Transmutation of 1,3-Dipoles. The Conversion of α-Diazo Ketones into Azomethine Ylides via Carbonyl Ylides

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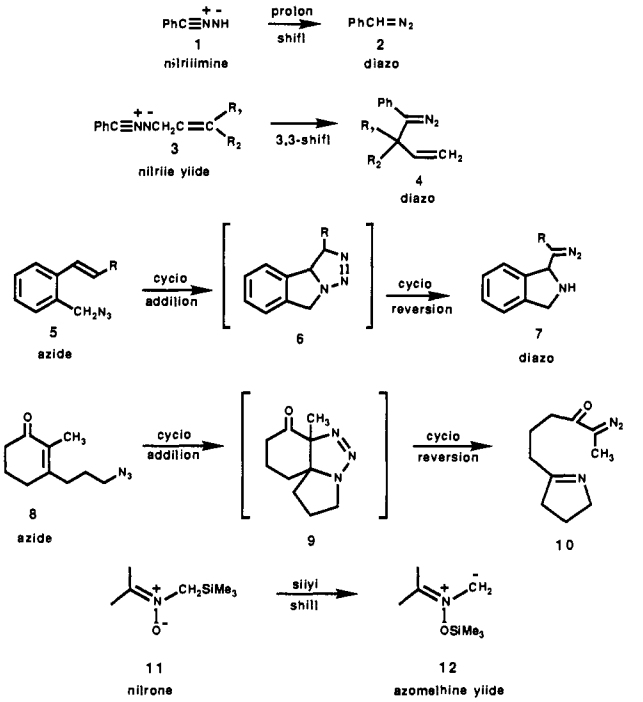
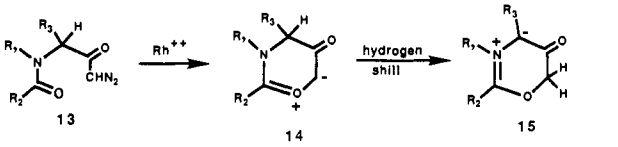
Abstract: A series of *N*-acyl-2-(1-diazoacetyl)pyrrolidines, when treated with a catalytic quantity of a rhodium(II) carboxylate, were found to afford tricyclic dihydropyrrolizines derived from an azomethine ylide intermediate. The initial reaction involves generation of the expected carbonyl ylide dipole by intramolecular cyclization of the keto carbenoid onto the oxygen atom of the amide group. In certain cases the carbonyl ylide dipole can be trapped by an added dipolarophile. When the α-position of the pyrrolidine ring was blocked by an alkyl group, the rhodium(II)-catalyzed cycloaddition with dimethyl acetylenedicarboxylate led to the carbonyl ylide cycloadduct in 95% yield. Usually, isomerization to the thermodynamically more stable azomethine ylide occurs via proton exchange with the small amount of water that was present in the reaction mixture. MNDO calculations show that these cyclic carbonyl ylides are ca. 18 kcal/mol higher in their heat of formation than the corresponding azomethine ylides. The initally formed azomethine ylide cycloadduct readily undergoes a subsequent alkoxy 1,3-shift to generate the tricyclic dihydropyrrolizine ring system.

The 1,3-dipolar cycloaddition reaction has long been recognized as a favored strategy for the synthesis of heterocyclic rings. Its popularity results from its high regio- and stereospecificity as well as its compatibility with a wide range of substitution patterns and functional groups.[2,3] As a consequence, knowledge of the mechanistic and synthetic aspects of 1,3-dipoles is quite extensive.[4] Less attention, however, has been placed upon the interconversion of one dipole into another.[5-9] Rearrangement of 1,3-dipoles is far less frequently encountered than analogous carbocation,[10-12] carbene,[13,14] or radical reorganizations.[15-17] Those rearrangements which do occur can be classified into a small number of types, defined either by the overall structural change or by the nature of the individual steps involved. In some instances, dipole rearrangements are quite elaborate and may be illustrated by several of the following transformations.



In a preliminary communication from our laboratory, we introduced a new strategy for azomethine ylide formation in which the key step involved a dipole rearrangement.[18] This reaction, which we have termed a "dipole cascade" involves three distinct classes of 1,3-dipoles. It is initiated by a rhodium(II)-catalyzed

Dipole Cascade



diazo ketone cyclization onto a neighboring carbonyl group to generate a carbonyl ylide dipole[19-22] which then undergoes a

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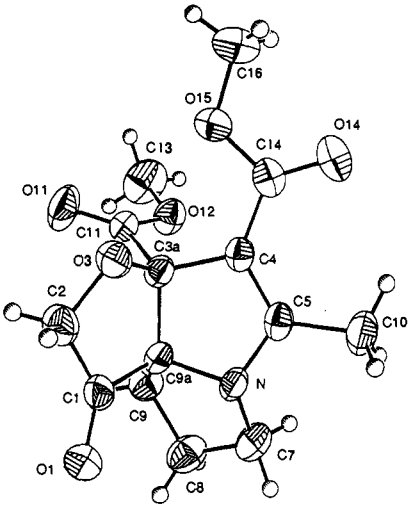


Figure 1. ORTEP drawing for 3a,4-dicarbomethoxy-5-methyl-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[3,2-*d*]pyrrolizin-1-one (**18**).

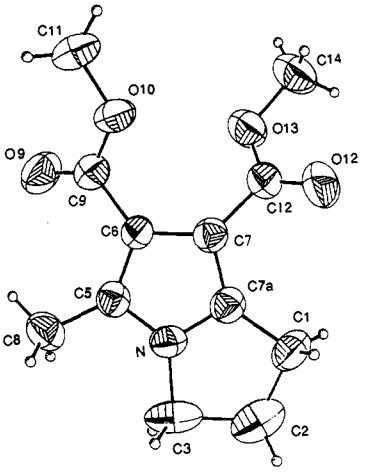
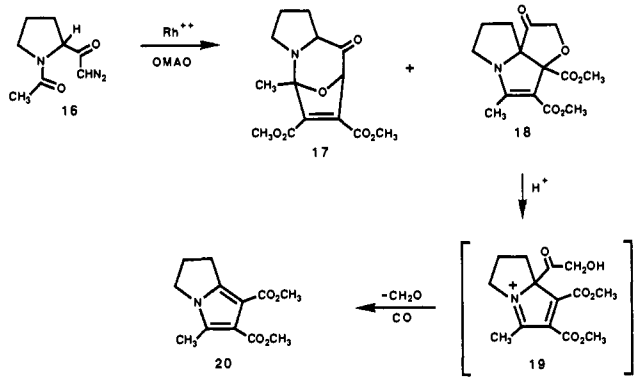


Figure 2. ORTEP drawing for 6,7-dicarbomethoxy-2,3-dihydro-5-methyl-1*H*-pyrrolizine (**20**).

subsequent proton shift. The wealth of strategically located functionality that could result from the rhodium-catalyzed reaction of α-diazo keto acyl amides of type **13** motivated us to focus on the possible utilization of the dipole cascade for heterocyclic synthesis. In this paper we present results which further define the scope, mechanism, and generality of the dipole cascade. In addition, we report that the azomethine ylide derived cycloadducts undergo a series of intriguing reactions to produce multiply functionalized pyrrole derivatives in excellent yield.

Results and Discussion

Our initial endeavors focused on the behavior of (*S*)-1-acetyl-2-(1-diazoacetyl)pyrrolidine (**16**). This diazo compound was obtained from *N*-acetyl-L-proline[23] by conventional sequences (see Experimental Section). Treatment of **16** with 1.2 equiv of



dimethyl acetylenedicarboxylate (DMAD) in the presence of a catalytic quantity of Rh_2OAc_4 at 25 °C afforded very little (10%) of the expected carbonyl ylide derived adduct **17**. Instead, the major product (87%) corresponded to cycloadduct **18**. The structure of pyrrolizin-1-one **18** was assigned on the basis of its NMR spectrum which showed a characteristic AB quartet (J = 17.0 Hz) centered at 4.24 ppm. The stereostructure of **18** was established unambiguously by single-crystal X-ray diffraction, and an ORTEP drawing of the molecular model is shown in Figure 1.

A novel fragmentation of **18** to give **20** was found to occur when it was subjected to silica gel chromatography. This same reaction also took place when **18** was stirred with a small amount of *p*-toluenesulfonic acid in benzene. The structure of **20** (98%) was assigned on the basis of its characteristic spectral data and was further established by an X-ray single-crystal structure analysis (see Figure 2). The conversion of **18** into **20** proceeds by an initial ring opening to give **19** as a transient species which either is attacked by water to give **20** and glycolic acid or else undergoes fragmentation to produce formaldehyde, carbon monoxide, and pyrrole **20**.

Among all the catalysts which have been developed for carbene addition to multiple π-bonds,[24] rhodium(II) carboxylates are the most effective for bimolecular reactions that employ α-diazo carbonyl compounds.[25,26] We have made similar observations with the above (α-diazoacetyl)pyrrolidine system.[27] Not only are yields significantly higher with rhodium catalysts, but the reaction conditions are frequently gentle enough to allow the reaction to be carried out at 10 °C. Several dirhodium(II) compounds with different electronic influences imparted on the rhodium(II) center by its ligands (i.e., octanoate, mandelate, trifluoroacetate) were prepared so as to determine their catalytic properties. The results obtained indicate very little difference in the yield or ratio of the two cycloadducts. We did find, however, that the more soluble rhodium octanoate was significantly more reactive than the mandelate or acetate catalyst.[28]

Several other dipolarophiles were examined so as to establish the scope and generality of the process. The cycloaddition proceeded readily with both methyl acrylate and methyl propiolate, giving rise to a rearranged cycloadduct in both cases. With methyl propiolate, a small amount (5%) of the dipolar cycloadduct **23** derived from a carbonyl ylide was also formed. Treatment of cycloadduct **22** with acid (or silica gel) gave rise to a 1:3 mixture of pyrroles **26** and **27**. As was the case with cycloadduct **18**, the first step involves ring opening to produce iminium ion **24** as a transient species. In this case, an acyl 1,5-shift to the unsubstituted carbon competes with loss of CH_2O and CO to give iminium ion **25** which subsequently loses a proton to produce pyrrole **27**.

