Rhodium(II)-Catalyzed Equilibration of Push-Pull Carbonyl and Ammonium Ylides. A Computationally Based Understanding of the Reaction Pathway

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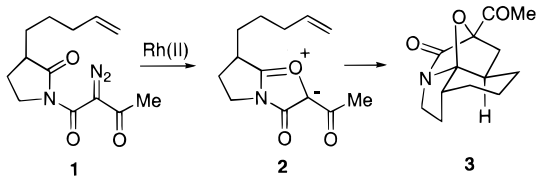
Received March 28, 2000

Abstract: α-Diazo esters containing an amido group in the γ-position have been found to undergo a rhodium(II)-catalyzed transformation, producing five-membered ammonium or carbonyl ylides depending on the reaction conditions used. In the absence of an external dipolarophile, ammonium ylides are the exclusive products formed. In most cases these ylides cannot be isolated as they readily undergo sigmatropic rearrangement or fragmentation reactions. In the presence of typical dipolarophiles such as DMAD or *N*-phenylmaleimide, cycloaddition products derived from cyclic carbonyl ylide dipoles are formed as the major products. The rhodium carbenoid intermediate generated in these reactions can either attack the lone pair of electrons on the amide nitrogen (ammonium ylide formation) or the lone pair of electrons on the carbonyl oxygen (carbonyl ylide formation). The experimental observations reflect a catalyst-promoted system of equilibria with a clear-cut thermodynamic bias. To examine the underlying mechanism in detail, density functional theory (DFT) calculations were performed on all plausible intermediates, including the full dirhodium tetracarboxylate functionality. A semiquantitative energy manifold is developed that rationalizes the empirical observations and provides a detailed picture of the role of the dirhodium(II) catalyst.

Introduction

The vast importance of nitrogen heterocycles has stimulated the development of new methodology for their construction.[1−8] Among the most useful methods recently developed are iminium ion initiated,[9−11] free radical induced,[12] and tandem Heck cyclizations.[13] Recent publications from our laboratories have introduced a new general strategy for ring-fused polyheterocycles in which metallo carbenoids derived from diazo carbonyl precursors play a central role.[14] A wide variety of aza-polycycles can be accessed with high efficiency from the rhodium(II)-catalyzed reaction of α-diazo keto amides.[15] For example, isomünchnone **2** was easily prepared by treating diazoimide **1** with $Rh_2(OAc)_4$ in CH_2Cl_2 at 80 °C.[16] The mesoionic oxazolium



1 2 3

ylide **2** is the cyclic equivalent of a carbonyl ylide dipole and

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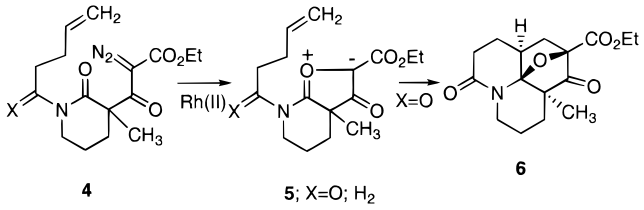
10.1021/ja001088j CCC: $19.00
Published on Web 08/10/2000

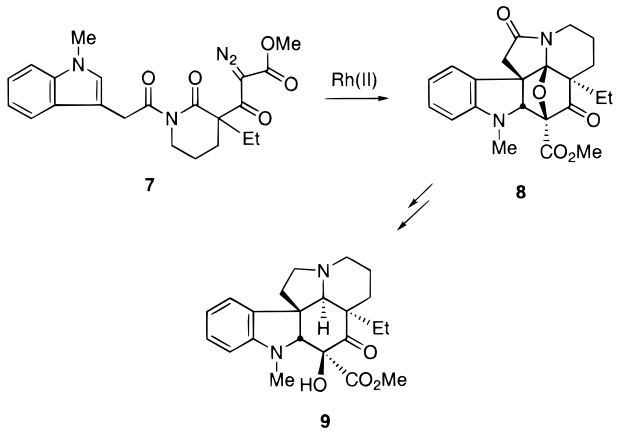
readily undergoes intramolecular 1,3-dipolar cycloaddition to give novel cycloadducts of type **3**. This reaction is an integral part of our program aimed at developing new cascade reactions and achieving the total synthesis of various alkaloids.[17]

Our more recent achievements in this area involve the use of diazo ketoamides such as **4**.[18] Attack of the amido oxygen at the rhodium carbenoid produces a *push*−*pull* carbonyl ylide dipole (i.e., **5**) that is isomeric with the isomünchnone class of mesoionic betaines. Intramolecular cycloaddition occurs to



4 **5**; X=O; H_2 **6**

furnish heterocycles such as **6** in good yield, provided that the tether engaged in ring formation carries a carbonyl group (i.e., X = O). In a recent report,[19] we demonstrated that these transient push−pull carbonyl ylides can be used as an entry to 2,3,3-trisubstituted indole alkaloids. The successful preparation of dihydrovindorosine **9** from diazo amide **7** (via cycloadduct **8**) establishes the merit of the method for constructing the pentacyclic skeleton of the aspidosperma alkaloid ring system.[20] This sequence is particularly attractive for further study as four of the stereocenters were formed in one step with a high degree of stereocontrol.



