.5, 58.4, 42.7, 30.0, 27.6, 26.8, 26.4; IR (neat) 1668 cm^{-1}; mass spectrum (CI) *m/z* 151.1002 [$C_9H_{13}NO$ (M^+) requires 151.0997], 152 (base), 129, 116.

1-Azabicyclo[6.3.0]undec-6-ene-11-one (16d). The RCM of **14d** was conducted for 4 h with 30–40 mol% of **6** according to Method A to give **16d** as a colorless oil in a 47% yield. ^{1}H NMR ($CDCl_3$) δ 5.81 (app. q, J = 8.0 Hz, 1 H), 5.44 (dd, J = 6.2, 11.0 Hz, 1 H), 4.29 (app. q, J = 6.5 Hz, 1 H), 3.49-3.41 (m, 2 H), 2.50-2.05 (comp, 6

H), 1.87-1.49 (comp, 4 H); ^{13}C NMR ($CDCl_3$) δ 174.4, 131.9, 130.4, 56.8, 41.0, 30.9, 27.0, 26.4, 25.9, 25.2; IR (neat) 1681 cm^{-1}; mass spectrum (CI) *m/z* 165.1149 ($C_{10}H_{15}NO$ (M+1) requires 165.1153), 166 (base), 152.

1-Azabicyclo[4.4.0]dec-4-ene-10-one (17b). The RCM of **15b** was conducted for 1 h at rt according to Method A to give **17b** as a pale yellow oil in 91% yield. ^1H NMR ($CDCl_3$) δ 5.86-5.83 (m, 1 H), 5.52 (ddt, *J* = 8.7, 2.8, 1.4 Hz, 1 H), 4.83 (dd, *J* = 12.9, 5.8 Hz, 1 H), 4.01-3.98 (m, 1 H), 2.61 (td, *J* = 12.9, 4.0 Hz, 1 H), 2.52-2.46 (m, 1 H), 2.36 (dd, *J* = 12.1, 6.4 Hz, 1 H), 2.29-2.25 (m, 1 H), 2.06-2.03 (m, 1 H), 2.02-1.99 (m, 1 H), 1.88-1.83 (m, 1 H), 1.75-1.65 (m, 1 H), 1.47-1.39 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 168.9, 128.9, 125.8, 55.1, 38.2, 32.4, 30.1, 25.1, 19.6; IR (CCl_4) 1696 cm^{-1}; mass spectrum (CI) *m/z* 152.1073 [$C_9H_{14}NO$ (M+1) requires 152.1075], 114, 152 (base).

1-Azabicyclo[5.4.0]undec-5-ene-10-one (17c). The RCM of **15c** was conducted for 3 h at rt according to Method A to give **17c** as a colorless oil in a 84% yield. ^1H NMR ($CDCl_3$) δ 5.79 (m, 1 H), 5.43 (d, *J* = 11.6 Hz, 1 H), 4.48 (m, 1 H), 4.12 (br s, 1 H), 2.80 (m, 1 H), 2.40-1.68 (comp, 10 H); ^{13}C NMR ($CDCl_3$) δ 169.5, 132.3, 131.4, 57.7, 46.0, 32.0, 29.3, 25.3, 25.2, 18.1; IR (neat) 1635 cm^{-1}; mass spectrum (CI) *m/z* 166.1239 [$C_{10}H_{16}NO$ (M+1) requires 166.1232], 166 (base), 154.

1-Azabicyclo[6.4.0]dodec-6-ene-11-one (17d). The RCM of **15d** was conducted for 3 h according to Method A to give **17d** (50%) as a pale yellow oil together with starting diene **15d** (24%). ^1H NMR ($CDCl_3$) δ 5.81-5.75 (m, 1 H), 5.40 (ddd, *J* = 11.4, 4.9, 1.2 Hz, 1 H), 4.16 (ddd, *J* = 13.7, 9.7, 2.7 Hz, 1 H), 4.11-4.08 (m, 1 H), 3.12 (ddd, *J* = 13.7, 7.2, 2.7 Hz, 1 H), 2.39 (comp, 2 H), 2.35-2.32 (m, 1 H), 2.18-2.04 (m, 1 H), 1.92-1.81 (comp, 3 H), 1.79-1.69 (comp, 3 H), 1.79-1.69 (m, 1 H), 1.55-1.50 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 170.2, 131.4, 130.7, 57.0, 45.5, 32.5, 29.1, 26.2, 24.7, 24.2, 18.1; IR (CCl_4) 1640 cm^{-1}; mass spectrum (CI) *m/z* 1801397 [$C_{11}H_{18}NO$ (M+1) requires 180.1388], 136, 179, 180 (base).