A number of experiments were conducted to determine the effect of the nitrogen acyl substituent on the cycloaddition product ratio. *N*-Benzoyl diazo pyrrolidine **28** reacted with DMAD at room temperature with Rh_2OAc_4 to give only the rearranged cycloadduct **29** in 95% isolated yield. The possibility of intra-

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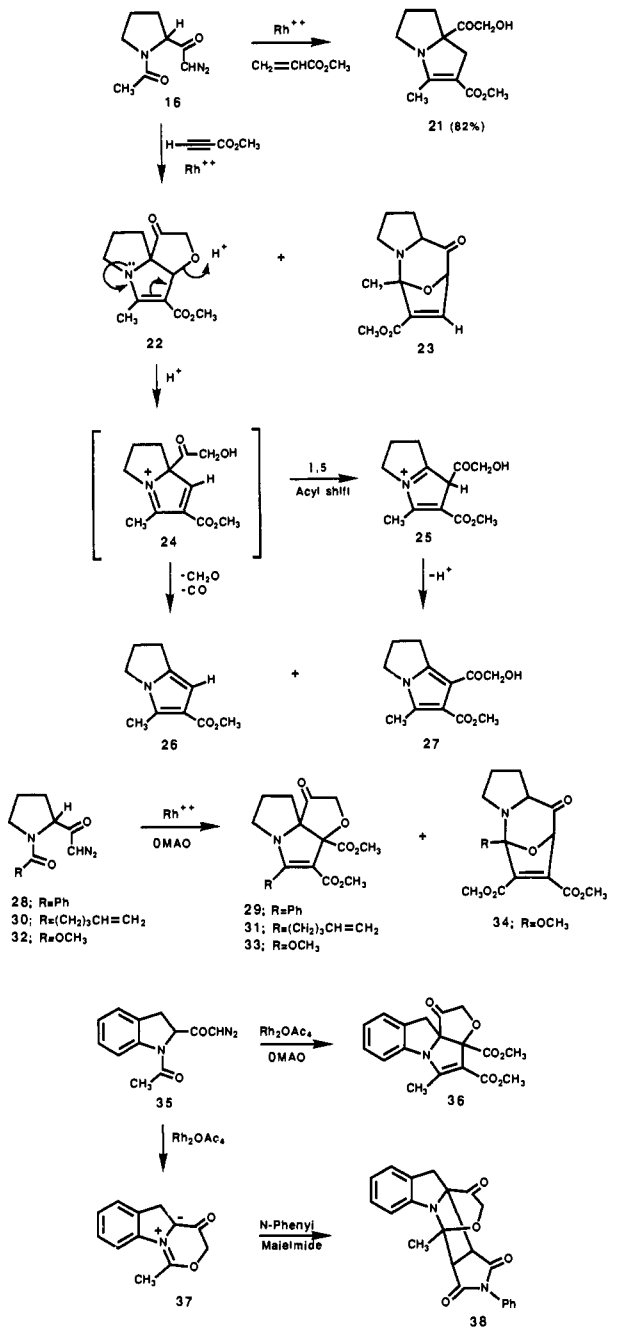
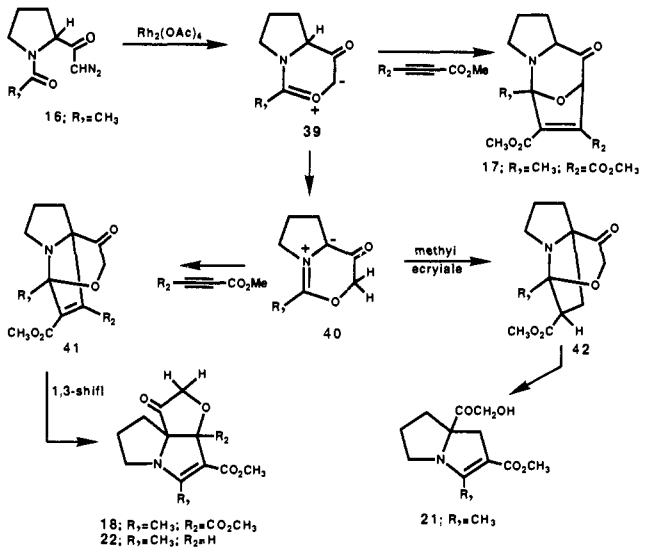
(27) Representative catalysts which have been examined include copper bronze, $Cu(acac)_2$, $Cu(OTf)_2$, $Mo(CO)_6$, $Fe(CO)_5$, and $Pd(OAc)_2$.
(28) A typical reaction using 2 mol % of rhodium acetate was complete in 60 min at 25 °C in benzene. Using similar amounts of rhodium octanoate as the catalyst, the reaction was generally finished in 20 min. Rhodium octanoate dimer can be purchased from Johnson-Matthey, Inc., Chemical Division, Winslow, NJ 08095.



molecular trapping of the initially formed carbonyl ylide was explored by using the *N*-(5-hexenylcarbonyl) analogue **30**. Exposure of **30** to Rh_2OAc_4 under standard conditions produced a complex mixture of products which contained none of the expected intramolecular cycloadduct. Addition of DMAD to the reaction mixture, however, led cleanly to the rearranged cycloadduct **31** in 85% yield. The absence of an internal adduct with diazo ketone **30** implies that the rearrangement of the initially formed carbonyl ylide **39** to azomethine ylide **40** (vide infra) is rapid relative to intramolecular dipolar cycloaddition to an unactivated π-bond.[29] In marked contrast to diazo pyrrolidines **28** and **30**, cycloaddition of the *N*-carbomethoxy-substituted diazo pyrrolidine **32** afforded a 1:1-mixture of cycloadducts **33** and **34**. This result indicates

Scheme I



that, in certain cases, the distribution of cycloadducts can be influenced by the electronic properties of the substituent group attached to the nitrogen atom.

The cycloaddition reaction of (diazoacetyl)indoline **35** and DMAD proceeded in a similar manner, giving rise to the rearranged cycloadduct **36** as the exclusive product in 91% yield. A key finding occurred when the cycloaddition of **35** was carried out using *N*-phenylmaleimide as the dipolarophile. This reaction produced cycloadduct **38** in 81% yield. The formation of **38** strongly suggests the involvement of an azomethine ylide intermediate (i.e., **37**) which undergoes 1,3-dipolar cycloaddition with the added dipolarophile. Presumably, a related process is involved in the formation of **36** (vide infra).

Mechanistic Overview. A mechanism that explains the formation of the products and that is consistent with all the data (vide supra) is outlined in Scheme I. The initial reaction involves generation of the expected carbonyl ylide dipole **39** by intramolecular cyclization of the keto carbenoid onto the oxygen atom of the amide group. Isomerization of **39** to azomethine ylide **40** is followed by 1,3-dipolar cycloaddition with DMAD. The initially formed cycloadduct **41** undergoes a subsequent alkoxy 1,3-shift to generate the tricyclic dihydropyrrolizine ring system. The reaction was followed by NMR spectroscopy, and the initially formed dipolar cycloadduct **41** could be readily detected in at least three different cases ($R_1 = CH_3$ (**41a**), $R_1 = Ph$ (**41b**), and $R_1 = CH_3$ in the indoline series **35** (**41c**)). Cycloadduct **41a** displayed a very characteristic AB pattern at 4.24 (d, 1 H, $J = 17.4$ Hz) and 4.33 ppm (d, 1 H, $J = 17.4$ Hz). This material was quantitatively converted to **18** upon standing for 1 h in the NMR tube. Similar results were also observed with diazo pyrrolidines **28** and **35**. In the case of **16**, the reaction with methyl propiolate proceeded in a highly regioselective manner, producing only cycloadduct **22**. This is perfectly consistent with the proposed mechanism outlined in Scheme I. According to frontier molecular orbital (FMO) theory,[31] regioselectivity is the result of best overlap of the interacting orbitals; i.e., the atoms with the largest coefficients combine preferentially. The dipolar HOMO–dipolarophile LUMO interaction with azomethine ylide **40** favors formation of cycloadduct **41d** which, in fact, can be detected by NMR spectroscopy. Over a period of 90 min, this transient rearranged to the thermodynamically more stable isomer **22**. When methyl acrylate was used as the dipolarophile, cycloadduct **42** was not seen as it readily rearranged to **21**, presumably via an iminium ion intermediate. The inability of the azomethine ylide to undergo intramolecular cycloaddition across the unactivated C–C double bond in **30** is in accord with FMO theory in that type I dipoles

(29) It should be noted that Maier and Evertz[30] have described a number of successful cases which involve the cycloaddition of mesoionic carbonyl ylides with nonactivated alkenes. The facility of cycloaddition of carbonyl ylides with simple alkenes, however, is dependent on the FMO interactions and is ultimately related to the nature of the substituent groups present on the dipole. With diazo ketone **30**, the dipole cascade occurs at a faster rate than intramolecular cycloaddition onto the alkenyl π-bond.

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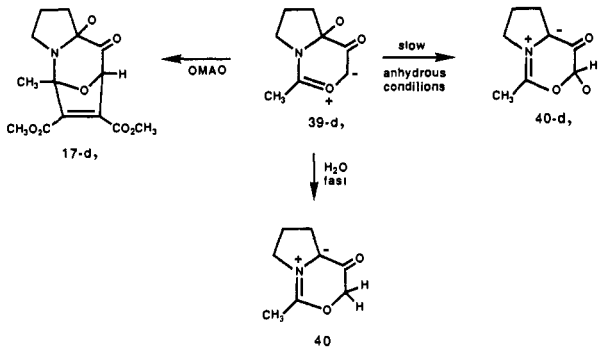
require electron-deficient dipolarophiles which possess low-lying LUMO levels.[32,33]

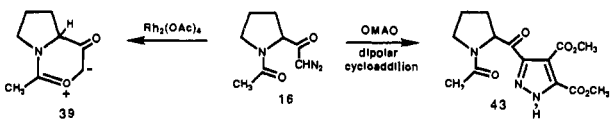
In order to provide more information regarding the details of the hydrogen-transfer step of the dipole cascade (i.e., **39** → **40**), we have examined the effect of deuteration on the cyclization reaction. The deuterated α-diazo pyrrolidine **16**-d_1 employed for the study was obtained from L-proline-2-d_1.[34] Treatment of this



material under fairly anhydrous conditions with Rh_2OAc_4 and DMAD afforded larger quantities of the carbonyl ylide derived cycloadduct **17** (45%) than was observed (10%) with the nondeuterated system. The increase in yield of the carbonyl ylide derived cycloadduct **17**-d_1 starting from **16**-d_1 suggests a slower rate of dipole interconversion (i.e., **39** → **40**), which is consistent with a significant deuterium isotope effect.[35]

During our investigations with **16**-d_1, we found that the ratio of cycloadducts **17** to **18** was critically dependent upon the amount of adventitious water present in the solvent. In fact, when one molar equivalent of water was deliberately added to the solvent, the carbonyl ylide derived cycloadduct **17** was totally absent. Moreover, carrying out the same reaction of **16**-d_1 in water-saturated $CDCl_3$ resulted in 94% loss of deuterium in the final rearranged cycloadduct **18**. We also note that 87% of deuterium was incorporated into **18** when the cycloaddition of **16** was carried out in a D_2O-saturated $CDCl_3$ solution. These results suggest that the hydrogen-transfer step in the dipole cascade process can best be depicted as proceeding through a bimolecular reaction of the carbonyl ylide **39** and a small amount of water present in solution.[36]

Some effort was invested in removing adventitious water present in the solvent which we suspected was intimately involved in the formation of the rearranged cycloadduct **18** (vide infra). When a mixture of **16** and DMAD was treated with rhodium(II) acetate in the presence of molecular sieves, the major product formed under these conditions (86%) corresponded to pyrazole **43**. More



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(35) Of course this suggestion is quite speculative since it involves a correlation of product yield with a kinetic isotope effect which is not always encountered.