7 **8** **9**

To further implement and develop this strategy, we have undertaken a study of the effect of different amido groups on the efficiency of dipole formation. The model system we selected allowed for good versatility in assembling the different amido substitution patterns and involved using cyclopropanated diazo ketoamides of type **10**. The results obtained show that the Rh(II)-catalyzed behavior of these compounds can lead to both push−pull carbonyl ylides and/or ammonium ylides.[21] A related process was encountered with the diazoacetylurea system. In this case, the product distribution was found to depend on the conformational flexibility of the carbenoid and the reaction conditions employed.[22]

Parallel to the application of dirhodium(II) tetracarboxylates to synthetic targets, we have initiated a computational examination of the structure and mechanism of intermediates along pathways facilitated by the bimetallic catalyst. While many previous theoretical studies have examined aspects of the electronic structure of $Rh_2(O_2CR)_4$ agents and their cations,[23,24] very few have investigated key reaction intermediates. Notable exceptions are the extended Huckel evaluation of a parent rhodium carbenoid, methylene(dirhodium tetraacetamide), which predicted a very low Rh−C barrier to rotation for the carbenoid ligand,[25a] a ZINDO estimate of charges and frontier orbital energies for $RhL_4Rh{=}CH_2$,[25b] and an MM2/ZINDO study of rhodium-mediated intramolecular C−H insertion.[26] More recently, we reported a density functional theory (DFT) examination of the solvated dirhodium cage structure and the corresponding methylene carbenoids. A novel proposal for Rh−C bonding emerged along with a proposition for the role played by the distal rhodium atom in the Rh−Rh−C train in the metal carbenoids.[27]

In the present contribution, we offer an intimate description of the action of the dirhodium catalyst on diazo ketone substrates followed by regeneration of the promoter concomitant with product formation. During the course of the overall transformation, a set of rhodium-containing organic complexes leads stepwise to the formation and release of carbonyl and ammonium ylides responsible for the ultimate catalyst-free steps in synthesis (Scheme 1). Each of the proposed structures has been treated to full DFT optimization to confirm existence as an energy minimum and to permit assessment of changes in bonding and relative energy. In sum, the mechanistic portrait links the experimental observations to unobserved intermediates and places the entire pathway on a semiquantitative footing.

Results and Discussion

Rhodium(II)-Catalyzed Decomposition of Cyclopropyl Diazo Ketoamides. Our earlier studies dealing with the Rh(II)-catalyzed reaction of cyclopropyl-substituted diazo carbonyls involved interaction of the metallo carbene with alkyl and aryl ketones.[28] We felt that it would prove enlightening to extend these earlier studies to include the related amido functionality

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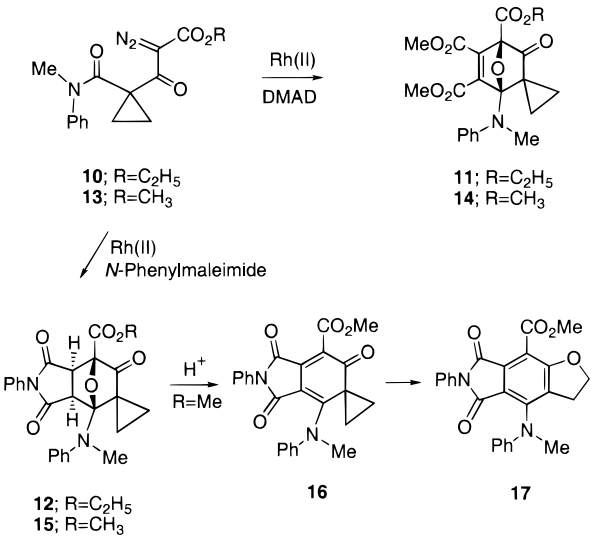
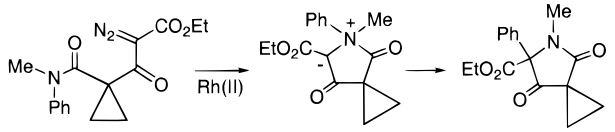
in order to more clearly define the role of the interacting carbonyl group for dipole formation. In this spirit, we prepared several amido-substituted diazo esters and examined their Rh(II)-catalyzed behavior. Treatment of α-diazo ketoamide **10** with $Rh_2(OAc)_4$ at 80 °C in benzene with dimethyl acetylenedicarboxylate afforded the expected dipolar cycloadduct **11** in 87% yield. The cycloaddition also proceeded readily with *N*-



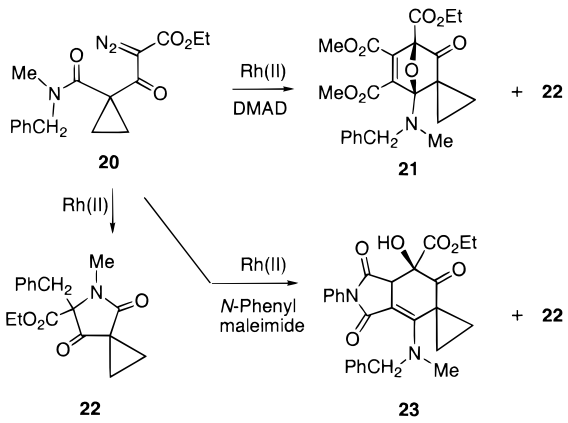
10; R=C_2H_5
13; R=CH_3
11; R=C_2H_5
14; R=CH_3
12; R=C_2H_5
15; R=CH_3
16
17

phenylmaleimide, giving rise to cycloadduct **12** in 42% isolated yield as a single diastereomer. We assume that **12** corresponds to the *exo* isomer, as previously established in the cycloaddition chemistry of related diazo ketones.[28,29] The transition state leading to the *endo* isomer suffers from unfavorable steric factors, and consequently, the *exo* orientation is favored. An analogous set of products [i.e. **14** (87%) and **15** (80%)] was obtained with the carbomethoxy-substituted amido diazoester **13**. While attempting to purify cycloadduct **15** on a silica gel column, we noted that it was partially converted to dihydrobenzofuran **17**. Assuming that the conversion of **15** to **17** was the consequence of an acid-catalyzed reaction, we treated a sample of **15** with $BF_3{\cdot}OEt_2$ and isolated **17** in 85% yield. The formation of **17** proceeds by an initial oxy-bridge ring opening followed by a subsequent dehydration to give **16** as a nonisolable intermediate which reacts further by an acid-catalyzed cyclopropyl ketone rearrangement.[30−32] The facility of the process is undoubtedly related to the aromaticity gained in the final step. When the reaction of **10** was carried out in the absence of an external dipolarophile, the rearranged lactam **19** was isolated in 62% yield. The formation of **19** can be attributed to the generation of ammonium ylide **18** followed by a 1,2-phenyl shift.



