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Nickel-Catalyzed Heterocycle Construction with Stereoselective Exocyclic Alkene Introduction[1]

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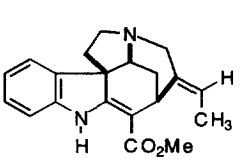
Abstract: A series of monocyclic and bicyclic heterocycles with exocyclic alkenes were constructed in a stereoselective fashion by an organozinc / $Ni(COD)_2$ - mediated cyclization of alkynyl enones. Both reductive and alkylative cyclization manifolds were accessible depending on the ligand and organozinc structure. Alkylative cyclizations were generally more efficient than reductive cyclizations, particularly with cyclic substrates. © 1997 Elsevier Science Ltd.

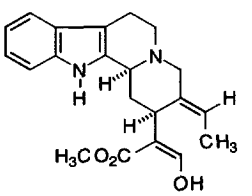
INTRODUCTION

The stereoselective introduction of exocyclic alkenes into complex molecules is a long-standing problem in organic synthesis.[2] The challenges associated with this transformation are frequently encountered in the total synthesis of heterocyclic natural products. Representative heterocyclic natural products that possess stereodefined trisubstituted alkenes include alkaloids of the strychnos and corynantheine families such as akuammicine[3] and geissoschizine,[4] and the oxepane diterpenoid zoapatanol[5] (Scheme 1). Whereas many previous synthetic entries to these alkaloids did not successfully address the issue of stereoselective introduction of the exocyclic alkene, the strategies that were successful in this regard[3-5] typically involved stereoselective creation of the trisubstituted alkene and construction of the heterocyclic core skeleton in separate, distinct operations.

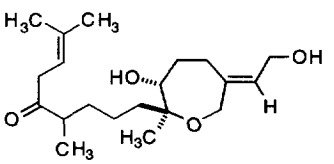
Scheme 1



akuammicine



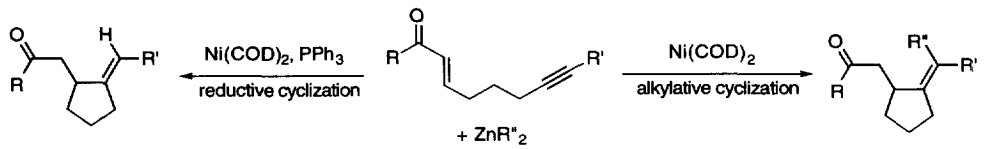
geissoschizine



zoapatanol

Recent studies from our laboratories have focused on the development of a nickel-catalyzed procedure for the cyclization of alkynylenones in the presence of organozincs.[6] We observed that tri- and tetra-substituted alkenes were efficiently assembled during the cyclization step with complete stereocontrol, and either alkylative or reductive cyclization pathways could be selected depending on the catalyst ligand structure (Scheme 2).[7,8] Catalysis by $Ni(COD)_2$ in the absence of phosphine ligands led to alkylative cyclizations, whereas catalysis by $Ni(COD)_2$ in the presence of three to four equivalents of triphenylphosphine led to reductive cyclizations if organozincs possessing β-hydrogens were employed.

Scheme 2

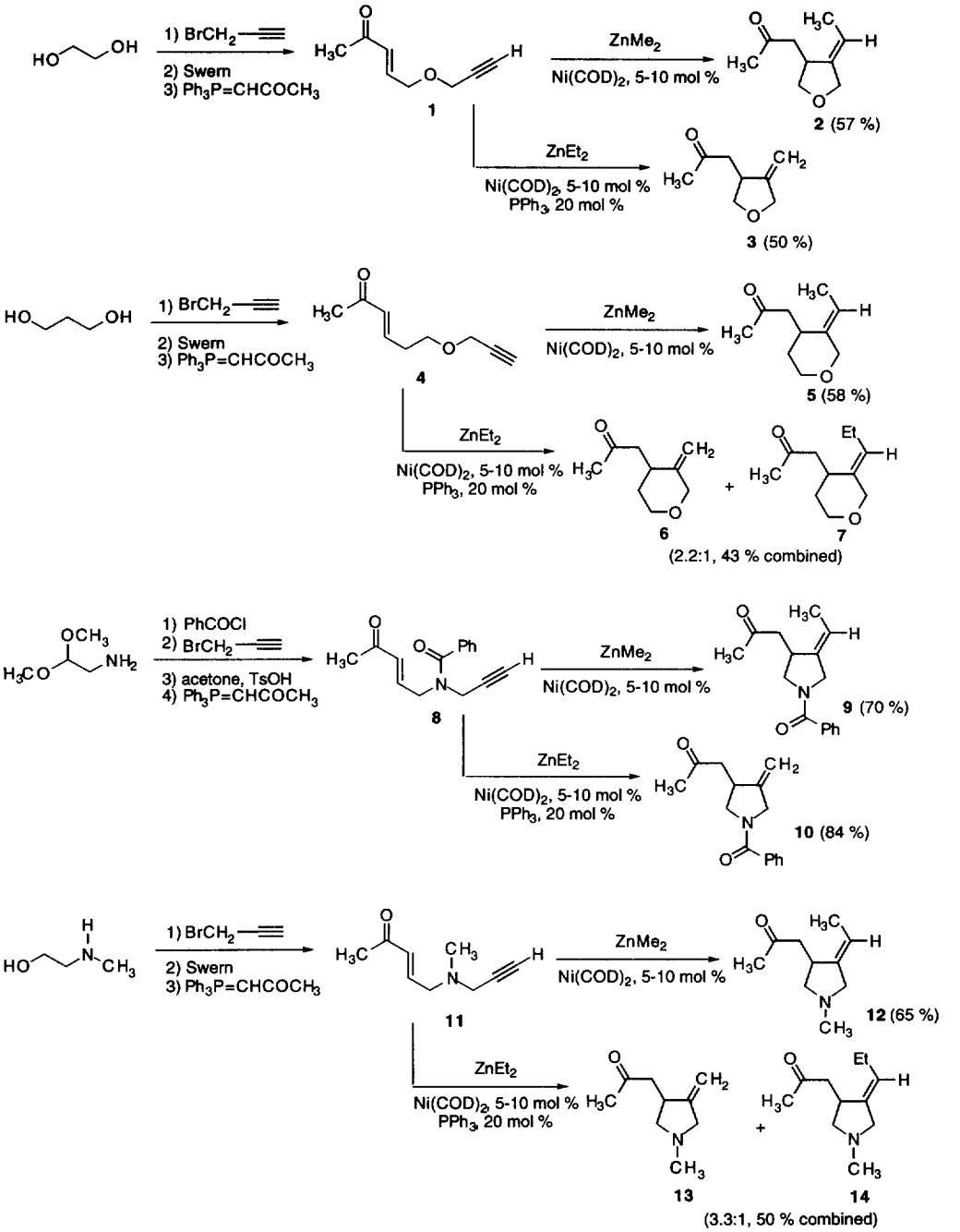


Since the nickel-mediated procedure is successful in catalyzing a ring closure with carbon-carbon bond formation and creation of a trisubstituted alkene in a single step, we felt that application of the carbocyclization method to the synthesis of complex heterocycles such as the natural products depicted above (Scheme 1) could simplify the synthetic challenges to a considerable extent. In order to probe the feasibility of applying the nickel-catalyzed alkynyl-enone cyclization method in complex molecule total synthesis, we have carried out a methodological study of the preparation of a variety of heterocyclic rings systems. Nitrogen- and oxygen-containing heterocycles with a variety of monocyclic and bicyclic skeletal frameworks have been prepared by both reductive cyclization and alkylative cyclization protocols.