Representative Procedure for (RCM) (Method B). Synthesis of 1-Azabicyclo[4.3.0]non-3-ene-9-one (21a). A solution of **20c** (50 mg, 0.28 mmol) or **20d** (40 mg, 0.24 mmol) containing the molybdenum catalyst **6** (15 mol%) in anhydrous, degassed dimethoxyethane (DME) (0.003 M in **6**) was stirred at rt in an inert atmosphere box for 24 h. The reaction was removed from the box, silica gel (200 mg) was added to the reaction mixture, and the solvent was removed under reduced pressure. The silica gel thus obtained was added to the top of a flash chromatography column containing silica gel, and the column was eluted with CH_2Cl_2 (100 mL) and then 3% acetone in CH_2Cl_2 to give **21a** in 77% yield from **20c** or in 73% yield from **20d**. ^1H NMR ($CDCl_3$) δ 5.80-5.72 (m, 1 H), 5.70-5.64 (m, 1 H), 4.22 (dd, *J* = 18.7, 2.7 Hz, 1 H), 3.62-3.46 (m, 2 H), 2.39-2.23 (comp, 3 H), 2.03-1.96 (comp, 2 H), 1.69-1.60 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 174.2, 124.1, 123.3, 52.9, 40.3, 32.4, 29.8, 25.4; IR ($CDCl_3$) 1678, 1445, 1266; mass spectrum (C/I) *m/z* 138.0914 [$C_8H_{12}NO$ (M+1) requires 138.0919].

1-Azabicyclo[5.3.0]dec-4-ene-10-one (21b). The RCM of **20b** was conducted for 12 h according to Method B to give **21b** in 95% yield. ^1H NMR ($CDCl_3$) δ 5.89 (p, *J* = 5.9 Hz, 1 H), 5.73 (p, *J* = 5.4 Hz, 1 H), 3.94-3.85 (m, 1 H), 3.67 (p, *J* = 7.1 Hz, 1 H), 3.07-2.97 (m, 1 H), 2.51-2.09 (comp, 7H), 1.64-1.50 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 174.3, 131.7, 128.4, 58.6, 41.3, 36.3, 30.5, 29.7, 27.8, 25.6; IR ($CDCl_3$) 2930, 2244, 1670, 1425 cm^{-1}; mass spectrum (C/I) *m/z* 152.1074 [$C_9H_{14}NO$ (M+1) requires 152.1075], 136, 106.

1-Azabicyclo[4.3.0]non-2-methyl-2-ene-9-one (21c). The RCM of **20c** was conducted according to Method B to give **21c** in 85% yield. ^1H NMR ($CDCl_3$) δ 5.41-5.49 (comp, 1 H), 4.11 (d, *J* = 18.1 Hz, 1 H), 3.62-3.50 (m, 1 H), 3.38 (d, *J* = 18.1 Hz, 1 H), 2.37 (q, *J* = 7.5 Hz, 2 H), 2.30-2.15 (m, 2 H), 2.02-1.86 (m, 1H), 1.67 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 173.9, 130.7, 118.6, 52.9, 43.8, 32.3, 30.2, 25.1, 20.4; IR 1732, 1662, 1450, 1252 cm^{-1}; mass spectrum (C/I) *m/z* 152.1077 [$C_9H_{14}NO$ (M+1) requires 152.1075].