10 **18** **19**

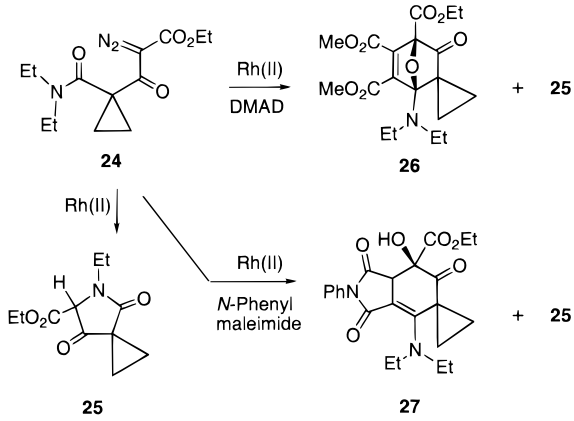
Extension of the carbenoid cyclization−cycloaddition sequence with the related *N*-benzyl-*N*-methyl amide **20** was also carried out. In this case, the reaction of **20** in the presence of DMAD afforded cycloadduct **21** (57%) together with the rearranged lactam **22** (42%). When *N*-phenylmaleimide was used as the trapping agent, a mixture of **22** (40%) and the ring-opened product **23** (60%), derived from the expected dipolar cycloadduct, was obtained. In the absence of an external



20 **21** **22** **23**

dipolarophile, lactam **22** was isolated in 70% yield. Once again, the formation of **22** can be attributed to the initial generation of an ammonium ylide followed by a 1,2-benzyl shift. Related 1,2-shifts of cyclic ammonium ylides derived from the reaction of tertiary amines with α-diazo carbonyl compounds have been described by West and co-workers,[33] thereby providing good analogy for the suggested mechanism. It would appear as though the highly electrophilic carbenoid center can either attack the lone pair of electrons on the amide nitrogen (ammonium ylide formation) or the lone pair of electrons on the carbonyl oxygen (carbonyl ylide formation).

Products derived from both a carbonyl ylide and an ammonium ylide were also encountered with diazo ketoamide **24**. When the Rh(II)-catalyzed reaction of **24** was carried out in the presence of DMAD, a mixture of lactam **25** (8%) and cycloadduct **26** (92%) was obtained. With *N*-phenylmaleimide,



24 **26** **25** **27**

a similar mixture of **25** (34%) and the ring-opened cycloadduct **27** (66%) was realized. In the absence of any trapping agent, **24** furnished lactam **25** in 93% yield. The formation of this product can readily be rationalized in terms of α,α-fragmentation of ethylene from a transient ammonium ylide. Indeed, ammonium ylides possessing an α-hydrogen are known to undergo an elimination reaction to provide the corresponding amine and alkene, thereby providing good precedent for the formation of **25**.[34−38]

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Rhodium(II)-Catalyzed Transformation of Diazo Acetyl Ureas. To compare the reactivity of the above push−pull carbonyl ylide dipoles (i.e., **5**) with the analogous isomünchnone systems (i.e., **2**), we next investigated the rhodium(II)-catalyzed decomposition of diazoacetylurea **28**. The reaction of **28** in the presence of rhodium(II) acetate led to both the isomünchnone dipole **31** and ammonium ylide **29**.[22,39] In contrast to ammonium ylides of type **18**, ylide **29** could be isolated as a crystalline solid (68%). The structure of this persistently stable five-membered *N*-acyl ammonium ylide was confirmed by X-ray analysis.[22,40] When the reaction was carried out in the presence of DMAD, a mixture of ylide **29** (28%), furan **33** (25%), and pyridine **30** (18%) was obtained. The formation of furan **33** strongly supports the involvement of a mesoionic betaine intermediate in this process.[15,41] 1,3-Dipolar cycloaddition of DMAD with isomünchnone dipole **31** followed by extrusion of methyl isocyanate from the primary cycloadduct **32** nicely accommodates the isolation of furan **33**. This reaction sequence is well established in isomünchnone cycloaddition chemistry.[41] Using *N*-methylmaleimide as the trapping reagent, a similar mixture of ylide **29** (46%) and pyrrolopyridine **35** (24%) derived from the expected dipolar isomünchnone cycloadduct was obtained.

Pyridine **30**, on the other hand, arises from the thermal addition of DMAD to ylide **29**. This reaction pathway was confirmed by an independent experiment in which **29** was treated with DMAD in refluxing toluene. The mechanism probably involves Michael addition of the anionic carbon center in ylide **29** to the triple bond in DMAD. The resulting zwitterion **36** then rearranges to pyridine **30** according to the pathway shown below (61%). The structure of pyridine **30** was established unambiguously by X-ray crystallographic analysis.[40] With *N*-methylmaleimide, no thermal cycloaddition reaction with ammonium ylide **29** was observed.

Common Features of Reactivity. The common feature in the rhodium(II)-catalyzed decompositions of the diazo amides reported above (i.e., **10 13**, **20**, **24**, and **28**) is the simultaneous formation of both ammonium ylides (**38**) and/or isomeric carbonyl ylides (**39**). Although these ylides cannot be isolated directly in most cases, the identification of trapped and/or rearranged products leaves little doubt that these species are formed as intermediates. It appears that in the decomposition of diazo amides **37** the presumed rhodium carbenoid intermediate (vide infra) can either attack the lone pair of electrons on the amide nitrogen (ammonium ylide formation, **37** → **38**), or the lone pair of electrons on the carbonyl oxygen (carbonyl ylide formation, **37** → **39**). The product distribution in all cases is markedly dependent on the reaction partner. Whereas in the absence of trapping agents ammonium ylides (or products derived thereof) are formed exclusively, the presence of dipolarophiles (i.e., DMAD or *N*-phenylmaleimide) can shift the product ratio toward carbonyl ylides which then undergo a 1,3-dipolar cycloaddition reaction.