(36) Control experiments demonstrated that cycloadduct **18** was stable to deuterium exchange under the reaction conditions used. The exchange reaction proceeds via the initially formed H_2O adduct i which subsequently eliminates a molecule of DOH, producing the thermodynamically more stable dipole **40** (vide infra).

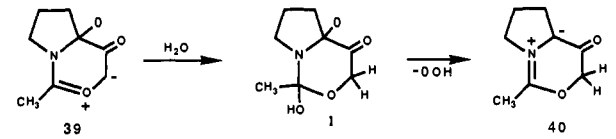
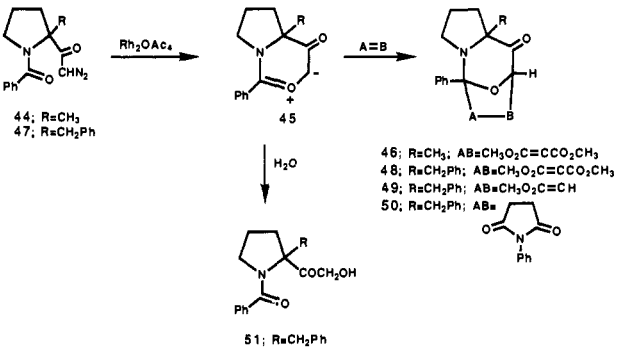


Table I. MOPAC Heats of Formation (kcal/mol) of Carbonyl and Azomethine Ylides

	carbonyl ylide **40**	ΔH	azomethine ylide **41**
R = H; X = H_2	−26.33	+17.42	−43.75
R = Me; X = H_2	−34.43	+18.06	−52.49
R = Ph; X = H_2	+2.70	+18.31	−15.61
R = OMe; X = H_2	−65.12	+6.81	−71.93
R = Me; X = O	−68.13	−7.93	−60.20

than likely the presence of molecular sieves destroys (or alters) the catalyst. In the absence of the rhodium catalyst, the α-diazo ketone simply undergoes 1,3-dipolar cycloaddition with DMAD to eventually give **43** after a hydrogen 1,3-shift from the initially formed cycloadduct. The rhodium(II)-catalyzed decomposition of α-diazo carbonyl compounds, on the other hand, involves a metallocarbenoid intermediate which retains the highly electrophilic properties associated with free carbenes.[25,26] Such an intermediate can be intercepted intramolecularly by the nonbonding electrons on the neighboring carbonyl group to effect overall cyclization to give carbonyl ylide **39**.

Cycloaddition would be expected to take place exclusively from the carbonyl ylide dipole if the α-position of the pyrrolidine ring was blocked by an alkyl group. Indeed, treatment of *N*-benzoyl diazo pyrrolidine **44** or **47** with several different dipolarophiles afforded only the carbonyl ylide derived cycloadducts in excellent yield. Attempts to obtain a cycloadduct from the reaction of the



diazo pyrrolidine with a nonactivated dipolarophile (e.g., 1-octene, propargyl ether, etc.) failed. The only product that could be isolated (70%) from the reaction mixture corresponded to *N*-benzoyl-2-benzyl-2-(hydroxyacetyl)pyrrolidine (**51**). The formation of **51** involves addition of a small amount of water that was present in the solvent to dipole **45**, and this is followed by a ring-opening reaction.

At this point in our studies, we felt it was necessary to address the question of why the carbonyl ylide dipole underwent rapid rearrangement to the azomethine ylide. To probe this point, we have carried out MO calculations using the semiempirical MNDO program, which has already been used successfully for the investigation of energy levels, heats of formation, and coefficients of a series of dipoles and dipolarophiles.[1] The size of the molecular systems involved in our study precluded the use of ab initio methodology. A variety of theoretical calculations have been performed on the 1,3-dipolar cycloaddition reaction over the past two decades.[37-43] These calculations, however, have generally

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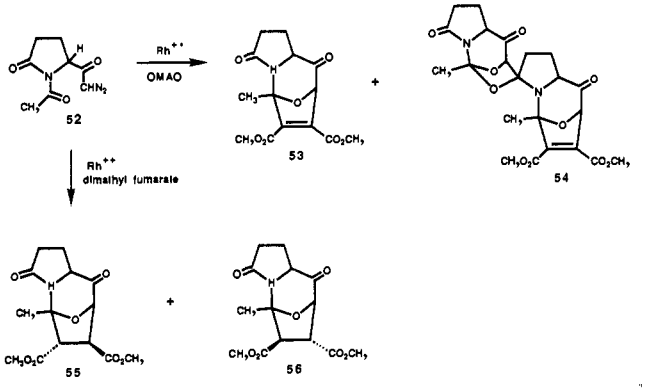
concerned themselves with problems of regioselectivity or the mechanistic details of the cycloaddition.

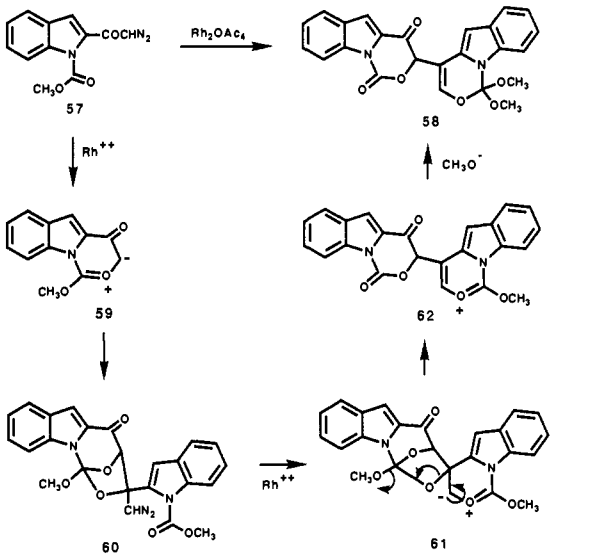
Global minima for each dipole were found by making use of multiconformer generation in Model (TTY, Conf, Statistical, Coordinate) followed by Batch minimization using Bakmdl.[44] The particular parameters used were those of the NOH (no hydrogen) field developed by Still and implemented by Steliou in the program Model. The resulting lowest energy conformation was submitted for a 1SCF determination of the heat of formation. Calculations were performed with the standard version of MNDO as implemented in the MOPAC package which includes the PM3 parameters. Determination of the calculated heats of formation of the cyclic carbonyl ylides of type **39** indicate that these dipoles are ca. 18 kcal/mol higher in energy than the corresponding azomethine ylides (see Table I). Some of this energy difference is presumably responsible for the facility with which the dipole reorganization occurs.[45,46] Thus, the product ratios are consistent with the calculated energy differences of the two dipoles. In almost all cases, the lower energy dipole corresponds to the azomethine ylide. This is a subtle effect that is not immediately obvious on inspection of the dipoles but for which MNDO calculations serve well to predict dipole stability. The calculations also reveal a smaller energy difference (6.81 kcal) between the two dipoles for the *N*-carbomethoxy case (i.e., **32**) relative to the *N*-acetyl (**16**) or *N*-benzoyl (**28**) systems. This would help account for why a nearly equimolar mixture of both cycloadducts is formed with the *N*-carbomethoxy-substituted diazo pyrrolidine **32**.

Comparison of the calculated heats of formation of the two dipoles (Table I) shows that the only exception to the "stability rule" comes with the diazo pyrrolidone system (X = O). In this case, the MNDO calculations reveal a 7.93-kcal energy difference, with the carbonyl ylide possessing the more negative heat of formation. This would suggest that the rhodium-catalyzed reaction of diazo pyrrolidione **52** should give predominantly the unrearranged cycloadduct. Indeed, this was borne out experimentally.



Exposure of **52** to Rh_2OAc_4 in benzene with DMAD afforded a mixture of two products. The minor component (36%) corresponds to the 1:1 cycloadduct **53** derived from a carbonyl ylide intermediate. Once the initial 1:1 cycloadduct is formed, it undergoes further dipolar cycloaddition across the carbonyl group to produce the 2:1 cycloadduct **54** as the second product isolated (47%). It is particularly noteworthy that no sign of a cycloadduct derived from an azomethine ylide was evident in the crude reaction mixture. When dimethyl fumarate was used as the trapping agent, a mixture of the exo/endo isomers of a carbonyl ylide cycloadduct was obtained (i.e., **55** and **56**).[47] Again, no rearranged adduct could be detected by NMR spectroscopy. Thus, a very good agreement between calculated values and experimental observations is observed here. These experimental results clearly indicate that diazo pyrrolidone **52** possesses a high barrier toward rearrangement, and this is certainly consistent with the calculated heats of formation.

One final point has to do with the rhodium-catalyzed reaction of *N*-carbomethoxy-2-(2-diazoacetyl)indole (**57**). In this case, the initially formed carbonyl ylide cannot undergo rearrangement since there is no hydrogen available at the α-position of the dipole. We found that treatment of **57** with Rh_2OAc_4 afforded the novel dimer **58**. Surprisingly, no bimolecular dipolar cycloadduct could



be detected, even in the presence of an excess of DMAD.[48] A speculative but reasonable mechanism for the formation of **58** is outlined below. The initially generated carbonyl ylide intermediate **59** adds across the carbonyl π-bond of another molecule of α-diazo ketone.[49] The resulting dimer **60** undergoes a subsequent rhodium-catalyzed cyclization, producing **61** which upon ring fragmentation and recombination with methoxide ion gives rise to the dimethoxy ketal **58**.

In conclusion, the high efficiency of the dipole cascade, in conjunction with the intriguing chemistry of the resulting cycloadducts, presents numerous synthetic possibilities. We are continuing to pursue further extensions of the dipole interconversion process and will report additional findings at a later date.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate–hexane mixture as the eluent unless specified otherwise.