***O*-Triethylsilyl-2-(*o*-aminophenyl)ethanol.** Triethylsilylchloride (7.13 g, 47.3 mmol) in dry CH_2Cl_2 (50 mL) was added to a stirred solution of 2-(*o*-aminophenyl)ethanol (**28**) (5.00 g, 36.4 mmol) and Et_3N (10.2 mL, 72.8 mmol) in CH_2Cl_2 (300 mL) at -20 °C. After 1 h, the reaction was warmed to rt, washed with sat. aq. $NaHCO_3$ (2 x 50 mL), and brine (1 x 50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1) to afford 8.88 g (97%) of protected alcohol as a light yellow oil. ^1H NMR ($CDCl_3$) δ 7.08-6.95 (comp, 2 H), 6.70

(dd, J = 7.9, 7.7 Hz, 1 H), 6.65 (d, J = 7.9 Hz, 1 H), 3.99 (br, 2 H), 3.84 (t, J = 6.3 Hz, 2 H), 2.77 (t, J = 6.3 Hz, 2 H), 0.90 (t, J = 8.0 Hz, 9 H), 0.55 (q, J = 8.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 145.6 130.4, 127.3, 125.0, 118.6, 115.8, 64.0, 35.3, 6.6, 4.2; IR 2954, 1624, 1498, 1094 cm^{-1}; mass spectrum (CI) *m/z* 251.1708 [$C_{14}H_{25}NOSi$ (M+1) requires 251.1705], 222 (base), 120.

***O*-Triethylsilyl-2-[*o*-(*N*-trifluoroacetamido)phenyl]ethanol.** Trifluoroacetic anhydride (13.6 mL, 96.0 mmol) was added dropwise over 15 min to a solution of the arylamine obtained in the previous experiment (8.00 g, 32.00 mmol) and Et_3N (27 mL, 190 mmol) in Et_2O (350 mL) at -20 °C. After stirring for 30 min, the reaction was washed with sat. aq. $NaHCO_3$ (3 x 60 mL), and brine (1 x 60 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1) to afford 10.47 g (94%) of product as a clear oil. ^{1}H NMR ($CDCl_3$) δ 10.09-10.00 (br s, 1 H), 7.77 (d, 1 H, J = 7.9 Hz), 7.32-7.20 (m, 1 H), 7.20-7.17 (comp, 2 H), 3.88 (t, J = 6.3 Hz, 2 H), 2.84 (t, J = 6.3 Hz, 2 H), 0.79 (t, J = 8.0 Hz, 9 H), 0.53 (t, J = 8.0 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 155.2 (q, J = 37 Hz), 134.4, 132.8, 130.2, 127.3, 126.7, 123.6, 116.2 (q, J = 289 Hz), 65.4, 34.7, 6.1, 3.6; IR (neat) 1771, 1751 cm^{-1}; mass spectrum (CI) *m/z* 348.1597 [$C_{16}H_{25}NO_2F_3Si$ (M+1) requires 348.1606], 318.

***O*-Triethylsilyl-2-[*o*-(*N*-allyl, *N*-trifluoroacetylamino)phenyl]ethanol (29).** A mixture of allylbromide (2.80 g, 23.2 mmol), the trifluoroacetamide from above (2.00 g, 5.80 mmol), and Na_2CO_3 (3.2 g, 23.2 mmol) were combined in acetone (120 mL) at 0 °C, and the mixture was stirred overnight at rt. The solids were removed by vacuum filtration, and the filtrate was concentrated under reduced pressure. The residue was suspended in CH_2Cl_2 (100 mL), and the solution was washed with sat. aq. $NaHCO_3$ (3 x 50 mL) and brine (1 x 50 mL). The organic layer was dried ($MgSO_4$), filtered, evaporated, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1) to afford 2.09 g (93%) of **29** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.44-7.32 (comp, 2 H), 7.21 (app t, J = 7.8 Hz, 1 H), 7.08 (d, J = 7.8 Hz, 1 H), 5.95-5.83 (m, 1 H), 5.24-5.09 (comp, 2 H), 4.85 (dd, J = 14.1, 5.7 Hz, 1 H), 3.88 (t, J = 6.9 Hz, 2 H), 3.72 (dd, J = 14.2, 5.7 Hz, 1 H), 2.86-2.71 (comp, 2 H), 0.91 (t, J = 8.5 Hz, 9 H), 0.56 (t, J = 8.5 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 156.9 (q, J = 36 Hz), 137.6, 137.4, 130.6, 130.0, 129.8, 129.2, 126.5, 120.0, 116.2 (q, J = 289 Hz), 62.5, 54.3, 33.4, 6.6, 4.2; IR ($CHCl_3$) 1697 cm^{-1}; mass spectrum (CI) *m/z* 388.1917 [$C_{19}H_{29}NO_2F_3Si$ (M+1) requires 388.1919], 358, 256.