The product distribution (ammonium ylide vs carbonyl ylide formation) is also a direct consequence of the conformational flexibility of the diazo amides. The rhodium(II)-catalyzed decomposition of a diazo imide of type **40**, where the urea moiety is constrained in a six-membered ring system, has been examined.[42] Here, the carbenoid intermediate can only attack the lone pair of electrons on the carbonyl oxygen, thereby generating exclusively the carbonyl ylide isomer. The "amino-iso-münchnone" of type **41** could be isolated as a stable crystalline solid and was found to undergo 1,3-dipolar cycloaddition reactions with various dipolarophiles.[42]

Since the decomposition of diazoacetylurea **28** gives rise to an isolable and stable ammonium ylide (i.e., **29**), we decided

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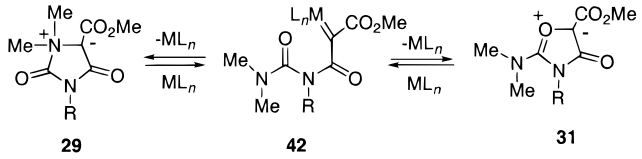
to investigate this particular system in more detail. We were particularly intrigued by the possible interconversion of the isomeric ammonium and carbonyl ylides. Toward this end, the reaction of ammonium ylide **29** with DMAD was carried out *in the presence of $Rh_2(OAc)_4$*. Whereas treatment of **29** with DMAD in the absence of a transition metal catalyst provided pyridine **30** in good yield (see above), the presence of $Rh_2(OAc)_4$ led also to the formation of furan **33**, along with the thermal adduct **30**. Although furan **33** is only formed in small amounts (ca. 10%) in this process, these results suggest that in the presence of a transition metal catalyst ($ML_n = Rh_2(OAc)_4$), the formation of ammonium ylide **29** is reversible, and that **29** rearranges to carbonyl ylide **31** via the carbenoid intermediate **42**. Because of the 1,3-dipolar character of ylide **31**, this mesoionic species can undergo cycloaddition with DMAD, ultimately giving furan **33**. In the first step of such a rearrangement process, the transition metal catalyst (ML_n) would have to add to the ammonium ylide (i.e., **29**) to form a metal-stabilized ylide intermediate which then ring opens to give carbenoid **42**. Attack of the electrophilic carbenoid on the lone pair of electrons on oxygen followed by dissociation then leads to the free carbonyl ylide (i.e., **31**) and the metal catalyst (ML_n). Reversibility of ylide formation from metallo carbenoids has been suggested to occur in the literature.[43,44] The relatively low yield of **33** can be rationalized by the competitive thermal process **29** → **30** and the significantly greater thermodynamic stability of the ammonium ylide vs the carbonyl ylide (vide infra). Therefore, the transition metal-mediated equilibrium between ylides **29** and **31** is expected to lie predominantly on the ammonium ylide side.

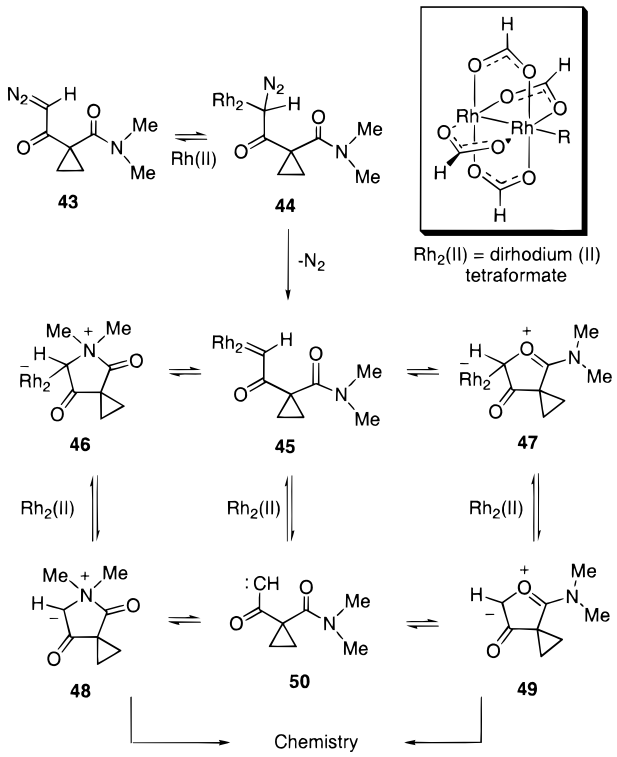


29 **42** **31**

A Plausible Mechanistic Scheme. An important element characterizing the work described above is the invisibility of the majority of intermediates that most certainly exist along the reaction pathways. In general, diazoketone and rhodium catalyst are mixed in the presence of an internal or external dipolarophile and the final dipolar cycloaddition adducts or the rearranged ammonium ylide are isolated. Only two examples of well-characterized intermediates have been observed: nitrogen ylide **29** and carbonyl ylides captured as isomünchnones[15] (e.g., **41**). A mechanistic map that considers plausible steps between starting materials and products is portrayed in Scheme 1.[45] Containing structural types proposed above and in numerous previous literature reports,[14] it rationalizes a number of key observations.

First, the scheme provides a role for the dirhodium tetracarboxylate catalyst and its release late in the pathway. Second, the early irreversible loss of N_2 commits the process to products, be they desired or undesired. That is, the pathway is overall exergonic. Third, the ambident properties of the amide group

Scheme 1. Reversible Dipole Formationin Rhodium(II)-Catalyzed Decomposition of α-Diazo Amides



43 **44** **46** **45** **47** **48** **50** **49**

in rhodium carbenoid **45** flanked by reversible equilibria permits both the interconversion of uncomplexed ylides **48** and **49** and their subsequent isolation or capture as cycloadducts. Finally, Scheme 1 allows for the possibility that the penultimate ylides interconvert through uncomplexed carbene intermediate **50**. An important aspect of the scheme we do not consider is the inhibition of dirhodium(II) catalyst with Lewis bases. Pirrung and Morehead have shown that both diazo ketone substrate and acetonitrile can divert the catalyst.[46]