Preparation of *N*-Acetyl-2-(diazoacetyl)-L-pyrrolidine (16). A 1.6-g sample of *N*-acetyl-L-proline[23] was suspended in 250 mL of ether, and 0.85 mL of methyl chloroformate was added. The mixture was allowed to stir for 30 min at 25 °C, and then 0.7 mL of triethylamine was added followed by another 0.7 mL after 30 min. The mixture was stirred for an additional 20 min and filtered from the white solid which had formed. The filtrate was allowed to react with 20 mmol of diazomethane in ether

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(42) Kormornicki, A.; Goddard, J. D.; Schaefer, H. F. *J. Am. Chem. Soc.* **1980**, *102*, 1763.
(43) McDouall, J. J. W.; Robb, M. A.; Niazi, U.; Bernardi, F.; Schlegel, H. B. *J. Am. Chem. Soc.* **1987**, *109*, 4642.
(44) We gratefully acknowledge Professor Kosta Steliou of the University of Montreal for a copy of the VMS Still-Steliou Model 2.94 program.
(45) We assume that the relative energy differences of the two dipoles will parallel the rate in which the carbonyl ylide dipole rearranges to the thermodynamically more stable azomethine ylide.
(46) Another possibility is that dipole **40** reacts faster than **39** and pulls the equilibrium toward the azomethine ylide.
(47) The relative stereochemistry at position 9a of cycloadducts **53–56** is still uncertain.
(48) The slow addition of **57** to an excess of DMAD and Rh_2OAc_4 in $CHCl_3$ did not afford any characterizable products other than a small amount of dimer **58**. We had previously noted that highly stabilized push–pull carbonyl ylides are reluctant to undergo dipolar cycloaddition with DMAD, and this may account for the absence of a bimolecular adduct with **57**; see: Padwa, A.; Zhi, L. *J. Am. Chem. Soc.* **1990**, *112*, 2037.
(49) Davies, J. S. *J. Chem. Soc., Perkin Trans. 2* **1978**, 1157.

at 0 °C for 12 h. Removal of the solvent followed by silica gel chromatography of the residue gave 1.3 g (75%) of a yellow solid whose structure was assigned as 1-acetyl-2-(diazoacetyl)-L-pyrrolidine (**16**): mp 82–83 °C; IR)KBr) 2115, 1645, 1430, 1375, 1335, and 1165 cm^{-1}. The high-field NMR spectrum showed that compound **16** exists as a 3:1 mixture of two nitrogen rotamers: NMR (300 MHz, $CDCl_3$) major (75%) δ 1.88–2.20 (m, 4 H), 2.11 (s, 3 H), 3.45–3.70 (m, 2 H), 4.48 (br, 1 H), and 5.60 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 23.9, 28.5, 47.4, 52.7, 62.3, 168.8, and 193.3; NMR (300 MHz, $CDCl_3$) minor (25%) δ 1.88–2.20 (m, 3 H), 2.01 (s, 3 H), 2.23–2.38 (m, 1 H), 3.45–3.70 (m, 2 H), 4.36 (br d, 1 H, J = 7.0 Hz), and 5.64 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 22.0, 31.2, 45.8, 52.7, 64.5, 169.0, and 193.6. Anal. Calcd for $C_8H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 53.13; H, 6.14; N, 23.14.

Cycloaddition Reaction of *N*-Acetyl-2-(diazoacetyl)-L-pyrrolidine (16) in the Presence of Dimethyl Acetylenedicarboxylate. A benzene solution containing 500 mg of **16** and 1.2 equiv of DMAD was allowed to react with a catalytic amount of rhodium acetate dimer. The resulting yellow solution was stirred at room temperature for 2 h until no further nitrogen was evolved. The solvent was removed under reduced pressure, and the residue was subjected to silica gel column using an ethyl acetate–hexane mixture as the eluent to give two fractions. The major product (87%) was identified as 3a,4-dicarbomethoxy-5-methyl-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[3,2-*d*]pyrrolizin-1-one (**18**) on the basis of an X-ray crystal structure analysis as well as its spectral properties: mp 119–120 °C; IR (KBr) 1765, 1748, 1695, 1590, 1445, 1205, 1170, and 1050 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.64–1.76 (m, 1 H), 1.91–2.04 (m, 2 H), 2.30 (s, 3 H), 2.30–2.35 (m, 1 H), 3.27 (ddd, 1 H, J = 11.0, 7.9, and 5.5 Hz), 3.45 (dt, 1 H, J = 11.0 and 6.8 Hz), 3.71 (s, 3 H), 3.80 (s, 3 H), 4.14 (d, 1 H, J = 17.0 Hz), and 4.34 (d, 1 H, J = 17.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 25.0, 27.1, 46.5, 50.8, 52.5, 68.4, 78.7, 93.8, 104.7, 164.7, 164.8, 169.8, and 210.5. Anal. Calcd for $C_{14}H_{17}NO_6$: C, 56.93; H, 5.81; N, 4.75. Found: C, 56.74; H, 5.67; N, 4.48.

Colorless crystals of **18** were grown from an ethyl acetate–hexane mixture. A suitable crystal approximately 0.43 × 0.40 × 0.32 mm was mounted on a glass fiber with glue. Unit-cell parameters were determined on a Syntex P2 automated diffractometer using Mo Kα radiation. Twenty-four reflections were machine centered and used in the least-squares refinement of the lattice parameters and orientation matrix. The unit-cell parameters obtained were a = 7.8351 (0.0017) Å, b = 8.1300 (0.0019) Å, c = 23.4004 (0.0037) Å, α = 89.983 (0.016)°, β = 89.939 (0.015)°, γ = 68.994 (0.017)°, V = 1391.52 (0.50) Å^3, d_{calcd} = 1.41 g cm^{-3}, $F(000)$ = 623.92, Z = 4, and space group $P2_1/C$. Intensity data were collected by using the 2θ scan technique with a scan rate of 4.88–29.30. A scan width of 1.0° was sufficient to collect all of the peak intensities. Check reflections, monitored after each set of 60 scans, showed no significant change during the course of data collection. Lorentz and polarization corrections were made in the usual way. No absorption correction was applied. Of the total of 2042 reflections collected with 3.0° < 2θ < 45.0°, 1585 were found to be unique and have $I > 3\sigma(I)$. The structure was solved by direct methods with the SHELXTL. Following anisotropic refinement of the skeleton atoms, all other hydrogen atoms were fixed into position. The final discrepancy index and weighted discrepancy index were R = 0.0479 and R_w = 0.0479, respectively. The final positional and thermal parameters are given in the supplementary material.

The minor product (10%) isolated from the reaction was assigned as 6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-methyl-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**17**): IR (neat) 1735, 1440, 1390, 1320, 1275, and 1255 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.65–1.84 (m, 2 H), 1.70 (s, 3 H), 1.86–1.98 (m, 1 H), 2.14–2.26 (m, 1 H), 2.90–3.04 (m, 2 H), 3.79 (s, 3 H), 3.84 (s, 3 H), 4.09 (td, 1 H, J = 8.1 and 1.5 Hz), and 4.95 (d, 1 H, J = 1.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 25.0, 30.2, 46.2, 52.1, 52.3, 67.6, 83.7, 99.6, 135.9, 147.9, 160.8, 163.9, and 198.6; HRMS for $C_{14}H_{17}NO_6$, calcd 295.1056, found 295.1061. Anal. Calcd for $C_{14}H_{17}NO_6$: C, 56.93; H, 5.81; N, 4.75. Found: C, 56.81; H, 5.73; N, 4.59.

When the cycloaddition reaction was followed by NMR spectroscopy, a transient intermediate was first formed which subsequently rearranged to **18** over a period of 60 min. This material was assigned as 10,11-dicarbomethoxy-1-methyl-2-aza-9-oxatricyclo[4.3.2.0^{2,6}]undec-10-en-7-one (**41a**): NMR (300 MHz, benzene-d_6) δ 1.20–1.45 (m, 2 H), 1.55–1.82 (m, 2 H), 1.51 (s, 3 H), 2.42–2.56 (m, 2 H), 3.21 (s, 3 H), 3.33 (s, 3 H), 4.24 (d, 1 H, J = 17.4 Hz), and 4.33 (d, 1 H, J = 17.4 Hz).

The reaction of a 100-mg sample of **16** was also carried out with 1.2 mol equiv of DMAD, a catalytic amount of rhodium acetate dimer, and 5 pellets of 4-Å molecular sieves. The yellow solution was stirred under a nitrogen atmosphere at 40 °C for 1 h until no more nitrogen gas evolved. The sieves and benzene were removed, and the residue was subjected to silica gel chromatography. The major product (86%) was identified as dimethyl 3-(1′-acetyl-2′-pyrrolidylcarbonyl)pyrazole-4,5-dicarboxylate (**43**): IR (neat) 1740, 1705, 1620, 1450, 1295, 1225, 1130, and 980 cm^{-1}; ^1H NMR (300 NMR (300 MHz, $CDCl_3$) δ 1.95–2.14 (m, 3 H), 2.23 (s, 3 H), 2.28–2.43 (m, 1 H), 3.56–3.80 (m, 2 H), 3.85 (s, 3 H), 3.87 (s, 3 H), and 5.80 (dd, 1 H, J = 9.0 and 2.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8, 23.4, 28.8, 47.9, 51.7, 52.0, 61.2, 117.2, 132.5, 144.4, 157.1, 163.1, 169.2, and 190.1. Anal. Calcd for $C_{14}H_{17}N_3O_6$: C, 51.99; H, 5.30; N, 13.01. Found: C, 51.81; H, 5.13; N, 12.86.

Acid-Catalyzed Reorganization of 3a,4-Dicarbomethoxy-5-methyl-1,3,8,9-tetrahydro-3a*H*,7*H*-furo[3,2-*d*]pyrrolizin-1-one (18). A 100-mg sample of **18** was treated with a trace of *p*-toluenesulfonic acid to give 6,7-dicarbomethoxy-2,3-dihydro-5-methyl-1*H*-pyrrolizine (**20**) in quantitative yield: NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3 H), 2.50 (quint, 2 H, J = 7.5 Hz), 3.04 (t, 2 H, J = 7.5 Hz), 3.78 (s, 3 H), 3.83 (s, 3 H), and 3.87 (t, 2 H, J = 7.75 Hz). The structure of this material was confirmed by an X-ray crystal structure analysis. Colorless crystals were grown from an ethyl acetate solution. A suitable crystal of **20** approximately 0.49 × 0.43 × 0.35 mm was mounted on a glass fiber with glue. Unit-cell parameters were determined on a Syntex P_2 automated diffractometer using Mo Kα radiation. Twenty-four reflections were machine centered and used in the least-squares refinement of the lattice parameters and orientation matrix. The unit-cell parameters obtained were a = 7.6106 (0.0023) Å, b = 8.4172 (0.0032) Å, c = 10.5378 (0.0046) Å, α = 112.271 (0.029)°, β = 101.307 (0.030)°, γ = 91.913 (0.028)°, V = 608.24 (0.39) Å^3, d_{calcd} = 1.30 g cm^{-3}, $F(000)$ = 253.96, Z = 2, and space group $P\bar{1}$. Intensity data were collected by using the 2θ scan technique with a scan rate of 29.30. A scan width of 1.0° was sufficient to collect all of the peak intensities. Check reflections, monitored after each set of 60 scans, showed no significant change during the course of data collection. Lorentz and polarization corrections were made in the usual way. No absorption correction was applied. Of the total of 1710 reflections collected with 3.0 < 2θ < 45.0°, 1605 were found to be unique and have $I > 3\sigma(I)$. The structure was solved by direct methods with SHELXTL. Following anisotropic refinement of the skeleton atoms, all other hydrogen atoms were fixed into position. The final discrepancy index and weighted discrepancy index were R = 0.0777 and R_w = 0.0870, respectively. The final positional and thermal parameters are given in the supplementary material.