RESULTS AND DISCUSSION

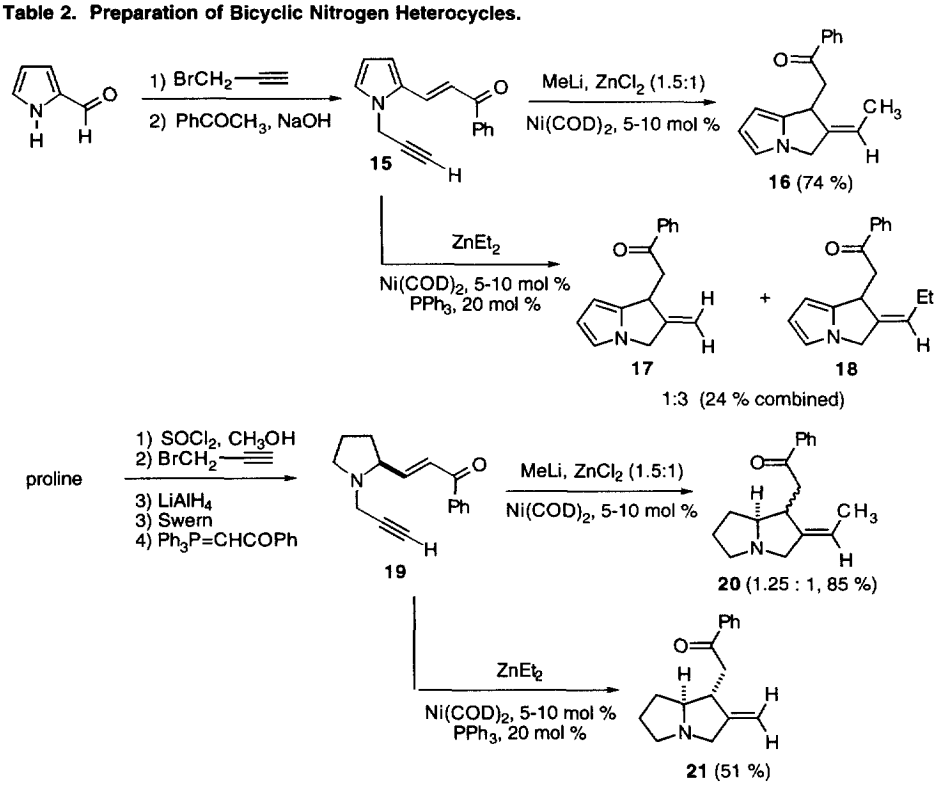
The application of the alkynyl enone cyclization method to heterocycle synthesis was first examined with linear substrates leading to monocyclic pyrrolidines and tetrahydrofurans (Table 1). The presence of basic nitrogens was a particular concern since this functionality is known to be problematic in many transition-metal-catalyzed processes involving coordinatively-unsaturated catalysts. We were pleased to observe that substrates possessing oxygen as well as *N*-alkyl and *N*-acyl groups in the tether chain were successfully cyclized. As expected, alkylative cyclizations with $Ni(COD)_2$ in the absence of triphenylphosphine employing dimethylzinc generated *in situ* from methyllithium and zinc chloride led to single isomers of trisubstituted exocyclic alkenes with a cis orientation between the carbonyl and the substituent derived from the organozinc. Reductive cyclizations with 1:4 $Ni(COD)_2$: PPh_3 employing commercial diethylzinc efficiently led to the exomethylene cycloadducts, with an ethyl-containing alkylative cyclization byproduct being observed in some cases. Alkylative cyclizations were generally developed with alkyllithium / zinc chloride mixtures to allow extrapolation to other readily available lithium reagents. Commercial dimethylzinc performed comparably, although reactions with organozincs derived from transmetallations with zinc chloride were generally faster.

Table 1. Preparation of Tetrahydrofurans, Tetrahydropyrans, and Pyrrolidines.



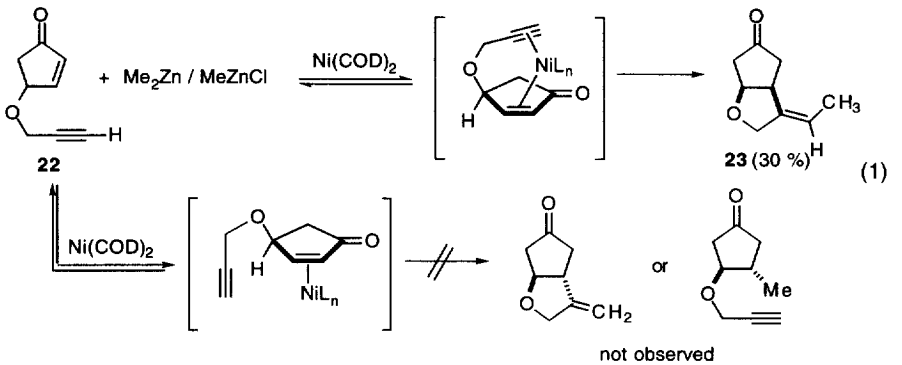
In order to prepare bicyclic skeletal frameworks, several heterocyclic substrates were studied. First, substrates in which a pre-existing ring was present in the tether chain were examined (Table 2). Substituted pyrrole **15** was efficiently cyclized under alkylative cyclization conditions to afford fused bicyclic product **16** in 74 % yield. Reductive cyclization of the same substrate, however, was less efficient and led to a 1:3 mixture of hydrogen- and ethyl-substituted products **17** and **18** in 24 % yield. Whereas cyclization efficiencies were generally highly sensitive to the electrophilicity of the enone component, the conjugation of the π-excessive pyrrole ring to the enone did not have an adverse effect on the process. The proline-derived framework of **19** was also tolerated in an alkylative cyclization sequence to produce the pyrrolizidine skeleton of **20** as a 1.25 : 1 mixture of two diastereomers in 85 % yield. Both diastereomers of **20** clearly possessed alkenes of the *E* configuration. Reductive cyclization of **19** afforded product **21** in 51 % yield as the single diastereomer depicted below after chromatography. A compound tentatively assigned as a diastereomer of **21** was obtained in < 5 % yield. The structure determinations of **20a**, **20b**, and **21** are described in the experimental section.

Table 2. Preparation of Bicyclic Nitrogen Heterocycles.