Optimized Structures. Taking the collection of intermediates in Scheme 1 as a reasonable hypothesis for the chemistry of both diazo ketoamides and diazo acetylureas, we have performed density functional theory (DFT) calculations for each of the structures. Diazo amide **43** with methyl substituents on nitrogen and a monosubstituted diazo group was selected for the calculations as a minimal system exemplifying the cyclopropyl diazo ketoamides. Subsequent complexes **44**−**47** incorporating the full rhodium tetracarboxylate cage were treated as the tetraformate. This level of structural truncation was necessitated by the desire to optimize geometries of the entire organometallic complexes including the demanding dirhodium cage. To achieve this result, we combined a nonlocal DFT method with an effective core potential at rhodium atoms and the 3-21G basis set at other atoms for both geometry refinement and initial energy evaluation. The latter was supplemented by single-point 6-31G* basis set energies and natural population analysis[47] (see Experimental Section for details). As a preliminary, the structure of ammonium ylide **29** was optimized with the 6-31G* basis set and compared with its X-ray structure[22,40] (Figure 1). For 13 bond lengths, the average absolute difference is 0.013 Å. For 19 bond angles, the absolute average deviation is 0.84° with

(43) Doyle, M. P. *Comprehensive Organometallic Chemistry II*; Hegedus, L. Ed.; Pergamon Press: Oxford; Vol. 12, 1995; p 431. Doyle, M. P.; McKervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; John Wiley and Sons: New York, 1998.

(44) (a) Pirrung, M. C.; Brown, W. L.; Rege, S.; Laughton, P. *J. Am. Chem. Soc.* **1991**, *113*, 8561. (b) Pirrung, M. C.; Morehead, A. J., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 8991.

(45) The Scheme 1 mechanism for carbenoid generation is essentially a variation of the original Yates proposal for copper-catalyzed decomposition of diazoketones; see: Yates, P. *J. Am. Chem. Soc.* **1952**, *74*, 5376.

(46) Pirrung, M. C.; Morehead, A. J., Jr. *J. Am. Chem. Soc.* **1996**, *118*, 8162.

(47) Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. NBO Version 3.1. Reed, A. E.; Curtiss, L. A.; Weinhold, F. *Chem. Rev.* **1988**, *88*, 899.

Table 1. DFT Optimized Structures and NBO Analysis; Selected Bond Distances

	basis set energies, au[a]		bond lengths, Å		bond orders, bo[b]	
no.	3-21G	6-31G*	C−Rh	Rh−Rh	C−Rh	Rh−Rh
43	−622.626 761	−626.077 928				
44	−1594.382 723	−1601.884 398	1.980	2.457	0.37	0.52
45	−1485.467 143	−1492.364 749	1.960	2.473	0.79	0.44
46	−1485.541 203	−1492.418 214	2.181	2.478	0.36	0.51
47	−1485.530 215	−1492.414 485	2.148	2.479	0.40	0.47
48	−513.740 173	−516.563 206				
49	−513.726 078	−516.551 762				
50	−513.652 747	−516.492 469				
Rh_2(II)	−971.728 675	−975.804 103		2.379		0.81
N_2	−108.892 471	−109.520 571				

[a] Becke3LYP/LANL2DZ/3-21G//Becke3LYP/LANL2DZ/3-21G and Becke3LYP/LANL2DZ/6-31G*//Becke3LYP/LANL2DZ/3-21G with LANL2DZ on Rh; 1 au = 627.5 kcal/mol. [b] Natural Population Analysis Wiberg NBO bond orders; see ref 47.

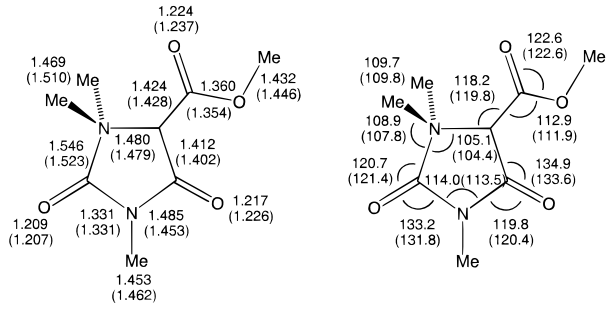
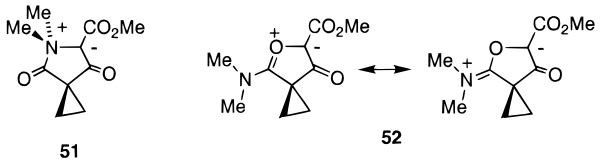


Figure 1. The Becke3LYP/6-31G* optimized geometry of *N*-acyl ammonium ylide **29** compared with the X-ray structure (refs 22 and 40); bond lengths (Å) to the left; selected bond angles (deg) to the right; X-ray values in parentheses.

the largest variation being 1.6°. Optimization with the 3-21G basis set yields a corresponding set of values that are about twice as large: 0.022 Å, 1.6°, and 3.4°, respectively.

A summary of the 6-31G* energies and selected bond lengths for the DFT/3-21G-refined structures in Scheme 1 is given in Table 1. The experimental work described above, in particular the Rh(II) tetraacetate catalyzed decomposition of diazo substrates in the absence of dipolarophile, strongly suggests that ammonium ylides are more stable than their carbonyl ylide isomers. In complete agreement, *N*-ylide **48** is found to be 7.2 kcal/mol lower in energy than *O*-ylide **49**. Given that the ester group in **51** and **52** was replaced with hydrogen in the latter



51 **52**

structures and in the corresponding Rh_2(II) complexes in Scheme 1 for the sake of computational economy, we checked to see if this substitution alters the energetic relationship.

It does not. *N*-Ylide **51** is 11.7 kcal/mol more stable than *O*-ylide **52** at the Becke3LYP/6-31G* level. The same obtains for urea intermediate *N*-**29** by comparison with *O*-**31**. The latter is calculated to be 12.6 kcal/mol higher in energy with the Becke3LYP/6-31+G* basis set. We surmise that the basis for the higher energy of the carbonyl ylide lies in the ability of the dimethylamino group to conjugate with $C{=}O^+$ in **52**. Although the resonance structure to the right delocalizes π-electrons by a means unavailable to **51**, the same structure separates the positive and negative charges over an additional two bonds. The latter would appear to be the dominating energetic effect.[48]

Numerous initial attempts were made to find local minima for singlet carbene **50** and the esterified analogue **53** (Me_2NCO-$C((CH_2)_2)$-CO-C:-CO_2Et, Figure 2). The structures have a great propensity for spontaneous cyclization to the corresponding ylides in the computer. Ultimately, we located conformations in which the dimethylamide moieties were unable to coordinate with the carbene carbon without passing over a moderate torsional barrier. The local minimum for **53** is depicted in Figure 2 along with the corresponding planar carbonyl ylide **52**. Truncated singlet carbene **50** is found to be 44.4 kcal/mol higher in energy than ammonium ylide **48** (Table 1). A similar energy differential was found for the esterified pair **51** and **53** (52.5 kcal/mol; 6-31G*), reinforcing the idea that ester removal does not alter the semiquantitative picture in the present series.