Cycloaddition of *N*-Acetyl-2-(diazoacetyl)-L-pyrrolidine (16) in the Presence of Methyl Acrylate. Treatment of a 200-mg sample of **16** with methyl acrylate in the presence of rhodium acetate dimer at 50 °C for 2 h afforded 2-carbomethoxy-7a-(hydroxyacetyl)-3-methyl-5,6,7,7a-tetrahydro-1*H*-pyrrolizine (**21**) (82%): IR (neat) 3460 (br), 1730, 1695, 1615, 1255, 1135, and 1060 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.60–1.74 (m, 2 H), 1.80–1.93 (m, 1 H), 2.22 (t, 3 H, J = 1.5 Hz), 2.47–2.59 (m, 1 H), 2.75 (dq, 1 H, J = 16.1 and 1.5 Hz), 2.97 (dq, 1 H, J = 16.1 and 1.5 Hz), 3.17 (ddd, 1 H, J = 11.0, 7.8, and 4.3 Hz), 3.29 (dt, 1 H, J = 11.0 and 7.6 Hz), 3.67 (s, 3 H), 3.81 (s, 1 H), 4.39 (d, 1 H, J = 19.9 Hz), and 4.53 (d, 1 H, J = 19.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.1, 24.0, 33.2, 38.1, 47.2, 49.9, 64.9, 77.9, 100.0, 161.0, 165.6, and 211.6; HRMS for $C_{12}H_{17}NO_4$, calcd 239.1158, found 239.1157.

Cycloaddition of *N*-Acetyl-2-(diazoacetyl)-L-pyrrolidine (16) in the Presence of Methyl Propiolate. The rhodium-catalyzed reaction of 200 mg of **16** was carried out in the presence of methyl propiolate at 50 °C for 1 h. The major product (90%) isolated was assigned as 4-carbomethoxy-5-methyl-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[2,3-*g*]pyrrolizin-1-one (**22**) on the basis of its spectral properties: IR (neat) 1765, 1695, 1595, 1440, 1390, and 1140 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.68 (dt, 1 H, J = 12.3 and 8.0 Hz), 1.85–1.95 (m, 1 H), 2.12–2.34 (m, 2 H), 2.26 (s, 3 H), 3.21 (dt, 1 H, J = 11.4 and 7.0 Hz), 3.41 (ddd, 1 H, J = 11.4, 6.7, and 5.5 Hz), 3.75 (s, 3 H), 4.04 (s, 2 H), and 5.60 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.0, 24.6, 27.0, 45.9, 50.2, 67.4, 75.4, 86.9, 103.3, 164.5, 165.4, and 211.4; NMR (300 MHz, benzene-d_6) δ 0.92–1.18 (m, 2 H), 1.58–1.91 (m, 2 H), 1.89 (s, 3 H), 2.46–2.65 (m, 2 H), 3.48 (s, 3 H), 3.59 (d, 1 H, J = 17.5 Hz), 3.69 (d, 1 H, J = 17.5 Hz) and 5.42 (s, 1 H). Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.73; H, 6.38; N, 5.91. Found: C, 60.51; H, 6.09; N, 5.74.

Compound **22** produced a 3:1 mixture of products when subjected to silica gel chromatography. The minor fraction (25%) was identified as 6-carbomethoxy-2,3-dihydro-5-methyl-1*H*-pyrrolizine (**26**): mp 87–88 °C; IR (KBr) 1700, 1530, 1445, 1370, 1220, 1155, and 1070 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3 H), 2.47 (quint, 2 H, J = 7.2 Hz), 2.80 (t, 2 H, J = 7.2 Hz), 3.77 (s, 3 H), 3.82 (t, 2 H, J = 7.2 Hz), and 6.15 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.2, 23.4, 26.8, 43.7, 49.9, 99.7, 113.9, 130.0, 133.9, and 165.6. Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.01; H, 7.32; N, 7.82. Found: C, 66.85; H, 7.23; N, 7.64.

The major fraction (70%) was identified as 6-carbomethoxy-2,3-dihydro-7-(hydroxyacetyl)-5-methyl-1*H*-pyrrolizine (**27**): mp 136–137 °C; IR (KBr) 1700, 1660, 1535, 1380, 1160, 1100, and 1015 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.38 (s. 3 H), 2.55 (quint, 2 H, J = 7.4 Hz), 3.09

(t, 2 H, J = 7.4 Hz), 3.72 (br, 1 H), 3.84 (s, 3 H), 3.91 (t, 2 H, J = 7.4 Hz), and 4.60 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.3, 25.4, 26.1, 44.5, 50.6, 66.7, 112.1, 113.2, 131.4, 143.8, 164.8, and 194.0; HRMS for $C_{12}H_{15}NO_4$; calcd 237.1001, found 237.0998.

When the cycloaddition reaction was followed by NMR spectroscopy, a transient intermediate was initially formed which subsequently rearranged to **22** over a period of 90 min. This material was assigned as 10-carbomethoxy-1-methyl-2-aza-9-oxatricyclo[4.3.2.0^{2,6}]undec-10-en-7-one (**41d**): NMR (300 MHz, benzene-d_6) δ 1.10–1.40 (m, 2 H), 1.40–1.65 (m, 2 H), 1.67 (s, 3 H), 2.19–2.32 (m, 1 H), 2.48–2.58 (m, 1 H), 3.30 (s, 3 H), 4.04 (d, 1 H, J = 19.0 Hz), 4.23 (d, 1 H, J = 19.0 Hz), and 6.27 (s, 1 H). The peak at 7.09 ppm (d, J = 2.5 Hz) in the NMR spectrum of the crude reaction mixture was assigned as the vinyl hydrogen of 6-carbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-methyl-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**23**) (5%).

Preparation of *N*-Benzoyl-2-(diazoacetyl)-L-pyrrolidine (28). *N*-Benzoylproline[50] was treated with methyl chloroformate–triethylamine and diazomethane according to the standard procedure to give *N*-benzoyl-2-(diazoacetyl)-L-pyrrolidine (**28**) in 73% yield as yellow solid: mp 100–101 °C; IR (KBr) 2105, 1620, 1415, 1375, 1325, and 1150 cm^{-1}. The high-field NMR spectrum showed that compound **28** consisted of a 6:1 mixture of nitrogen rotamers: NMR (300 MHz, $CDCl_3$) major δ 1.76–2.28 (m, 4 H), 3.46–3.70 (m, 2 H), 4.70 (br t, 1 H, J = 6.0 Hz), 5.61 (br s, 1 H), and 7.30–7.62 (m, 5 H); NMR minor δ 1.76–2.28 (m, 4 H), 3.68–3.90 (m, 2 H), 4.28 (br d, 1 H, J = 6.0 Hz) 5.28 (br s, 1 H), and 7.30–7.62 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) major δ 24.7, 28.3, 49.8, 53.1, 62.8, 126.6, 127.6, 129.7, 135.4, 169.3, and 192.9; ^{13}C NMR minor δ 21.9, 31.1, 46.2, 53.0, 65.4, 126.0, 127.8, 129.3, 136.1, 169.3, and 192.9. Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27. Found: C, 64.23; H, 5.41; N, 17.21.

Rhodium-Catalyzed Cycloaddition of *N*-Benzoyl-2-(diazoacetyl)-L-pyrrolidine (28) in the Presence of Dimethyl Acetylenedicarboxylate. Treatment of a 200-mg sample of **28** with DMAD under standard reaction conditions afforded 3a,4-dicarbomethoxy-5-phenyl-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[2,3-*g*]pyrrolizin-1-one (**29**) (95%): IR (neat) 1770, 1755, 1705, 1370, 1210, and 1140 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.75–1.93 (m, 2 H), 2.20–2.12 (m, 1 H), 2.15–2.28 (m, 1 H), 2.98–3.16 (m, 2 H), 3.60 (s, 3 H), 3.86 (s, 3 H), 4.26 (d, 1 H, J = 17.0 Hz), 4.41 (d, 1 H, J = 17.0 Hz), and 7.38–7.55 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.6, 27.1, 48.6, 50.4, 52.2, 68.2, 78.0, 94.5, 104.2, 127.3, 129.1, 129.8, 129.9, 163.4, 165.0, 169.3, and 210.2; HRMS for $C_{19}H_{19}NO_6$, calcd 357.1212, found 357.1223.

When the cycloaddition reaction was followed by NMR spectroscopy, a transient intermediate was first formed which subsequently rearranged to **29**. This material was assigned as 10,11-dicarbomethoxy-1-phenyl-2-aza-9-oxatricyclo[4.3.2.0^{2,6}]undec-10-en-7-one (**41b**): NMR (300 MHz, $CDCl_3$) δ 1.70–1.90 (m, 2 H), 2.11 (dt, 1 H, J = 12.0 and 7.5 Hz), 2.35 (t, 1 H, J = 7.2 Hz), 2.45–2.64 (m, 2 H), 3.72 (s, 3 H), 3.83 (s, 3 H), 4.61 (d, 1 H, J = 17.5 Hz), 4.68 (d, 1 H, J = 17.5 Hz), and 7.35–7.64 (m, 5 H).

Preparation and Rhodium(II) Acetate Reaction of 1-(5-Hexenoyl)-2-(2-diazoacetyl)pyrrolidine (30). A solution containing 0.72 g of 5-hexenoyl chloride[51] in 5 mL of acetone was added dropwise (with simultaneous addition of 2.0 N sodium hydroxide to maintain the solution at pH 8–9) to a stirred solution (pH 9–10) containing 0.76 g of L-proline in 4 mL of a 2.0 N sodium hydroxide solution, 5 mL of 1.0 N sodium bicarbonate, and 7 mL of acetone at 0 °C. The mixture was stirred for 2 h at 0 °C and at room temperature for an additional h. The solution was concentrated under reduced pressure and acidified to pH 2–3 using concentrated hydrochloric acid. The aqueous solution was extracted with dichloromethane, and the combined extracts were washed with saline and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give 1.16 g (84%) of *N*-(5-hexenoyl)-L-proline as a viscous oil which was used in the next step without further purification: IR (neat) 3000, 1735, 1645, 1445, and 1200 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.00 (m, 8 H), 2.45 (t, 2 H, J = 6.5 Hz), 3.55 (m, 2 H), 4.60 (m, 1 H), 5.0 (m, 2 H), 5.70 (m, 1 H), and 11.20 (br s, 1 H).

A solution containing 0.70 g of the above compound and 0.40 g of methyl chloroformate in 10 mL of dichloromethane at 0 °C was treated with 0.47 mL of triethylamine. The solution was stirred at 0 °C for 1 h and room temperature for 2 h. The solvent was removed under reduced pressure, and the residue was taken up in 10 mL of anhydrous ether. The solution was filtered, and the filtrate was added to a 10 mmol solution of diazomethane in ether. The solution was stirred for 4 h at room temperature, and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography using ethyl acetate as the eluent to give 0.35 g (43%) of 1-(5-hexenoyl)-2-(2-diazoacetyl)pyrrolidine (**30**) as a yellow oil: IR (neat) 2120, 1715, 1655, 1440, 1365, and 1170 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.05 (m, 8 H), 2.30 (t, 2 H, J = 6.5 Hz), 3.72 (m, 2 H), 4.60 (m, 1 H), 5.05 (m, 2 H), 5.55 (s, 1 H), and 5.78 (m, 1 H); HRMS for $C_{12}H_{17}N_3O_2$, calcd 235.13211, found 235.1333.