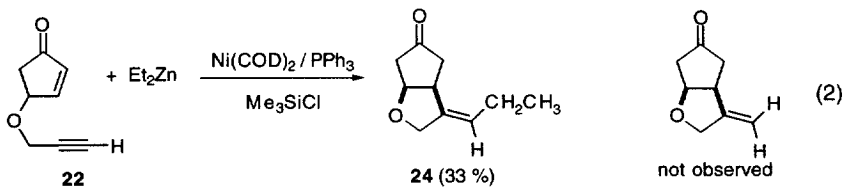
Next, substrate **22** was examined in which the enone was incorporated into a cyclic framework (eq 1). Although yields were somewhat lower than with acyclic enones, cis-fused diastereomer **23** was observed in 30 % yield as a single diastereomer upon alkylative cyclization of **22**. Apparently, either complexation of nickel to

the enone is reversible, or the tethered alkyne directs nickel complexation to the enone face that is syn to the tether chain, thus selectively affording the cis-fused bicycle. Irreversible complexation of nickel to the opposite diastereotopic enone face would likely result in the formation of either the trans-fused bicycle, or more likely, the product of direct conjugate addition to the enone, neither of which were observed.



(1)

Consistent with the bicyclic pyrrole preparation, reductive cyclization of **22** with hydrogen atom incorporation was not observed under the diethylzinc / $Ni(COD)_2$ / PPh_3 - promoted conditions. The standard reaction conditions led to sluggish reactions, and the addition of trimethylsilyl chloride resulted in ethyl incorporation by an alkylative cyclization providing **24** in 33 % yield. In general, the alkylative cyclization protocol tolerates increasing structural complexity well, whereas the reductive cyclization protocol becomes less efficient when steric hindrance is incorporated either at the enone or alkyne functionality. The reason behind this empirical observation as well as efforts to overcome the current limitations of the reductive cyclization procedure are in progress.



(2)

CONCLUSION

These studies demonstrate that a variety of monocyclic and bicyclic heterocycles with diverse heteroatom substitution patterns and cyclization topographies may be prepared by the organozinc / nickel (0)-promoted cyclization of alkynyl enones. Further methodological extensions, applications in the total synthesis of structurally-complex heterocyclic natural products, and mechanistic studies are in progress and will be reported in due course.

EXPERIMENTAL SECTION

Unless otherwise noted, reagents were commercially available and were used without purification. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium/benzophenone ketyl. Dichloromethane and DMSO were distilled from calcium hydride. All organolithium reagents were freshly titrated with 2,5-dimethoxybenzyl alcohol. Zinc chloride was dried at 150 °C at 0.1 mm overnight, then thoroughly ground by mortar and pestle in an inert atmosphere glovebox, and then dried again overnight at 150 °C at 0.1 mm Hg. $Ni(COD)_2$ and anhydrous $ZnCl_2$ were stored and weighed in an inert atmosphere glovebox. All reactions were conducted in flame-dried glassware under a nitrogen or argon atmosphere. Phosphoranes were prepared by literature methods.[9]

General Procedures for Nickel-Catalyzed Reactions

General Procedure A. A flame-dried, round-bottom flask, equipped with a magnetic stirring bar was charged with $Ni(COD)_2$ (0.05 - 0.1 equiv.) in THF (0.02 M solution) under argon. The solution was cooled to 0 °C, and Me_2Zn (1.2 - 1.5 equiv., 2.0 M toluene solution, used as received from Aldrich) was added dropwise and stirred for 5 - 10 min. The enone substrate (1.0 equiv.) in THF (0.25 M) was transferred to the $Ni(COD)_2$ / $ZnMe_2$ solution via cannula. The reaction was stirred at 0 °C for 15 min and then at 25 °C until starting material consumption was observed by TLC analysis (generally 1 h). The reaction was quenched by the addition of aqueous NH_4Cl / NH_4OH (pH 8), and the aqueous layer was extracted with EtOAc. The combined organic layers were dried with anhydrous Na_2SO_4, filtered, and concentrated, and the residue was purified by flash chromatography on SiO_2.

General Procedure B. Method A was followed except that Me_2Zn was generated *in situ* by the addition of MeLi (1.1 M ether solution, 1.8 equiv.) to a freshly prepared THF solution of anhydrous $ZnCl_2$ (0.5 M THF solution, 1.0 equiv.) at 0 °C.

General Procedure C. Method A was followed except that Et_2Zn (15 wt. % in hexanes, 1.5 equiv, used as received from ACROS) was employed. The nickel catalyst was freshly prepared as a 0.02 M THF solution by cannula transfer of a Ph_3P solution (0.1 M in THF, 0.2 - 0.4 equiv.) to a 0 °C $Ni(COD)_2$ solution (0.03 M THF solution, 0.05 - 0.1 equiv.).

(*E*)-5-(Prop-2-ynyloxy)pent-3-en-2-one (1). Oxalyl chloride (0.38 g, 3.0 mmol) was added dropwise to DMSO (0.47 g, 6.0 mmol) in 10 ml CH_2Cl_2 at -78°C. After stirring for 10-15 min. at -78 °C, 2-(2-propynyloxy)ethanol[10] (0.20 g, 2 mmol) was added dropwise, and mixture was stirred for 20-30 min. at -78°C. After the reaction mixture was allowed to warm to -50 °C, Et_3N (1.42 g, 14.0 mmol) was added by a syringe and the mixture was stirred for 2 h at 25 °C. The mixture was quenched with 0.1 N HCl, the CH_2Cl_2 layer was separated, dried with $MgSO_4$ and filtered, and $Ph_3P{=}CHC(O)CH_3$ (0.95 g, 3.0 mmol) was added at 25 °C. After stirring for 12 h, the reaction mixture was concentrated, and the mixture was chromatographed on SiO_2 (hexanes / EtOAc 2:1), to produce 90 mg (31% overall) of **1** as a pale yellow oil that was homogeneous by TLC analysis. ^1H NMR (500 MHz, $CDCl_3$) δ 6.74 (dt, J = 16.5, 4.5 Hz, 1H), 6.27 (dt, J = 16.0, 2.0 Hz, 1H), 4.22 (dd, J = 4.5, 2.0 Hz, 2H), 4.16 (d, J = 2.5 Hz, 2H), 2.45 (t, J = 2.5 Hz, 1H), 2.22 (s, 3H); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 198.0, 142.0, 130.5, 79.0, 75.1, 68.3, 58.0, 27.3; IR (film) 1697, 1676, 1635 cm^{-1}; HRMS (EI) *m/e* calcd for $C_8H_{10}O_2$ 123.0446, found 123.0449 ($(M-CH_3)^+$).