The optimized structure for diazo ketone **43** is unexceptional. Complexes **44** and **45**, however, are portrayed in Figure 3. Formation of the former, derived from combination of diazo ketone **43** and Rh_2(II), is symbolized in Figure 4. In the reaction of **43**, shortening of the N−N bond is accompanied by lengthening of both the C−N and Rh−Rh bonds as complexation takes place. The parenthesized NBO bond orders follow the same trend. Clearly the sp^2 diazo carbon has served as a nucleophile in its transformation to a sp^3 center in **44**. Loss of nitrogen to give rhodium carbenoid **45** is complemented by rehybridization of the former diazo carbon back to sp^2 (Figures 3 and 4). The overall geometry, e.g., Rh−C and Rh−Rh bond lengths and bond orders, is precisely what is to be expected for a RhRhC train in which a weak Rh−C single bond in **44** has been converted into a somewhat stronger single bond with dual character in **45**. That is, the carbenoid Rh−C connection is characterized by a nearly equal mix of C to Rh σ dative bonding and Rh to C π dative bonding.[27] The latter was foreshadowed by a number of previous investigations,[44b,49] although the classical Rh−C σ/π scheme differs considerably from our double "half-bond" model. Accompanying Rh−C bond strengthening from **43** to **44** is Rh−Rh bond weakening. Although negative charge resides entirely on the bridging carboxylates, the metal positive charge drops 1% at Rh−C and 23% at the distal rhodium center in the transformation from Rh_2(II) to **45**.

(48) Although charge delocalization by resonance is an energy-lowering effect, this notation strictly applies to singly charged systems. Zwitterionic systems, supporting two oppositely charged centers, need to accommodate both charge *delocalization* and charge *separation*. The former stabilizes; the latter destabilizes.

(49) (a) Drago, R. S.; Tanner, S. P.; Richman, R. M.; Long, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 2897. Drago, R. S.; Long. J. R.; Cosmano, R. *Inorg. Chem.* **1981**, *20*, 2920. (b) King, R. B.; King, A. D., Jr.; Iqbal, M. Z. *J. Am. Chem. Soc.* **1979**, *101*, 4893. Drago, R. S. *Inorg. Chem.* **1982**, *21*, 1697. Dennis, A. M.; Howard, R. A.; Bear, J. L. *Inorg. Chim. Acta* **1982**, *66*, L31. Chavan, M. Y.; Ahsan, M. Q.; Lifsey, R. S.; Bear, J. L.; Kadish, K. M. *Inorg. Chem.* **1986**, *25*, 3218. Eagle, C. T.; Farrar, D. G.; Pfaff, C. U. *Organometallics* **1998**, *17*, 4523;

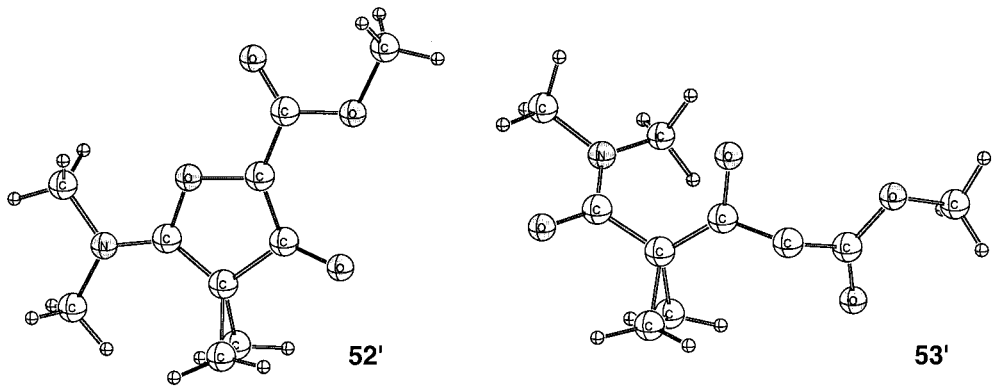


Figure 2. Becke3LYP/3-21G optimized geometries for carbonyl ylide **52** and singlet carbene **53**.

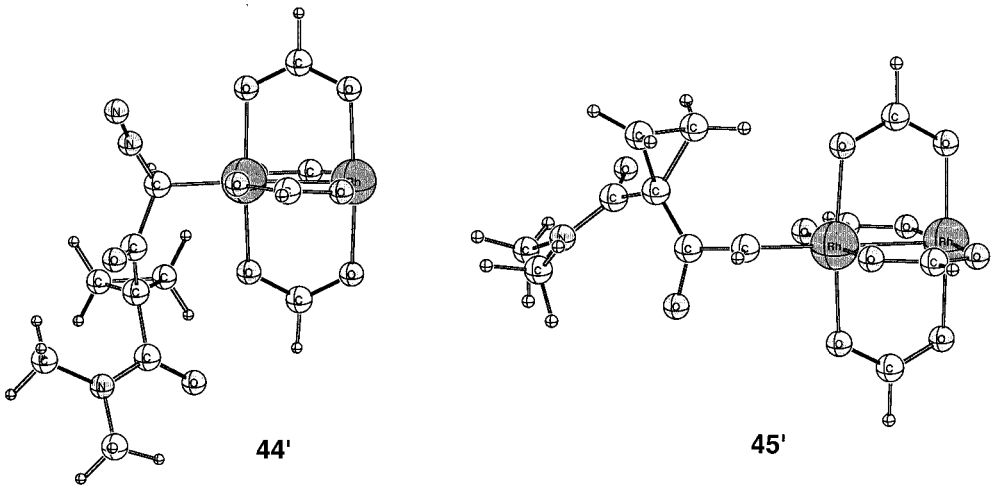


Figure 3. Becke3LYP/3-21G optimized geometries for the initial catalytic complex **44** (from diazo ketone **43** and Rh_2(II)) and the subsequent rhodium carbenoid **45** resulting from loss of N_2.