A solution containing 87 mg of **30** in 3 mL of benzene was treated with a catalytic amount of rhodium(II) acetate, and the solution was stirred at room temperature until nitrogen evolution had ceased (ca. 30 min). The mixture was filtered through a pad of Celite, and the solvent was removed under reduced pressure. The resulting residue contained a complex mixture of compounds which resisted all attempts at separation and purification. Examination of this material by NMR spectroscopy indicated that the olefinic hydrogens were still present. A cycloadduct could be obtained from (diazoacetyl)pyrrolidine **30** when this material was allowed to react with DMAD as the dipolarophile. A solution containing 115 mg of **30** and 870 mg of dimethyl acetylenedicarboxylate in 3 mL of benzene was treated with a catalytic amount of rhodium(II) acetate. The solution was stirred at room temperature until nitrogen evolution had ceased (ca. 15 min). The mixture was filtered through a pad of Celite, and the solvent was removed under reduced pressure. The resulting residue was subjected to flash silica gel chromatography using a 50% ethyl acetate–hexane mixture as eluent to give 112 mg (67%) of 3a,4-dicarbomethoxy-5-(4-hexenyl)-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[2,3-*g*]pyrrolizin-1-one (**31**) as a clear oil: IR (neat) 1760, 1750, 1700, 1615, 1600, 1385, and 1235 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.62 (m, 4 H), 1.95 (m, 2 H), 2.11 (q, 2 H, J = 6.9 Hz), 2.36 (m, 2 H), 3.21 (m, 2 H), 3.68 (s, 3 H), 3.77 (s, 3 H), 4.11 (d, 1 H, J = 16.9 Hz), 4.30 (d, 1 H, J = 16.9 Hz), 4.75 (d, 1 H, J = 8.8 Hz), 5.05 (d, 1 H, J = 15.2 Hz), and 5.78 (m, 1 H); HRMS for M – $C_2H_2O_2$, calcd 291.1584, found 291.1591.

Preparation of *N*-Acetyl-2-(diazoacetyl)-DL-indoline (35). This compound was prepared from 1.7 g of indoline-2-carboxylic acid via the standard three-step sequence in 55% overall yield and was isolated as a yellow solid: mp 100–101 °C; IR (KBr) 2110, 1670, 1645, 1630, 1483, 1385, 1150, and 758 cm^{-1}. The high-field NMR spectrum showed that **35** exists as a 3:2 mixture of two nitrogen rotamers: ^{1}H NMR (300 MHz, $CDCl_3$) major (60%) δ 2.19 (s, 3 H), 3.17 (d, 1 H, J = 16.8 Hz), 3.62 (dd, 1 H, J = 16.8 and 10.2 Hz), 4.81 (d, 1 H, J = 10.2 Hz), 5.35 (s, 3 H), 7.00–7.25 (m, 3 H), and 8.19 (d, 1 H, J = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 30.5, 52.9, 64.3, 116.6, 123.8, 124.1, 127.4, 128.4, 141.7, 168.3, and 193.1; NMR (300 MHz, $CDCl_3$) minor (40%) δ 2.47 (s, 3 H), 3.10–3.45 (m, 2 H), 5.14 (br s, 1 H), 5.51 (s, 1 H), and 7.00–7.25 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.8, 30.5, 64.3, 65.9, 113.9, 123.4, 125.2, 127.0, 131.2, 138.2, 168.3, and 193.1. Anal. Calcd for $C_{12}H_{11}N_3O_2$: C, 62.87; H, 4.83; N, 18.33. Found: C, 62.94; H, 4.89; N, 18.38.

Cycloaddition Reaction of *N*-Acetyl-2-(diazoacetyl)-DL-indoline (35) with Dimethyl Acetylenedicarboxylate. The rhodium(II) acetate catalyzed reaction of 230 mg of diazo keto amide **35** in the presence of 150 mg of DMAD was carried out at room temperature for 30 min in 5 mL of chloroform to give 3a,4-dicarbomethoxy-1,2-dihydro-5-methyl-3a*H*,11*H*-furo[3′,2′-*b*]pyrrolo[1,2-*a*]indo-1-one (**36**) (91%): mp 147–148 °C; IR (KBr) 1770, 1750, 1700, 1605, 1220, and 735 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.55 (s, 3 H), 3.07 (d, 1 H, J = 16.0 Hz), 3.25 (d, 1 H, J = 16.0 Hz), 3.75 (s, 3 H), 3.82 (s, 3 H), 4.17 (d, 1 H, J = 16.8 Hz), 4.38 (d, 1 H, J = 16.8 Hz), and 7.06–7.28 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 31.3, 50.7, 52.3, 67.2, 78.1, 93.0, 106.6, 115.4, 124.5, 124.9, 127.2, 131.5, 141.1, 161.3, 164.2, 168.8, and 206.2. Anal. Calcd for $C_{18}H_{17}NO_6$: C, 62.97; H, 4.99; N, 4.08. Found: C, 62.85; H, 4.96; N, 4.07.

When the cycloaddition reaction was followed by NMR spectroscopy, a transient intermediate was first formed which subsequently rearranged to **36** over a period of several hours. The transient intermediate was assigned as 10,11-dicarbomethoxy-1-methyl-2-aza-9-oxa-3-benzotricyclo[4.3.2.0^{2,6}]undec-10-en-7-one (**41c**) on the basis of its NMR spectrum: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3 H), 3.39 (d, 1 H, J = 16.3 Hz), 3.45 (d, 1 H, J = 16.3 Hz), 3.81 (s, 3 H), 3.84 (s, 3 H), 4.42 (d, 1 H, J = 17.2 Hz), 4.57 (d, 1 H, J = 17.2 Hz), and 6.92–7.22 (m, 4 H).

Cycloaddition Reaction of *N*-Acetyl-2-(diazoacetyl)-DL-indoline (35) with *N*-Phenylmaleimide. Treatment of 170 mg of diazo keto amide **35** in 3 mL of chloroform with a catalytic amount of rhodium acetate dimer in the presence of 170 mg of *N*-phenylmaleimide gave 1-methyl-4-phenyl-4,11-diaza-12-oxa-9-benzotetracyclo[5.4.3.0^{2,6}.0^{7,11}]tetradecane-3,5,14-trione (**38**) (81%): mp 178–179 °C; IR (neat) 1750, 1715, 1385, 1200, 755, and 740 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 3.34 (d, 1 H, J = 16.7 Hz), 3.36 (d, 1 H, J = 7.4 Hz), 3.66 (d, 1 H, J = 7.4 Hz), 3.88 (d, 1 H, J = 16.7 Hz), 4.29 (d, 1 H, J = 17.4 Hz), 4.48 (d, 1 H, J = 17.4 Hz), 6.39 (d, 1 H, J = 7.6 Hz), 6.41 (d, 1 H, J = 5.2

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Hz), and 6.89–7.31 (m, 7 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.2, 28.9, 47.9, 55.8, 67.4, 80.2, 96.4, 111.0, 121.7, 125.8, 127.7, 127.8, 128.3, 130.5, 133.6, 144.9, 172.4, and 201.5. Anal. Calcd for $C_{22}H_{18}N_2O_4$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.41; H, 4.86; N, 7.40.

Preparation of *N*-Carbomethoxy-2-(diazoacetyl)-L-pyrrolidine (32). A 4.73-g sample of *N*-carbomethoxyproline[52] was converted to *N*-carbomethoxy-2-(diazoacetyl)-L-pyrrolidine (**32**) in 80% yield by a method similar to that outlined above for compound **16**: IR (neat) 2110, 1710, 1645, 1455, 1385, and 1125 cm^{-1}. The high-field NMR spectrum showed that compound **32** consisted of a 4:3 mixture of two nitrogen rotamers: NMR (300 MHz, $CDCl_3$) major (57%) δ 1.82–2.20 (m, 4 H), 3.41–3.62 (m, 2 H), 3.74 (s, 3 H), 4.32 (m, 1 H), and 5.53 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.7, 29.0, 46.2, 52.0, 52.7, 63.3, 155.1, and 194.0; NMR (300 MHz, $CDCl_3$) minor (43%) δ 1.82–2.32 (m, 4 H), 3.41–3.62 (m, 2 H), 3.71 (s, 3 H), 4.28 (m, 1 H), and 5.46 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 30.6, 46.7, 52.0, 52.7, 63.3, 154.7, and 194.7. Anal. Calcd for $C_8H_{11}N_3O_3$: C, 48.73; H, 5.62; N, 21.31. Found: C, 48.59; H, 5.58; N, 21.09.

Cycloaddition of *N*-Carbomethoxy-2-(diazoacetyl)-L-pyrrolidine (32) in the Presence of Dimethyl Acetylenedicarboxylate. The rhodium-catalyzed reaction of a sample of 200 mg of **32** in the presence of 1.2 equiv of DMAD was carried out at 60 °C for 2 h and afforded a 1:1 mixture of two products in 95% yield. Chromatography of the crude residue gave 3a,4-dicarboxmethoxy-5-methoxy-1,2,8,9-tetrahydro-3a*H*,7*H*-furo[3,2-*d*]pyrrolizin-1-one (**33**): IR (neat) 1750, 1705, 1595, 1455, 1390, 1270, and 1125 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.68–1.77 (m, 1 H), 1.92–2.06 (m, 2 H), 2.21–2.23 (m, 1 H), 3.21 (dt, 1 H, J = 11.5 and 6.5 Hz), 3.47 (dt, 1 H, J = 11.5 and 6.3 Hz), 3.70 (s, 3 H), 3.80 (s, 3 H), 4.13 (s, 3 H), 4.19 (d, 1 H, J = 17.0 Hz), and 4.35 (d, 1 H, J = 17.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.7, 27.7, 47.4, 50.4, 52.1, 60.8, 67.9, 74.0, 92.9, 163.1, 169.3, 169.4, and 210.1. Anal. Calcd for $C_{14}H_{17}NO_7$: C, 54.02; H, 5.50; N, 4.50. Found: C, 54.18; H, 5.39; N, 4.33.

The other product observed in the crude NMR spectrum was assigned as 6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-methoxy-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**34**): NMR (300 MHz, $CDCl_3$) δ 1.70–2.00 (m, 3 H), 2.12–2.25 (m, 1 H), 2.87–2.96 (m, 1 H), 3.15–3.25 (m, 1 H), 3.57 (s, 3 H), 3.81 (s, 3 H), 3.87 (s, 3 H), 4.22 (m, 1 H), and 5.00 (d, 1 H, J = 1.0 Hz). All attempts to obtain a pure sample of this material failed.