(*E*)-3-Ethylidene-4-(2-oxopropyl)tetrahydrofuran (2). Following the general method A, enone **1** (70 mg, 0.50 mmol), Me_2Zn (0.70 mmol), and $Ni(COD)_2$ (13 mg, 0.05 mmol) were employed to produce, after flash chromatography (hexanes/EtOAc 2:1), 37 mg (48%) of **2** as a colorless oil that was homogeneous by TLC analysis. ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (m, 1H), 4.31 (dq, J = 12.6, 1.8 Hz, 1H), 4.13 (dt, J = 12.6, 1.8 Hz, 1H), 3.89 (dd, J = 9.0, 5.9 Hz, 1H), 3.66 (dd, J = 6.3, 2.4 Hz, 3H), 3.22 (m, 1H), 2.62 (m, 2H), 2.15 (s, 3H), 1.65 (dt, J = 6.3, 2.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.7, 142.0, 114.5, 74.1, 70.9, 46.2, 36.1, 30.2, 14.6; IR (film) 1715, 1649, 1636 cm^{-1}; HRMS (EI) *m/e* calcd for $C_9H_{14}O_2$ 154.0994, found 154.0989 (M^+).

Following the general method B, enone **1** (50 mg, 0.36 mmol), MeLi (1.20 mmol), $ZnCl_2$ (89 mg, 0.65 mmol), and $Ni(COD)_2$ (12 mg, 0.04 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 2:1), 32 mg (57%) of **2** as a colorless oil that was homogeneous by TLC analysis. Spectral data were identical to that reported above.

3-Methylidene-4-(2-oxopropyl)tetrahydrofuran (3). Following the general method C, enone **1** (60 mg, 0.43 mmol), Et_2Zn (0.75 mmol), Ph_3P (52 mg, 0.20 mmol), and $Ni(COD)_2$ (12 mg, 0.04 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 2:1), 30 mg (50%) of **3** as a colorless oil that was homogeneous by TLC analysis. ^1H NMR (500 MHz, $CDCl_3$) δ 4.94 (q, J = 2.0 Hz, 1H), 4.89 (q, J = 2.0 Hz, 1H), 4.29 (m, 2H), 4.11 (dd, J = 9.0, 7.5 Hz, 1H), 3.43 (dd, J = 9.0, 6.3 Hz, 1H), 3.08 (m, 1H), 2.73 (dd, J = 18.0, 5.0 Hz, 1H), 2.55 (dd, J = 18.0, 9.0 Hz, 1H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 151.1, 104.0, 74.0, 71.2, 46.7, 38.8, 30.2; IR (film) 1715, 1666 cm^1; HRMS (CI) *m/e* calcd for $C_8H_{12}O_2$ 140.0837, found 140.0833 (M^+).

(*E*)-6-(Prop-2-ynyloxy)hex-3-en-2-one (4). The procedure for compound **1** was followed starting with 3-(2-propynyloxy)propanol[10] to afford 2.24 g of **4** (42 % overall yield) on a 35 mmol scale. ^1H NMR (300 MHz, $CDCl_3$) δ 6.74 (dt, J = 15.9, 6.9 Hz, 1H), 6.07 (dt, J = 16.2, 1.5 Hz, 1H), 4.09 (m, 2H), 3.60 (t, J = 6.3 Hz, 2H), 2.46 (dq, J = 6.3, 1.5 Hz, 2H), 2.41 (t, J = 2.1 Hz, 1H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.3, 144.3, 132.6, 79.4, 74.6, 67.8, 58.1, 32.5, 26.8; IR (film) 3263, 2865, 2115, 1696, 1675 cm^{-1}; HRMS (EI) calcd for $C_9H_{13}O_2$ 153.0914, found 153.0918 ($(M + 1)^+$).

(*E*)-3-Ethylidene-4-(2-oxopropyl)tetrahydropyran (5). Following the general method A, enone **4** (152 mg, 1.0 mmol), Me_2Zn (1.5 mmol), and $Ni(COD)_2$ (27.5 mg, 0.10 mmol) were employed to produce, after flash chromatography (hexanes/EtOAc 4:1) 97 mg (58%) of **5**. ^1H NMR (300 MHz, $CDCl_3$) δ 5.36 (q, J = 6.9 Hz, 1H), 4.08 (d, J = 12.6 Hz, 1H), 3.90 (d, J = 12.6 Hz, 1H), 3.81 (dd, J = 11.4, 4.5 Hz, 1H), 3.63 (dt, J = 11.7, 2.4 Hz, 1H), 3.36 (q, J = 6.3 Hz, 1H), 2.75 (dd, J = 15.9, 8.1 Hz, 1H), 2.61 (J = 16.2, 6.3 Hz, 1H), 2.14 (s, 3H), 1.92 (m, 1H), 1.60 (dd, J = 6.9, 1.8 Hz, 1H), 1.48 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4, 136.3, 120.8, 70.9, 63.6, 44.9, 31.0, 30.7, 28.6, 12.3; IR (film) 2954, 1714, 1360, 1081 cm^{-1}; HRMS (EI) calcd for $C_{10}H_{16}O_2$ 168.1150, found 168.1154 (M^+).

(*E*)-3-Methylidene-4-(2-oxopropyl)tetrahydropyran (6). Following the general method C, enone **4** (152 mg, 1.0 mmol), Et_2Zn (247 mg, 2.0 mmol), PPh_3 (105 mg, 0.4 mmol), and $Ni(COD)_2$ (28 mg, 0.1 mmol) were employed to produce, after flash chromatography (hexanes/EtOAc 4:1) 63 mg (43%) of a 2.2:1 ratio of **6** and **7**. ^1H NMR (300 MHz, $CDCl_3$) δ 4.87 (s, 1H), 4.65 (s, 1H), 4.15 (d, J = 12.0 Hz, 1H), 3.94 (m, 2H), 3.63 (dt, J = 11.1, 2.4 Hz, 1H), 2.82 (m, 2H), 2.49 (m, 1H), 2.19 (s, 3H), 1.81 (dq, J = 13.1, 4.2 Hz, 1H), 1.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 146.4, 108.0, 73.0, 67.4, 46.0, 35.6, 34.1, 30.5; IR (film) 2956, 2843, 1712, 1357, 1092 cm^{-1}. HRMS (EI) calcd for $C_9H_{13}O_2$ 153.0916, found 153.0919 ($(M-1)^+$).

***N*-(2,2-Dimethoxyethyl)-*N*-(prop-2-ynyl)benzamide.** Benzoylation[11] and propargylation[12] of 2,2-dimethoxyethylamine were carried out in 57 % overall yield on a 2.1 mmol scale to afford the product as a pale yellow oil that was homogeneous by TLC analysis. NMR data were broad due to rotamer interconversion. ^1H NMR (300 MHz, $CDCl_3$) δ 7.43 (br s, 2H), 7.34 (s, 3H), 4.65, 4.37 (br s, 1H (both)), 4.06 (br s, 1H), 3.65 (br s, 2H), 3.59-3.21 (br m, 7H), 2.30 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.5, 135.4, 129.9, 128.4, 126.9, 103.0, 78.9, 72.8, 54.6, 46.5, 40.4; IR (film) 1629, 1578 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{13}H_{14}NO_2$ 216.1025, found 216.1020 ($(M-OCH_3)^+$).