2-[*o*-(*N*-Allyl, *N*-trifluoroacetylamino)phenyl]ethanol. A solution of **29** (8.90 g, 23.0 mmol) in THF (200 mL) at 0 °C and hydrogen fluoride-pyridine (4.6 mL) was stirred at 0 °C for 3 h. The reaction solution was then washed with sat. aq. $NaHCO_3$ (2 x 50 mL), and brine (1 x 50 mL). The organic layer was dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography eluting with hexanes/EtOAc (4:1) yielding 5.84 g (93%) of alcohol as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.42-7.7.30 (comp, 2 H), 7.21 (dd, J = 7.5, 10.3 Hz, 1 H), 7.08 (d, J = 7.5 Hz, 1 H), 5.99-5.82 (m, 1 H), 5.22-5.04 (comp, 2 H), 4.79 (dd, J = 14.2, 5.7 Hz, 1 H), 3.88 (t, J = 6.9 Hz, 2 H), 3.70 (dd, J = 14.2, 5.7 Hz, 1 H), 2.92-2.68 (comp, 3 H); ^{13}C NMR ($CDCl_3$) δ 156.9 (q, J = 35 Hz), 137.6, 136.8, 130.6, 129.8, 129.7, 129.5, 126.8, 118.4, 116.2 (q, J = 289 Hz), 62.0, 54.3, 33.2; IR ($CHCl_3$) 3455, 1696 cm^{-1}; mass spectrum (CI) *m/z* 274.1053 [$C_{13}H_{15}NO_2F_3$ (M+1) requires 274.1055], 256 (base).

***N*-Allyl, *N*-trifluoroacetyl-2-(2'-hydroxy-3'-buten-1'-yl) aniline.** DMSO (1.22 mL, 17.2 mmol) in THF (10 mL) was added to a stirred solution of oxalyl chloride (1.38 mL, 15.7 mmol) in THF (200 mL) at -78 °C. After 20 min a solution of the phenethyl alcohol from above (3.90 g, 14.3 mmol) in THF (50 mL) was added. After 45 min, Et_3N (4.58 mL, 32.9 mmol) was added, and the solution was allowed to warm to rt and stirred for 10 min. The reaction was again cooled to -78 °C, and vinylmagnesium bromide (51.0 mL of 1 M in THF, 51.0 mmol) was added dropwise. The reaction was stirred for 1.5 h, and MeOH (22 mL) and sat. aq. NH_4Cl (50 mL) were added. The yellow solution was warmed to rt, and Et_2O (100 mL) was added. The mixture was washed with sat. aq. NH_4Cl (2 x 100 mL), and the combined aq. layers were extracted with Et_2O (3 x 50 mL). The combined organics were washed with brine (1 x 50 mL), dried ($MgSO_4$), and evaporated. The residue was purified by flash chromatography eluting with hexanes/EtOAc (7:3) to furnish 3.80 g (88%) of 1,9-diene alcohol as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.50 (d, J = 7.8 Hz, 1 H), 7.44-7.30 (m, 1 H), 7.21 (dd, J = 8.0, 7.8 Hz, 1 H), 7.08 (d, J = 7.8 Hz, 1 H), 6.02-5.81 (comp, 2 H), 5.35-5.09 (comp, 4 H), 4.92-4.79 (m, 1 H), 4.58-4.40 (m, 1 H), 3.80 (dd, J =

14.1, 7.5 Hz, 0.5 H), 3.63 (dd, J = 14.1, 7.5 Hz, 0.5 H), 2.82-2.71 (comp, 2 H), 2.23-2.08 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 156.9 (q, J = 38 Hz), 140.4, 140.2, 137.8, 137.7, 136.7, 135.3, 130.9, 130.6, 130.3, 130.0, 129.8, 129.4, 129.2, 126.9, 126.7, 120.2, 120.1, 116.2 (q, J = 289 Hz, 115.4, 115.2, 72.7, 72.3, 54.3, 54.0, 37.8, 37.5; IR ($CHCl_3$) 3431, 1647 cm^{-1}; mass spectrum (CI) m/z 300.1207 [$C_{15}H_{17}NO_2F_3$ (M+1) requires 300.1211].