Preparation and Rhodium-Catalyzed Reaction of *N*-Benzoyl-2-(diazoacetyl)-2-methylpyrrolidine (44). Diazo compound **44** was obtained from *N*-benzoyl-2-methylproline by the standard method in 47% overall yield: IR (neat) 2105, 1745, 1635, 1415, 1365, 745, and 710 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.71 (s, 3 H), 1.82–2.05 (m, 3 H), 2.12–2.30 (m, 1 H), 3.48–3.66 (m, 2 H), 5.58 (s, 1 H), and 7.35–7.58 (m, 5 H). A sample containing 500 mg of **44** and 1.2 equiv of dimethyl acetylenedicarboxylate in benzene was allowed to react in the normal fashion. The major product obtained from the reaction mixture (70%) was assigned as 6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-9a-methyl-5-phenyl-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**46**): mp 87–88 °C; IR (neat) 1730, 1320, 1240, 1130, and 770 cm^{-1}; UV (methanol) 312 nm (ϵ 870) and 362 (800); NMR (300 MHz, $CDCl_3$) δ 1.55 (s, 3 H), 1.75–1.98 (m, 3 H), 2.07–2.18 (m, 1 H), 3.03–3.18 (m, 2 H), 3.70 (s, 3 H), 3.85 (s, 3 H), 5.16 (s, 1 H), 7.36–7.45 (m, 3 H), and 7.62–7.68 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 30.3, 36.6, 47.9, 52.1, 52.2, 73.2, 84.3, 102.7, 127.2, 127.7, 129.0, 136.8, 138.6, 149.3, 160.8, 163.7, and 202.2. Anal. Calcd for $C_{20}H_{21}NO_6$: C, 64.68; H, 5.70; N, 3.77. Found: C, 64.48; H, 5.77; N, 3.72.

Cycloaddition Reactions of *N*-Benzoyl-2-benzyl-2-(diazoacetyl)-pyrrolidine (47). A 5.4-g sample of *N*-benzoyl-2-benzylproline[53] was converted into *N*-benzoyl-2-benzyl-2-(diazoacetyl)pyrrolidine (**47**) by the standard method in 40% overall yield: IR (neat) 2105, 1735, 1625, 1445, 1410, 1355, 730, and 705 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.30–1.42 (m, 1 H), 1.68–1.85 (m, 1 H), 2.06–2.32 (m, 2 H), 2.86 (ddd, 1 H, J = 10.2, 9.7, and 6.7 Hz), 3.10 (d, 1 H, J = 13.5 Hz), 3.38 (ddd, 1 H, J = 10.2, 7.0, and 3.4 Hz), 4.02 (d, 1 H, J = 13.5 Hz), 5.55 (s, 1 H), and 7.21–7.56 (m, 10 H). Treatment of 200 mg of **47** with a catalytic amount of rhodium acetate in the presence of 1.2 mol equiv of dimethyl acetylenedicarboxylate afforded 9a-benzyl-6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-phenyl-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**48**) in 85% yield as a yellow oil: IR (neat) 1730, 1320, 1260, 765, and 705 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.38–1.54 (m, 1 H), 1.58–1.74 (m, 1 H), 2.02–2.19 (m, 2 H), 2.88 (dd, 1 H, J = 10.6 and 6.1 Hz), 2.94 (d, 1 H, J = 13.0 Hz), 3.14 (dt, 1 H, J = 10.6 and 6.9 Hz), 3.29 (d, 1 H, J = 13.0 Hz), 3.65 (s, 3 H), 3.84 (s, 3 H), 5.12 (s, 1 H), 7.24 (s, 5 H), 7.38–7.46 (m, 3 H), and 7.57–7.66 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 34.6, 47.0, 48.2, 52.1, 52.2, 77.6, 84.3, 102.8, 126.1, 127.2, 127.4, 127.5, 128.9, 130.6, 135.9, 136.8, 138.1, 149.7, 160.8, 163.7, and 210.2; HRMS for $C_{26}H_{25}NO_6$, calcd 447.1682, found 447.1667.

The reaction of **47** with rhodium acetate in the presence of 1.2 equiv of methyl propiolate gave 9a-benzyl-6-carbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-phenyl-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**49**) in 80% yield: IR (neat) 1725, 1305, 1265, 1220, 740, and 700 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.24–1.53 (m, 2 H), 1.97–2.10 (m, 2 H), 2.71 (ddd, 1 H, J = 10.5, 8.1, and 6.0 Hz), 2.86 (ddd, 1 H, J = 10.5, 6.1, and 4.7 Hz), 3.29 (d, 1 H, J = 12.9 Hz), 2.95 (d, 1 H, J = 12.9 Hz), 3.61 (s, 3 H), 5.01 (d, 1 H, J = 2.8 Hz), 7.26 (s, 5 H), 7.35 (d, 1 H, J = 2.8 Hz), 7.36–7.47 (m, 3 H), and 7.58–7.65 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 33.6, 47.8, 48.5, 51.5, 77.5, 84.2, 99.9, 126.0, 127.1, 127.2, 127.4, 128.3, 130.7, 135.9, 138.3, 141.2, 143.9, 162.7, and 202.9; HRMS for $C_{17}H_{16}NO_4$ ($M^+ - C_7H_7$), calcd 298.1079, found 298.1083.

Treatment of **47** with a catalytic amount of rhodium acetate in the presence of 1.2 equiv of *N*-phenylmaleimide gave 9a-benzyl-5,8-epoxy-1,2,3,6,7,8,9,9a-octahydro-5-phenyl-6,7-[*exo*-(phenylimino)dicarbonyl]-5*H*-pyrrolo[1,2-*a*]azepin-9-one (**50**) in 70% yield: IR (neat) 1720, 1500, 1450, 1385, 1185, 740, and 705 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.23–1.45 (m, 2 H), 1.85 (dt, 1 H, J = 13.0 and 6.5 Hz), 2.15 (dt, 1 H, J = 13.0 and 7.3 Hz), 2.87 (d, 1 H, J = 13.1 Hz), 3.05 (t, 2 H, J = 6.2 Hz), 3.12 (d, 1 H, J = 13.1 Hz), 3.40 (d, 1 H, J = 7.5 Hz), 3.86 (d, 1 H, J = 7.5 Hz), 5.21 (s, 1 H), and 6.95–7.60 (m, 15 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.3, 31.5, 45.6, 48.5, 49.2, 49.4, 72.9, 81.6, 99.6, 125.2, 125.4, 126.0, 127.2, 127.3, 127.9, 128.0, 128.5, 130.2, 130.9, 135.1, 137.2, 172.0, 173.6, and 206.6. Anal. Calcd for $C_{30}H_{26}N_2O_4$: C, 75.28; H, 5.48; N, 5.86. Found: C, 75.13; H, 5.41; N, 5.75.

When the rhodium-catalyzed reaction of **47** was carried out in the presence of an unreactive dipolarophile, the major product (70%) isolated was *N*-benzoyl-2-benzyl-2-(hydroxyacetyl)pyrrolidine (**51**): IR (neat) 1720, 1455, 1410, 1280, 1125, 1070, and 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.63–1.90 (m, 3 H), 1.90 (br s, 1 H), 2.18–2.29 (m, 1 H), 2.75 (d, 1 H, J = 13.5 Hz), 2.97 (dt, 1 H, J = 10.3 and 6.5 Hz), 3.08 (dt, 1 H, J = 10.3 and 6.8 Hz), 3.38 (d, 1 H, J = 13.5 Hz), 4.96 (d, 1 H, J = 17.7 Hz), 5.32 (d, 1 H, J = 17.7 Hz), 7.12–7.63 (m, 8 H), and 8.09 (d, 2 H, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.6, 35.3, 42.0, 46.3, 67.3, 73.0, 126.4, 127.7, 128.0, 129.1, 129.2, 129.4, 132.5, 135.9, 165.5, and 108.6; MS m/e 324 (M^+ + H), 264, 202, and 160 (base). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.27; H, 6.55; N, 4.33. Found: C, 74.08; H, 6.42; N, 4.07.

Preparation and Cycloaddition Reactions of (*S*)-1-Acetyl-5-(2′-diazoacetyl)-2-pyrrolidone (52). The N-acylation of (*S*)-2-pyrrolidone-5-carboxylic acid was carried out according to the method of Imaki and co-workers,[53] producing (*S*)-1-acetyl-2-pyrrolidone-5-carboxylic acid in 95% yield as a clear oil: NMR (300 MHz, $CDCl_3$) δ 2.14–2.24 (m, 1 H), 2.39 (ddd, 1 H, J = 19.7, 13.0, and 9.6 Hz), 2.54 (s, 3 H), 2.62 (ddd, 1 H, J = 17.8, 9.1, and 3.3 Hz), 2.77 (ddd, 1 H, J = 17.8, 13.0, and 7.0 Hz), 4.78 (dd, 1 H, J = 9.6 and 2.7 Hz), and 8.75 (br s, 1 H). This material was converted to the corresponding diazo compound (**52**) in the usual manner in 60% overall yield: mp 101–102 °C; IR (KBr) 2140, 1740, 1710, 1622, and 1400 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.07 (dddd, 1 H, J = 19.8, 8.4, 7.0, and 2.9 Hz), 2.26 (ddd, 1 H, J = 19.8, 13.1, and 9.4 Hz), 2.53 (s, 3 H), 2.55 (ddd, 1 H, J = 17.7, 9.4, and 2.9 Hz), 2.79 (ddd, 1 H, J = 17.7, 13.1, and 7.0 Hz), 4.69 (d, 1 H, J = 8.4 Hz), and 5.48 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 24.0, 31.3, 53.5, 60.6, 170.3, 174.2, and 190.9. Anal. Calcd for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.53. Found: C, 49.33; H, 4.68; N, 21.60.

A chloroform solution containing 400 mg of **52** and 1.2 equiv of DMAD was allowed to stir in the presence of a catalytic amount of rhodium acetate dimer. The reaction was complete in 10 min. Removal of the solvent under reduced pressure followed by crystallization of the crude residue gave 238 mg (47%) of a white solid whose structure was assigned as spiro[6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-methyl-5*H*-pyrrolo[1,2-*a*]azepin-3-one-9,7′-5′-methyl-1′,2′,3′,6′,7′,8′,9′,9a′-octahydro-6′-oxa-5*H*-pyrrolo[1,2-*a*]azepine-3′,9′-dione] (**54**), on the basis of its spectral properties: mp 240–241 °C; IR (neat) 1750, 1740, 1720, 1703, 1690, 1395, and 1296 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.93 (s, 3 H), 2.17 (s, 3 H), 1.96–2.56 (m, 8 H), 3.74 (s, 3 H), 3.84 (s, 3 H), 4.30 (t, 1 H, J = 8.5 Hz), 4.43 (t, 1 H, J = 7.1 Hz), 4.61 (s, 1 H), and 4.95 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.5, 18.7, 18.8, 19.5, 30.0, 31.3, 51.9, 52.3, 59.2, 63.1, 78.3, 80.1, 84.7, 98.0, 112.0, 135.7, 144.3, 161.5, 162.9, 172.0, 173.1, and 204.1. Anal. Calcd for $C_{22}H_{24}N_2O_{10}$: C, 55.46, H, 5.08, N, 5.88. Found: C, 55.39, H, 5.11, N, 5.84.