(*E*)-*N*-(4-Oxopent-2-enyl)-*N*-(prop-2-ynyl)benzamide (8). The acetal prepared above (500 mg, 2.0 mmol) was stirred with p-TsOH (100 mg, 0.53 mmol) in acetone (20 mL) at 56 °C for 2.5 h. The reaction was quenched with NH_4Cl / NH_4OH (pH 8), extracted with EtOAc, dried with Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography (hexanes / EtOAc 2:1) to afford 239 mg (60 %) of the desired aldehyde and 164 mg (33%) of recovered starting acetal. The aldehyde was stirred in 11 mL CH_2Cl_2 with 1-(triphenylphosphoranylidene)-2-propanone (380 mg, 1.5 mmol) at 40 °C for 1 h. The reaction mixture was directly concentrated and purified by silica gel chromatography (hexanes / EtOAc 2:1) to afford 242 mg (85 %) of **8** as a pale yellow oil that was homogeneous by TLC analysis. NMR data were broad due to rotamer interconversion. ^1H NMR (300 MHz, $CDCl_3$) δ 7.60-7.30 (m, 5H), 6.74 (br s, 1H), 6.18 (dt, J = 16.2, 1.5 Hz, 1H), 4.46-3.90 (br m, 4H), 2.40-2.30 (br s, 1H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8, 134.7, 132.3, 130.4, 128.6, 126.9, 78.2; IR (film) 1677, 1639 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{15}H_{15}NO_2$ 241.1103, found 241.1105 (M^+).

(*E*)-1-Benzoyl-3-ethylidene-4-(2-oxopropyl)pyrrolidine (9). Following the general method A, enone **7** (77 mg, 0.38 mmol), Me_2Zn (0.45 mmol), and $Ni(COD)_2$ (7 mg, 0.03 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 1:2), 40 mg (49%) of **9** as a colorless oil that was homogeneous by TLC analysis. NMR data were broad due to rotamer interconversion. ^1H NMR (300 MHz, DMSO-d_6, 25°C) δ 7.45 (m, 5H), 5.45 (m), 5.30 (m), 4.28-3.76 (m), 3.64 (dd, J = 11.1, 6.9 Hz), 3.51 (m), 3.34-3.10 (m), 2.70-2.45 (m), 2.10 (s), 2.01 (s), 1.58 (m); ^1H NMR (300 MHz, DMSO, 95° C) δ 7.40 (m, 5H), 5.40 (m, 1H), 4.17 (d, J = 15.0 Hz, 1H), 3.91 (d, J = 15.3 Hz, 1H), 3.59 (dd, J = 6.9, 11.4 Hz) 3.38 (m, 1H), 3.23 (q, J = 6.9 Hz, 1H), 2.57 (d, J = 6.9 Hz, 2H), 2.06 (s, 3H), 1.60 (d, J = 6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) δ 130.0, 128.6, 128.5, 128.3, 127.7, 127.1, 117.9, 54.8, 53.0, 51.6, 49.8,

46.9, 46.1, 35.4, 33.7, 30.4, 14.1; IR (film) 1713, 1626, 1576; HRMS (EI) *m/e* calcd for $C_{15}H_{19}NO_2$ 257.1416, found 257.1413 (M^+).

Following the general method B, enone **8** (50 mg, 0.25 mmol), MeLi (0.83 mmol), $ZnCl_2$ (61 mg, 0.45 mmol), and $Ni(COD)_2$ (7 mg, 0.03 mmol) were employed to produce, after flash chromatography (hexanes/EtOAc 1:2), 38 mg (70%) of **9** as a colorless oil that was homogeneous by TLC analysis. Spectral data were identical to that reported above.

1-Benzoyl-3-methylidene-4-(2-oxopropyl)pyrrolidine (10). Following the general procedure C, enone **7** (50 mg, 0.25 mmol), Et_2Zn (0.30 mmol), Ph_3P (26 mg, 0.10 mmol), and $Ni(COD)_2$ (7 mg, 0.03 mmol) were employed to produce, after flash chromatography (hexanes : EtOAc 1:2), 42 mg (84 %) of **10** as a colorless oil that was homogeneous by TLC analysis. NMR data were broad due to rotamer interconversion. ^1H NMR (300 MHz, DMSO-d_6, 25°C) δ 7.42 (m), 5.06 (s, major), 4.95 (s, major), 4.92 (s, minor), 4.87 (s, minor), 4.22 (d, J = 16.2 Hz), 4.00 (m), 3.71 (dd, J = 9.8, 8.0 Hz), 3.14-2.82 (m), 2.55 (m), 2.12 (s), 2.04 (s); ^1H NMR (300 MHz, DMSO-d_6, 90°C) δ 7.42 (m, 5H), 5.00 (br s, 1H), 4.92 (q, J = 2.1 Hz, 1H), 4.10 (m, 2H), 3.81 (t, J = 8.6 Hz, 1H), 3.14 (m, 1H), 3.05 (m, 1H), 2.82 (dd, J = 5.2, 17.7 Hz, 1H), 2.55 (dd, J = 8.1, 17.7 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 146.8, 136.1, 130.0, 128.3, 127.1, 127.0, 106.7, 54.8, 53.6, 51.4, 50.4, 46.1, 45.3, 38.5, 36.7, 30.2; IR (film) 1714, 1667, 1632, 1576 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{15}H_{17}NO_2$ 243.1259, found 243.1263 (M^+).

(*E*)-*N*-Methyl-*N*-4-oxopent-2-enyl-*N*-prop-2-ynylamine (11). 2-(Methyl-prop-2-ynyl-amino)ethanol[13] was oxidized by the Taber modification of the Swern oxidation.[14] Extraction from NH_4Cl / NH_4OH (pH 8) with CH_2Cl_2 followed by Wittig olefination of the crude product as described for compound **1** afforded a 38 % yield over two steps of **11** as a yellow oil on a 14 mmol scale. ^1H NMR (300 MHz, $CDCl_3$) δ 6.69 (dt, J = 16.2, 6.0 Hz, 1H), 6.16 (dt, J = 16.2, 1.8 Hz, 1H), 3.28 (d, J = 2.4 Hz, 2H), 3.17 (dd, J = 6.3, 1.5 Hz, 2H), 2.27 (s, 3H), 2.24 (t, J = 2.1 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2, 144.0, 132.7, 78.0, 73.6, 56.8, 45.5, 41.8, 26.9; IR (film) 1677, 1630 cm^{-1}; HRMS (EI) *m/e* calcd for $C_9H_{13}NO$ 151.0997, found 151.1000 (M^+).

(*E*)-1-Methyl-3-ethylidene-4-(2-oxopropyl)pyrrolidine (12). Following the general method A, enone **11** (70 mg, 0.46 mmol), Me_2Zn (0.7 mmol), and $Ni(COD)_2$ (12 mg, 0.046 mmol) were employed to produce, after flash chromatography (EtOAc / MeOH 1:1), 50 mg (65 %) of **12** as a yellow oil that was homogeneous by TLC analysis: ^1H (500 MHz, $CDCl_3$) δ 5.29 (qq, J = 6.9, 1.8 Hz, 1H), 3.30 (dd, J = 12.9, 1.5 Hz, 1H), 3.16 (m, 1H), 2.81 (dt, J = 12.6, 2.1 Hz, 1H), 2.72-2.57 (m, 3H), 2.46 (dd, J = 9.3, 3.0 Hz, 1H), 2.28 (s, 3H), 2.13 (s, 3H), 1.58 (dq, J = 1.5, 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1, 142.8, 115.2, 62.7, 61.4, 47.5, 42.3, 35.7, 30.3, 14.1; IR (film) 2360, 1714, 1447 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{10}H_{17}NO$ 167.1310, found 167.1313 (M^+).