***N*-Allyl, *N*-trifluoroacetyl-2-(2'-benzyloxy-3'-buten-1'-yl)aniline (30).** Triflic acid (30 μL) was added with stirring at rt to a solution of allyl alcohol from above (0.60 g, 2.00 mmol) and benzyl-2,2,2-trichloroacetimidate (0.56 mL, 0.76 g, 3.00 mmol) in a mixture of hexane (3 mL) and CH_2Cl_2 (1 mL), and the solution was stirred for 1 h. The crystalline trichloroacetamide was removed by filtration, and the filtrate was diluted with CH_2Cl_2 (50 mL). The organics were washed with sat. aq. $NaHCO_3$ (2 x 15 mL), water (1 x 10 mL), brine (1 x 10 mL), dried ($MgSO_4$), and filtered. The filtrate was concentrated under reduced pressure, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1) to give 0.59 g (76%) of **30** as a golden oil. ^{1}H NMR ($CDCl_3$) δ 7.51-7.01 (comp, 9 H), 6.01-5.74 (comp, 2 H), 5.79-5.50 (comp, 3 H), 4.98-3.95 (comp, 5 H), 3.75 (dd, J = 14.3, 7.5 Hz, 0.5 H), 3.51 (dd, J = 14.3, 7.5 Hz, 0.5 H), 2.86-2.61 (comp, 2 H); ^{13}C NMR ($CDCl_3$) δ 156.9 (q, J = 35 Hz), 138.6, 138.1, 137.9, 137.2, 135.7, 131.7, 130.8, 130.5, 130.0, 129.7, 129.0, 129.1, 128.9, 128.4, 128.0, 126.4, 126.1, 120.1, 119.9, 117.9, 117.4, 116.1 (q, J = 289 Hz), 80.8, 79.5, 70.4, 70.1, 54.5, 53.8, 36.6; IR ($CHCl_3$) 1704 cm^{-1}; mass spectrum (CI) m/z 390.1675 [$C_{22}H_{23}NO_2F_3$ (M+1) requires 390.1681], 282 (base).

1-(*N*-Trifluoroacetyl)-1,2,5,6-tetrahydro-5-(benzoxy)-1-benzazocine (31). A dry round bottom flask equipped with a magnetic stir bar under argon atmosphere was charged with the molybdenum catalyst **6** (57 mg, 0.075 mmol), and a solution the protected aniline **30** (0.19 g, 0.50 mmol) in degassed benzene (2 mL) was added. The reaction was heated at 50 °C (oil bath temperature) for 4 h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography eluting with hexanes/EtOAc (9:1) to deliver 0.14 g (78%) of **31** as a light yellow oil. ^{1}H NMR ($CDCl_3$) δ 7.40-7.11 (comp, 9 H), 5.74-5.65 (m, 1 H), 5.45-5.37 (comp, 2 H), 4.94-4.76 (comp, 1 H), 4.65 (d, J = 11.4, 1 H), 4.52 (d, J = 11.4, 1 H), 3.65-5.53 (comp, 2 H), 2.89 (dd, J = 16.2, 10.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 156.9 (q, J = 36 Hz), 138.6, 137.9, 135.8, 131.5, 130.9, 130.6, 129.5, 128.9, 128.6, 128.2, 127.5, 125.1, 116.0 (q, J = 289 Hz), 73.6, 71.4, 49.3, 38.4; IR ($CHCl_3$) 1695 cm^{-1}; mass spectrum (CI) m/z 362.1368 [$C_{20}H_{19}NO_2F_3$ (M+1) requires 362.1368].

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