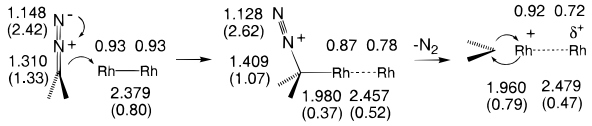


Figure 4. Symbolic coupling of **43** and Rh_2(II) to give **44** and the subsequent loss of dinitrogen to produce **45**. Bond lengths in Å are given beside the reactive bonds; bond orders are shown in parentheses; NBO charges at rhodium are reported above the atoms.

Thus, the distal metal center serves as an electron sink to accommodate polarization of the Rh−Rh bond in both complex **44** and carbenoid **45**. That the influence of the distal rhodium atom in RhRhC appears to be a decisive factor in catalysis is entirely consistent with early studies by Drago,[49a,c] the inhibition work of Pirrung and Morehead,[46] and the more recent application of a novel series of dirhodium(II) catalysts to 1-diazo-5-penten-2-one cyclization by Lahuerta and co-workers.[50]

The final structures to be considered are the ylide−Rh_2(II) complexes **46** and **47** (Figure 5) formed by ambident cyclization onto the carbenoid carbon of **45**, either by the lone electron pair on the amide nitrogen or that on the amide carbonyl, respectively. To a large degree, the C−Rh σ-bonds in **46** and **47** should resemble that for complex **44**. In both cases, an anionic center is formed in the corresponding ylides **48** and **49** upon subsequent dissociation. Indeed, Table 1 shows the C−Rh and Rh−Rh bond orders to be similar for the three complexes. NBO analysis concurs. In all three cases the overwhelming contribution to the C−Rh bond is dative bonding by a lone electron pair on carbon; i.e., a C-LP (σ*(Rh−Rh) interaction. At the same time, however, the C−Rh bond lengths in **46** and **47** are considerably longer than that in **44**. This can be understood as a molecular response to significant steric effects between the five-membered rings and the Rh_2(II) cage. Ring closure brings the oxygens of the dirhodium tetraformate moiety in close proximity to both hydrogens and heavy atoms of the pendant rings. Nonetheless, as will be discussed below, complexes **46** and **47** are the two most stable species among those considered in Scheme 1. A balance of forces is obviously at work. Steric effects destabilize the complexes, but the formation of a new bond as a result of ring closure more than compensates for the compression effect. The mark of the compromise is the stretched C−Rh bond distances.

The DFT Energy Profile. The goals of the present work are 3-fold. First we seek to establish the existence of the various species as genuine intermediates residing in well-defined energy wells as described above. Second, we want to understand the energy relationships along the pathway, at the very least, in a semiquantitative sense. Third, we hope to lay a general mechanistic foundation for the function of the dirhodium tetracarboxylate(II) catalyst to stimulate further experimentation and theoretical evaluation. This section focuses on the second and third goals. Figure 6 compiles and compares the energy relationships. In the present work, no transition states have been examined explicitly. We have, however, depicted the elimination of dinitrogen from **44** as rate determining ($E_a \sim 10$ kcal/mol) in accord with the kinetic studies of Pirrung and Morehead.[45] The fact that the intermediates are high above product ground

(50) Lahuerta, P.; Pérez-Pieto, J.; Stiriba, S.-E.; Ubeda, M. A. *Tetrahedron Lett.* **1999**, *40*, 1751.

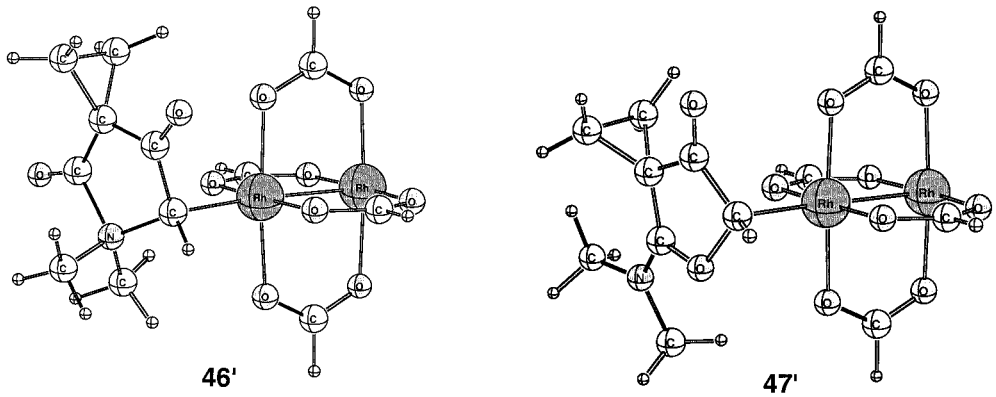


Figure 5. Becke3LYP/3-21G optimized geometries for the complexes (**46**, and **47**) between $Rh_2(II)$ and the five-membered ring 1,3-dipoles **48** and **49**, respectively.