1-Methyl-3-methylidene-4-(2-oxopropyl)pyrrolidine (13). Following the general method C, enone **11** (100mg, 0.66 mmol), Et_2Zn (1 mmol), Ph_3P (69 mg, 0.26 mmol), and $Ni(COD)_2$ (18 mg, 0.066 mmol) were employed to produce, after flash chromatography (EtOAc / MeOH 1:1), 55 mg (50 %) of an

inseparable mixture of **13** and **14** as a 3.3:1 ratio. ^{1}H NMR of **13** (500 MHz, $CDCl_3$) δ 4.90 (q, J = 2.3 Hz, 1H), 4.78 (q, J = 2.3, 1H), 3.18-3.02 (m, 3H), 2.86 (dd, J = 7.0, 9.5 Hz, 1H), 2.68 (m, 1H), 2.59 (m, 1H), 2.30 (s, 3H), 2.22 (dd, J = 6.0, 9.0 Hz, 1H), 2.12 (s, 3H). Distinct signals for **14**: δ 5.20 (tq, J = 7.0, 1.8 Hz, 1H), 3.28 (d, J = 13.0 Hz, 1H), 2.82 (d, J = 13.0 Hz, 1H), 2.43 (dd, J = 2.5, 9.5 Hz, 1H), 2.27 (s, 3H), 2.11 (s, 3H), 1.94 (m, 2H), 0.93 (t, J = 7.5 Hz, 3H). ^{13}C NMR of mixture (125 MHz, $CDCl_3$) δ 208.0, 207.8, 152.2, 141.1, 123.1, 104.8, 62.7, 62.5, 61.3, 48.4, 48.1, 42.3, 38.5, 35.8, 30.3, 30.2, 22.2, 14.3; IR (film) 2931, 2767, 1708, 1443 cm^{-1}; HRMS (EI) *m/e* calcd for $C_9H_{15}NO$ 153.1153, found 153.1149 (M^+).

1-(Prop-2-ynyl)pyrrole-2-carbaldehyde. 2-Formylpyrrole was alkylated with propargyl bromide under phase transfer catalysis[12] in 78 % yield as a yellow oil on a 1.6 mol scale. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (d, J = 0.9 Hz, 1H), 7.22 (s, 1H), 6.94 (dd, J = 3.9, 1.5 Hz, 1H), 6.26 (dd, J = 3.9, 2.7 Hz, 1H), 2.46 (t, J = 2.7 Hz, 2H), 5.18 (d, J = 2.7 Hz, 1H), 2.45 (t, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.5, 131.0, 130.3, 124.9, 110.1, 77.5, 74.4, 38.1; IR (film) 1670, 1529 cm^{-1}; HRMS (EI) *m/e* calcd for C_8H_7NO 133.0527, found 133.0520. (M^+).

(*E*)-3-(1-Prop-2-ynyl-pyrrol-2-yl)-1-phenylprop-2-en-1-one (15). The aldehyde prepared above was subjected to an aldol condensation with acetophenone.[15] Chromatography on SiO_2 (hexanes / EtOAc 2:1), afforded **15** (34%) as a yellow solid on a 1.9 mmol scale. mp 64-65 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (dt, J = 6.3, 1.5 Hz, 2H), 7.84 (d, J = 15.3 Hz, 1H), 7.60-7.46 (m, 3H), 7.34 (d, J = 15.3 Hz, 1H), 7.01 (m, 1H), 6.87 (dd, J = 3.9, 1.5 Hz, 1H), 6.27 (t, J = 3.3 Hz, 1H), 4.82 (d, J = 2.1 Hz, 2H), 2.48 (t, J = 2.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.8, 138.6, 132.4, 131.6, 129.7, 128.5, 128.3, 126.5, 117.5, 113.3, 110.3, 77.3, 74.6, 36.8; IR (film) 1650, 1585, 1569 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{16}H_{13}NO$ 235.0997, found 235.0994 (M^+).

(*E*)-2-Ethylidene-1-(2-oxo-2-phenylethyl)-2,3-dihydro-*1H*-pyrrolizine (16). Following the general method B, enone **15** (40 mg, 0.172 mmol), MeLi (0.567 mmol), $ZnCl_2$ (42 mg, 0.310 mmol), and $Ni(COD)_2$ (5 mg, 0.017 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 3:1), 31.4 mg (74%) of **16** as a yellow solid that was homogeneous by TLC analysis: ^{1}H (300 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.54 (m, 1H), 7.44 (m, 2H), 6.57 (dd, J = 1.5, 3.0 Hz, 1H), 6.16 (t, J = 3.2 Hz, 1H), 5.81 (d, J = 3.6 Hz, 1H), 5.60 (m, 1H), 4.71 (d, J = 14.7 Hz, 1H), 4.51 (m, 2H), 3.32 (m, 2H), 1.74 (d, J = 7.2 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 198.1, 141.8, 139.5, 137.1, 133.0, 128.5, 128.1, 119.2, 113.4, 111.9, 100.5, 50.8, 43.7, 35.1, 14.1; IR (film) 1682, 1596, 1487 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{17}H_{17}NO$ 251.1310, found 251.1307 (M^+).

(*E*)-2-Propylidene-1-(2-oxo-2-phenylethyl)-2,3-dihydro-1*H*-pyrrolizine (18) and 2-methylidene-1-(2-oxo-2-phenylethyl)-2,3-dihydro-1*H*-pyrrolizine (17). Following the general procedure C, enone **15** (75 mg, 0.32 mmol), Et_2Zn (0.64 mmol), $Ni(COD)_2$ (9mg, 0.03 mmol), and Ph_3P (25 mg, 0.1 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 19:1), 15 mg (18%) of **18** as a yellow oil and 5 mg (6%) of **17** as a yellow solid. Compound **18**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.54 (tt, J = 1.3, 7.5 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 6.56 (dd, J = 1.5, 2.5 Hz, 1H), 6.15 (t, J =

3 Hz, 1H), 5.79 (d, J = 3.5 Hz, 1H), 5.50 (m, 1H), 4.71 (d, J = 14.0 Hz, 1H), 4.51 (d, J = 14.0 Hz, 1H), 4.48 (d, J = 9.5 Hz, 1H), 3.35 (dd, J = 17.5, 10.0 Hz, 1H), 3.25 (dd, J = 17.5, 3.5 Hz, 1H), 2.13 (m, 2H), 1.01 (t, J = 7.5 Hz, 3H). Stereochemical assignments were made on the basis of homonuclear decoupling and NOE experiments. ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.0, 140.2, 139.4, 137.1, 133.0, 128.5, 128.0, 126.7, 113.4, 111.9, 100.5, 50.8, 44.3, 35.3, 22.1, 14.1; IR (film) 1686, 1596 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{18}H_{19}NO$ 265.1467, found 265.1474 (M^+).