Chromatography of the residual oil afforded 6,7-dicarbomethoxy-5,8-epoxy-1,2,3,8,9,9a-hexahydro-5-methyl-5*H*-pyrrolo[1,2-*a*]azepine-3,9-dione (**53**) (36%): IR (neat) 1740, 1730, 1330, 1285, and 1210 cm^{-1};

(52) Crooks, P. A.; Rosenberg, H. E. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2721.

(53) Imaki, K.; Niwa, H.; Sakuyama, S.; Okada, T.; Toda, M.; Hayashi, M. *Chem. Pharm. Bull.* **1981**, *29*, 2699.

NMR (300 MHz, $CDCl_3$) δ 2.12 (s, 3 H), 2.15-2.52 (m, 4 H), 3.82 (s, 3 H), 3.86 (s, 3 H), 4.81 (t, 1 H, J = 8.7 Hz), and 5.14 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.2, 20.2, 29.7, 52.2, 52.4, 65.0, 84.1, 97.8, 133.3, 148.6, 160.4, 161.9, 172.1, and 196.6; HRMS for $C_{14}H_{15}NO_7$, calcd 309.0848, found 309.0844.

Another fraction that was also isolated from the column was assigned as 1-acetyl-5-(hydroxyacetyl)-2-pyrrolidone (8%): mp 122-123 °C; IR (neat) 3450, 1745, 1692, 1290, and 1242 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.16 (dddd, 1 H, J = 13.4, 9.5, 4.0, and 3.2 Hz), 2.29 (dddd, 1 H, J = 13.4, 9.6, 9.4, and 9.3 Hz), 2.52 (s, 3 H), 2.60 (ddd, 1 H, J = 17.9, 9.3, and 4.0 Hz), 2.73 (ddd, 1 H, J = 17.9, 9.4, and 9.5 Hz), 3.18 (br s, 1 H), 4.44 (d, 1 H, J = 19.2 Hz), 4.51 (d, 1 H, J = 19.2 Hz), and 4.92 (dd, 1 H, J = 9.6 and 3.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) 19.3, 23.8, 31.4, 58.6, 66.0, 170.1, 173.8, and 206.6. Anal. Calcd for $C_8H_{11}NO_4$: C, 51.87, H, 5.99, N, 7.57. Found: C, 51.74, H, 5.81, N, 7.48.

Treatment of **52** with 1.2 equiv of dimethyl fumarate according to the standard procedure afforded a mixture of two cycloadducts. Chromatography of the crude reaction mixture using a 10-40% ethyl acetate-hexane mixture as the eluent afforded 6(*endo*),7(*exo*)-dicarbomethoxy-5-methyl-1,2,3,6,7,8,9,9a-octahydro-5*H*-pyrrolo[1,2-*a*]azepine-3,9-dione (**55**) as a colorless oil (30% yield): IR (neat) 1730, 1680, 1380, 1268, and 1177 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 1.81 (s, 3 H), 2.04-2.59 (m, 4 H), 3.65 (s, 3 H), 3.80 (s, 3 H), 3.98 (d, 1 H, J = 3.5 Hz), 4.07 (dd, 1 H, J = 9.4 and 3.5 Hz), 4.35 (dd, 1 H, J = 9.0 and 6.3 Hz), and 4.86 (d, 1 H, J = 9.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 18.9, 30.4, 49.9, 52.0, 52.2, 53.2, 58.3, 82.0, 96.3, 170.2, 170.4, 173.4, and 205.4; HRMS for $C_{14}H_{17}NO_7$, calcd 311.1005, found 311.1006.

The second cycloadduct isolated from the column was assigned as 6(*exo*),7(*endo*)-dicarbomethoxy-5-methyl-1,2,3,6,7,8,9,9a-octahydro-5*H*-pyrrolo[1,2-*a*]azepine-3,9-dione (**56**) (12%): IR (neat) 1738, 1696, 1380, 1260, and 1174 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3 H), 2.22-2.56 (m, 4 H), 3.34 (d, 1 H, J = 6.7 Hz), 3.46 (dd, 1 H, J = 6.7 and 2.3 Hz), 3.74 (s, 3 H), 3.77 (s, 3 H), 4.41 (dd, 1 H, J = 8.9 and 7.9 Hz), and 4.89 (d, 1 H, J = 2.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 20.5, 30.8, 49.3, 52.3, 52.5, 56.2, 59.7, 82.0, 95.6, 168.6, 170.3, 172.6, and 204.8. Anal. Calcd for $C_{14}H_{17}NO_7$: C, 54.01, H, 5.51, N, 4.50. Found: C, 53.85, H, 5.36, N, 4.24.

Preparation and Rhodium-Catalyzed Reaction of *N*-Carbomethoxy-2-(2-diazoacetyl)indole (57). To a suspension containing 1.6 g of sodium hydride (50% mineral oil) in 40 mL of tetrahydrofuran was slowly added 3.2 g of indole-2-carboxylic acid. The resulting suspension was allowed to stir at room temperature for 3 h until no more hydrogen had evolved and the reaction mixture had become clear. To this mixture was added 3.2 mL of methyl chloroformate. The resulting solution was washed with a 1.0 N hydrochloric acid solution, dried over sodium sulfate, and concentrated under reduced pressure. The residue was treated with a diazomethane ether solution and after workup gave (diazoacetyl)indole **57** as a yellow solid in 65% yield: mp 101-102 °C; IR (KBr) 2100, 1750, 1610, 1545, 1455, 1400, and 1320 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.96 (s, 3 H), 5.74 (s, 1 H), 6.89 (s, 1 H), 7.22 (t, 1 H, J = 7.8 Hz), 7.37 (t, 1 H, J = 7.8 Hz), 7.52 (d, 1 H, J = 7.8 Hz), and 8.00 (d, 1 H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.7, 55.9, 113.1, 114.2, 121.6, 123.0, 126.4, 126.9, 135.7, 137.1, 150.8, and 179.0. Anal. Calcd for $C_{12}H_9N_3O_3$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.27; H, 3.76; N, 17.22.

Treatment of a 500-mg sample of diazo keto amide **57** in 5 mL of chloroform with a catalytic amount of rhodium acetate dimer in either the presence (1.2 equiv) or absence of dimethyl acetylenedicarboxylate gave rise to 1,2-dihydro-4',4'-dimethoxy-1,4-dioxo-2,1'-bi(4*H*-[1,3]oxazino[3,4-*a*]indole) (**58**) (56%): mp 145-146 °C; IR (neat) 1740, 1690, 1535, 1450, 910, and 750 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 3 H), 4.02 (s, 3 H), 5.46 (s, 1 H), 6.83 (s, 1 H), 6.95 (s, 1 H), 7.11-7.26 (m, 3 H), 7.39 (s, 1 H), 7.40-7.51 (m, 2 H), 7.69 (d, 1 H, J = 8.1 Hz), 7.92 (d, 1 H, J = 8.5 Hz), and 7.97 (d, 1 H, J = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.6, 53.1, 82.5, 93.5, 109.8, 109.9, 110.7, 113.0, 115.0, 119.8, 121.7, 122.7, 122.9, 123.9, 126.3, 127.0, 128.9, 130.1, 132.2, 134.3, 135.0, 146.7, 151.9, and 180.2. Anal. Calcd for $C_{24}H_{18}N_2O_6$: C, 66.97; H, 4.22; N, 6.50. Found: C, 67.00; H, 4.25; N, 6.48.

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Supplementary Material Available: Final positional and thermal parameters (Tables I-X) for the X-ray crystal structures of compounds **18** and **20** (6 pages). Ordering information is given on any current masthead page.

Toward a Molecular-Size "Tinkertoy" Construction Set. Preparation of Terminally Functionalized [*n*]Staffanes from [1.1.1]Propellane

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Abstract: A facile but low-yield synthesis of [*n*]staffanes (the oligomers of [1.1.1]propellane **1**, n = 1-5) functionalized on one or both ends is described, and their properties are summarized. The substituents are $-COOCH_3$, $-n-C_4H_9$, $-C_6H_5$, -Br, -I, and $-SCOCH_3$, and their conversion to others, such as -COOH, $-COCH_3$ and -SH, is demonstrated. It is proposed that these rod-shaped molecules will be useful in the development of a molecular-size civil engineering construction set analogous to children's toy construction sets.

In preliminary communications[2,3] we identified the development of a molecular-size civil engineering construction set, analogous to the children's "Tinkertoy"[4] play set, as a long-term goal worthy of pursuit. The Tinkertoy set consists of straight rods and spoollike connectors (Figure 1). Its molecular analogue would offer a

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(2) (a) Kaszynski, P.; Michl, J. *J. Am. Chem. Soc.* **1988**, *110*, 5225. (b) Kaszynski, P.; Friedli, A. C.; Michl, J. The Third Chemical Congress of North America, Toronto, Canada, June 4-10, 1988, Book of Abstracts, ORGN 218, American Chemical Society: Washington, D.C., 1988. (c) The carbon atoms in each bicyclo[1.1.1]pentane cage of an [*n*]staffane are numbered in the usual way and primes are used to distinguish the individual cages.[3] For instance, the methylene positions in the terminal cages of [3]staffane are 2, 4, 5, 2'', 4'', and 5''; those on the internal cage are 2', 4', and 5'. A general position characterized by k primes is indicated by $2^{(k)}$, $4^{(k)}$, etc., following the usage common in mathematics, where a first derivative is labeled f', a second derivative f'', and an kth derivative, $f^{(k)}$.

(3) Michl, J.; Kaszynski, P.; Friedli, A. C.; Murthy, G. S.; Yang, H.-C.; Robinson, R. E.; McMurdie, N. D.; Kim, T. In *Strain and Its Implications in Organic Chemistry*; de Meijere, A., Blechert, S., Eds.; NATO ASI Series, Vol. 273; Kluwer: Dordrecht, 1989; p 463.

(4) Tinkertoy is a trademark of Playskool, Inc., Pawtucket, RI 02862, and designates a children's toy construction set consisting of straight wooden sticks and other simple elements insertable into spool-like connectors. The assembly of triangular trinuclear metal cluster units into polyhedra and stacks has been referred to as "Tinker-Toy" construction: Underwood, D. J.; Hoffmann, R.; Tatsumi, K.; Nakamura, A.; Yamamoto, Y. *J. Am. Chem. Soc.* **1985**, *107*, 5968. We use the expression in a related but different sense.

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