Compound **17**: ^1H NMR (500 MHz, $CDCl_3$) δ 7.97 (m, 2H), 7.56 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 2H), 6.61 (dd, J = 1.5, 2.5 Hz, 1H), 6.21 (t, J = 3 Hz, 1H), 5.80 (d, J = 3.5 Hz, 1H), 5.20 (quintet, J = 2.5 Hz, 2H), 4.68 (qq, J = 1.5, 15.0 Hz, 2H), 4.43 (m, 1H), 3.42 (dd J = 7.5, 17.5 Hz, 1H), 3.37 (dd, J = 6.5, 17.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.1, 151.2, 139.0, 137.0, 133.1, 128.6, 128.1, 113.6, 112.2, 109.0, 100.0, 51.0, 45.2, 37.4; IR (film) 1685, 1596, 1580 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{16}H_{15}NO$ 237.1154, found 237.1157 (M^+).

Methyl 1-(prop-2-ynyl)-pyrrolidine-2-carboxylate. This compound was prepared by a closely-related literature procedure[16] from proline in 87 % yield on a 0.25 mol scale. Bp 80-81 °C at 2.1 mm Hg. ^1H NMR (300 MHz, $CDCl_3$) δ 3.67 (s, 3H), 3.54 (dd, J = 2.4, 1.5 Hz, 2H), 3.37 (dd, J = 9.3, 6.6 Hz, 1H). 2.99 (m, 1H), 2.66 (dt, J = 9.2, 7.6 Hz, 1H), 2.16 (t, J = 2.4 Hz, 1H), 2.02-2.12 (m, 1H), 1.70-2.00 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 78.2, 73.1, 62.3, 52.0, 51.8, 41.0, 29.4, 23.1; IR (film) 3286, 2952, 2100, 1744, 1435 cm^{-1}; HRMS (EI) calcd for $C_9H_{13}NO_2$ 167.0946, found 167.0948 (M^+).

1-(Prop-2-ynylpyrrolidin-2-yl)-2-methanol. To a solution of $LiAlH_4$ (4.54 g, 0.12 mol) in Et_2O (200 mL) was added the ester prepared above (10.0 g, 0.060 mol). After 1 h the mixture was quenched with NH_4Cl / NH_4OH (pH 8 buffered), vacuum filtered through diatomaceous earth, dried ($MgSO_4$) and concentrated. Vacuum distillation provided 7.4 g (89%) of the alcohol as a colorless oil, bp 60-62 °C at 0.3 mm Hg. ^1H NMR (300 MHz, $CDCl_3$) δ 3.57 (dd, J = 11.1, 3.6 Hz, 1H), 3.49 (dd, J = 14.9, 2.2 Hz, 1H), 3.38 (m, 2H), 2.96 (m, 2H), 2.78 (m, 1H), 2.62 (q, J = 8.4 Hz, 1H), 2.16 (t, J = 2.1 Hz, 1H), 1.84 (m, 1H), 1.70 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 79.2, 72.6, 62.2, 61.8, 53.3, 41.0, 27.6, 23.3; IR (film) 3296, 2102, 1330 cm^{-1}; HRMS (EI) calcd for $C_7H_{10}N$ 108.0813, found 108.0816 ($(M - CH_2OH)^+$).

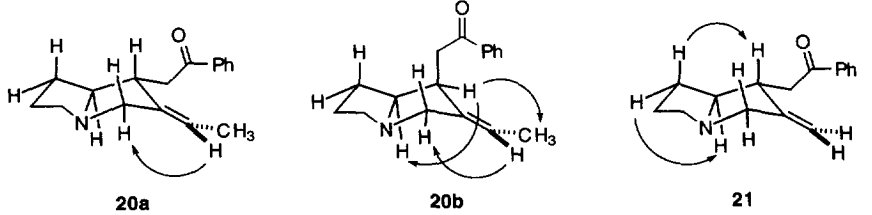
(*E*)-(1-Prop-2-ynyl)-2-(3-oxo-3-phenyl-prop-1-enyl)pyrrolidine (19). The alcohol prepared above was oxidized by a Swern oxidation as described for compound **1** on a 5.0 mmol scale. The mixture was then quenched with H_2O, extracted with CH_2Cl_2, the organic layer was washed with brine, dried ($MgSO_4$), and filtered. The crude aldehyde in CH_2Cl_2 was then treated with $Ph_3P{=}CH\text{-}C(O)CH_3$ and was heated at reflux for 24 h. Evaporation and flash chromatography (hexane / EtOAc 9:1) followed by washing with aq. sodium bisulfite, drying ($MgSO_4$) and concentration provided 455 mg (38% overall yield) of **19** as a pale yellow powder. ^1H NMR (300 MHz, $CDCl_3$) δ 7.84-7.87 (m, 2H), 7.43-7.49 (m, 1H), 7.34-7.40 (m, 2H), 6.97 (d, J = 15.6 Hz, 1H), 6.78 (dd, J = 15.6, 10.8 Hz, 1H), 3.45 (dd, J = 17.4, 2.4 Hz, 1H), 3.28 (m, 2H), 2.99 (dt, J = 6.0, 1.8 Hz, 1H), 2.60 (dd, J = 17.4, 8.6 Hz, 1H), 2.20 (t, J = 2.4 Hz, 1H), 1.91-2.01 (m, 1H), 1.61-1.80 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5, 149.6, 149.6, 137.6, 132.7, 128.6, 126.5,

78.7, 73.1, 63.2, 52.2, 40.6, 31.7, 22.7; IR (film) 3297, 2966, 1670, 1622 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{17}NO$ 239.1310, found 239.1304 (M^+).

(*E*)-2-Ethylidene-1-(2-oxo-2-phenylethyl)hexahydro-pyrrolizine (20). Following the general method B, enone **19** (50 mg, 0.21 mmol), MeLi (1.12 mmol), $ZnCl_2$ (86 mg, 0.63 mmol), and $Ni(COD)_2$ (5.8 mg, 0.02 mmol) were employed to produce, after flash chromatography (basic alumina, EtOAc) 45 mg (85%) of **20a** and **20b** as a 1.25:1 mixture of diastereomers. Small quantities of **20a** and **20b** were obtained in diastereomerically pure form by careful chromatography (SiO_2, 99.5 acetone/0.5 $EtNH_2$). For **20a**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.84-7.94 (m, 2H), 7.46-7.54 (m, 1H), 7.36-7.43 (m, 2H), 5.35 (q, J = 7.0 Hz, 1H), 3.70 (br d, J = 14.0 Hz, 1H), 3.04-3.24 (m, 4H), 2.85-2.93 (m, 1H), 2.50-2.57 (m, 1H), 2.02-2.10 (m, 1H), 1.77-1.85 (m, 1H), 1.60-1.68 (m, 1H), 1.57 (d, J = 7.0 Hz, 3H), 1.48-1.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.3, 142.8, 137.0, 133.0, 128.5, 128.0, 116.4, 72.0, 58.6, 54.0, 42.9, 41.6, 31.4, 24.9, 14.5; For **20b**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.93-7.97 (m, 2H), 7.52-7.58 (m, 1H), 7.41-7.47 (m, 2H), 5.35 (dq, J = 6.9, 1.5 Hz, 1H), 3.69 (dt, J = 6.6, 2.5 Hz, 1H), 3.57 (br m, 1H), 3.36 (d, J = 12.0 Hz, 1H), 3.18-3.27 (m, 4H), 3.04 (d, J = 5.4 Hz, 1H), 2.91-2.99 (m, 1H), 2.59-2.67 (m, 1H), 1.82-1.94 (m, 1H), 1.73-1.81 (m, 1H), 1.56 (dd, J = 6.9, 1.5 Hz, 1H), 1.52-1.62 (m, 1H), 1.26-1.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 144.8, 136.7, 133.1, 128.6, 127.9, 116.1, 68.7, 58.4, 53.5, 39.8, 36.5, 26.7, 25.9, 13.9; IR of mixture (film) 2959, 1684, 1447 cm^{-1}; HRMS (EI) of mixture, calcd for $C_{17}H_{21}NO$ 255.1623, found 255.1620 (M^+). The structures of **20a** and **20b** were rigorously established by NOE difference spectroscopy.

2-Methylidene-1-(2-oxo-2-phenylethyl)hexahydro-pyrrolizine (21). Following the general method C, enone **19** (120 mg, 0.50 mmol), Et_2Zn (93 mg, 0.75 mmol), PPh_3 (53 mg, 0.2 mmol), and $Ni(COD)_2$ (14 mg, 0.05 mmol) were employed to produce, after flash chromatography (basic alumina, hexanes/EtOAc 1:4) 61 mg (51%) of **21** as a single diastereomer. ^1H NMR (300 MHz, $CDCl_3$) δ 7.94-7.97 (m, 2H), 7.51-7.54 (m, 1H), 7.42-7.47 (m, 2H), 4.87 (d, J = 1.8 Hz, 1H), 4.82 (d, J = 1.8 Hz, 1H), 3.70 (d, J = 14.7 Hz, 1H), 2.95-3.32 (m, 6H), 2.57-2.60 (m, 1H), 1.57-2.09 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 153.5, 137.0, 133.1, 128.6, 128.0, 105.2, 71.4, 58.9, 54.5, 44.2, 42.5, 30.7, 25.4; IR (film) 2959, 1682, 1447 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{19}NO$ 241.1466, found 241.1461 (M^+). The structure of **21** was rigorously established by NOE difference spectroscopy.

Selected NOE's



4-(Prop-2-ynyloxy)cyclopent-2-enone (22). ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (dd, J = 2.3, 5.8, 1H), 6.27 (dd, J = 1.5, 5.5 Hz, 1H), 4.91 (m, 1H), 4.29 (dd, J = 2.3, 16.3 Hz, 1H), 4.22 (dd, J = 2.5,

16.0 Hz, 1H), 2.71 (dd, J = 6.0, 18.0 Hz, 1H), 2.50 (t, J = 2.3 Hz, 1H), 2.35 (dd, J = 2.5 Hz, 18.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5, 160.6, 136.0, 79.2, 76.6, 75.4, 57.1, 41.5; IR (film) 1719, 1587 cm^{-1}; HRMS (EI) calcd for $C_8H_8O_2$ 136.0524, found 136.0521 (M^+).

(*E*)-4-Ethylidene-2-oxa-*cis*-bicyclo[3.3.0]octan-7-one (23). Following the general method A, enone **22** (50 mg, 0.37 mmol), $ZnMe_2$ (0.42 mmol), and $Ni(COD)_2$ (10 mg, 0.037 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 1:1) 17 mg (30%) of **23** as a colorless oil that was homogeneous by TLC analysis: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.36 (qq, J = 2.0, 6.5 Hz, 1H), 4.57 (t, J = 5.0 Hz, 1H), 4.47 (dq, J = 12.8, 1.5 Hz, 1H), 4.29 (ddt, J = 1.0, 12.5, 2.5 Hz, 1H), 3.35 (q, J = 6.5 Hz, 1H), 2.66 (dd, J = 19.0, 10.0 Hz, 1H), 2.55 (d, J = 19.0 Hz, 1H), 2.47 (ddd, J = 19.0, 5.0, 1.0 Hz, 1H), 2.07 (ddd, J = 19.3, 8.5, 1.0 Hz), 1.66 (ddt, J = 7.0, 2.0, 1.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.2, 143.5, 115.2, 81.4, 71.8, 44.4, 41.9, 41.4, 15.2; IR (film) 1745, 1649, 1636 cm^{-1}; HRMS (EI) *m/e* calcd for $C_9H_{12}O_2$ 152.0837, found 152.0836 (M^+). Stereochemical assignments were made on the basis of homonuclear decoupling and NOE experiments.

2-Oxa-(*E*)-4-propylidene-*cis*-bicyclo[3.3.0]octan-7-one (24). General method C was followed, except that trimethylsilyl chloride was pre-mixed with enone **22** prior to addition to the catalyst solution, and 0.1 N HCl was added to the reaction mixture prior to extraction. Enone **22** (50 mg, 0.37 mmol), Et_2Zn (0.55 mmol), TMSCl (79 mg, 0.73 mmol), Ph_3P (38 mg, 0.146 mmol), and $Ni(COD)_2$ (10 mg, 0.037 mmol) were employed to produce, after flash chromatography (hexanes / EtOAc 1.2:1), 20 mg (33%) of **24** as a colorless oil that was homogeneous by TLC analysis: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.3 (dt, J = 7.0, 2.0 Hz, 1H), 4.57 (t, J = 5.0 Hz, 1H), 4.48 (dt, J = 12.5, 1.5 Hz, 1H), 4.31 (dd, J = 12.5, 1.5 Hz, 1H), 3.35 (q, J = 6.5 Hz, 1H), 2.65 (dd, J = 19.0, 10.0 Hz, 1H), 2.55 (d, J = 19.0 Hz, 1H), 2.47 (ddd, J = 19.0, 5.0, 1.0 Hz, 1H), 2.11-2.00 (m, 3H), 0.99 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.2, 141.9, 122.7, 81.4, 71.8, 44.5, 42.4, 41.5, 23.5, 14.1; IR (film) 1743, 1643 cm^{-1}; HRMS (EI) *m/e* calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0998 (M^+).

REFERENCES AND NOTES

1. Dedicated to Professor Carl Johnson on the occasion of his sixtieth birthday.
2. For an excellent review, see Negishi, E. in *Advances in Metal-Organic Chemistry* Liebeskind, L. S., Ed. JAI Press Inc., Greenwich, Conn., 1989; Vol. 1, 177.
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