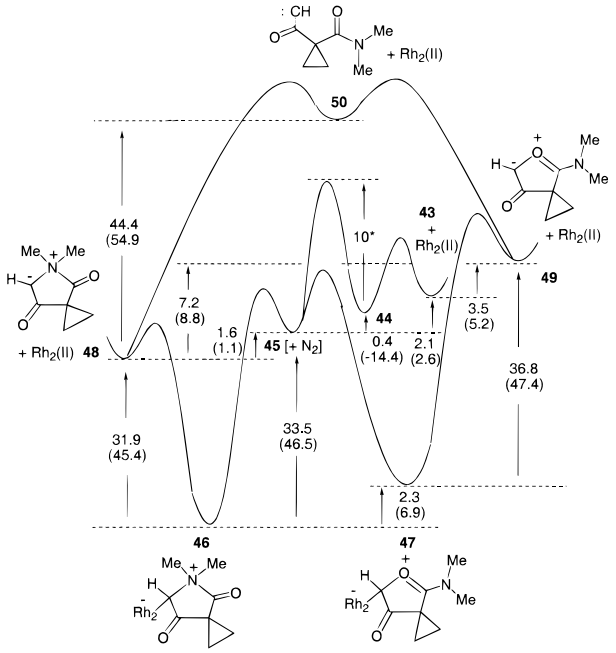


Figure 6. Energy diagram for rhodium(II) catalytic pathway. The 6-31G* energies are in kcal/mol; 3-21G energies are in parentheses. The value of 10* kcal/mol has been taken from ref 46. N_2 in (**45** + N_2) correlates only with **44** and (**43** + $Rh_2(II)$). $Rh_2(II)$ refers to the tetraformate structure given in Scheme 1.

states (e.g., **46** and **47** as well as the ultimate isolated cycloaddition and rearrangement products) suggests that the barriers can be readily surmounted in accord with Hammond's postulate.

The first revealing feature of the energy diagram in Figure 6 is that the rhodium tetraformate complexed ylides **46** and **47** reside in energy basins; this occurs despite significant intramolecular steric effects. Furthermore, complex **46** is favored by 2.3 kcal/mol over the isomeric carbonyl ylide complex **47**. Combined with the prediction that ammonium ylide **48** is likewise stabilized by 7.2 kcal/mol relative to *O*-ylide **49**, the result implies that for a fully equilibrated system the dissociation of complex **46** to *N*-ylide **48** is predicted to be 4.9 kcal more facile than the release of *O*-ylide **49** from complex **47**. This picture is fully consistent with the thermodynamically controlled formation of ammonium ylide-rearranged products obtained from cyclopropyl diazo amides under the influence of dirhodium(II) tetraacetate. It likewise comports with the isolation of nitrogen ylide **29** in the urea series where the *N*-ylide is calculated to be 12.6 kcal/mol (6-31+G*) more stable than the corresponding *O*-ylide **31**.

A second interesting point depicted by Figure 6 is the importance of diazoketone **43** as a substrate for the process. The high energy of the diazoketone moiety places it only 3.5 kcal/mol below *O*-ylide **49** (+ N_2). The starting materials are consequently located at an ideal entry point on the energy surface to deliver the key complex **45** exergonically. A third and general characteristic of the energy scheme is its profiling of the action of the rhodium tetracarboxylate catalyst. Two important roles are played by the organometallic reagent. First and foremost the compound serves to keep the reaction intermediates (i.e., **44**−**47**) at energies that permit product formation under mild conditions. The ultimate zwitterionic reactants **48** and **49** are formed by strongly exergonic ring closure at the rhodium carbenoid carbon followed by regeneration of the Rh(II) catalyst in preference to reopening of the rings.

Insight into these final two steps is gained by examining the concomitant structural changes at the reacting carbon center. Optimized carbenoid **45** sustains a relatively short Rh−C bond length of 1.960 Å and an NBO bond order of bo = 0.79. As alluded to above, these values are comparable to those derived for the simpler $[Rh_2(II)]-CH_2$ system: 1.920 Å and bo = 0.98.[27] During cyclization to **46** and **47**, the Rh−C bonds lengthen by 0.22 and 0.19 Å and thereby weaken substantially; bo = 0.36 and 0.40, respectively (Table 1). Consequently, the stretched metal−carbon bonds offer only moderate resistance to dissociative cleavage (32−37 kcal/mol, Figure 6).

The second role played by $Rh_2(RCO_2)_4$ concerns initiation of the diazo carbonyl chemistry. Coordination to **43** to give intermediate **44** sets up the original diazoketone for dinitrogen loss without the need to employ harsh reaction conditions (i.e., heat or light). Clearly the end-game zwitterions **48** and **49** can be generated directly from carbene **50**. However, were it necessary to take this route instead of passing through complex **45**, the additional energy cost is estimated to be around 40−50 kcal/mol. Thus, the dirhodium tetracarboxylate triggers diazo ketone decomposition and maintains it under highly controlled conditions at relatively low energies as expected for an efficient catalyst.

Conclusions

The experiments described in the first section of this report fall into four categories: (1) a potent dipolarophile such as DMAD reacts with diazo keto substrates in the presence of $Rh_2(OAc)_4$ to capture carbonyl ylides such as **31**, **39**, and **49** in excellent yields; (2) a weaker trapping agent such as *N*-

phenylmaleimide routinely elicits lower yields of cycloadduct and increasing quantities of rearranged lactam; (3) in the absence of a dipolarophile, the rhodium(II) catalyst promotes exclusive formation of lactam; and (4) ammonium ylide **29** in the presence of $Rh_2(OAc)_4$ and DMAD yields 10% of furan **33** derived from the carbonyl ylide intermediate.

These observations reflect a catalyst-promoted system of equilibria with a clear-cut thermodynamic bias. In the case of the cyclopropyl diazo keto amides, if we assume that DMAD trapping of carbonyl ylide is faster than rearrangement of ammonium ylide but that *N*-phenylmaleimide is competitive with it, Scheme 1 and Figure 6 explain observations (1) and (2) as arising from a rapidly established equilibrium between ylides **48** and **49**. Slower cycloaddition to **49** provides the thermodynamically more stable *N*-ylide **48** an opportunity for intramolecular transposition. In the presence of rhodium catalyst alone, the energetically favored **48** provides the sole reaction channel to products accounting for observation (3). In the case of diazoacetyl ureas (e.g., **28**), we believe the energy profile of Figure 6 also obtains. The low yield of furan **33** in observation (4) is readily accommodated by the competition of *N*-ylide **29** for DMAD, a reaction course not taken by cyclopropyl intermediates such as **48** and **51**. For the latter, the out-of-plane *N*-CH_3 and cyclopropyl carbons may well block effective approach by the acetylene to the carbanionic center.

For all of the reactions examined here, the nuances in relative stabilities and barrier heights will, of course, vary depending on substituents and ring constraints in the diazo ketone substrates as found, for example, for compounds **1**, **4**, and **40**. Given that the rhodium(II)-catalyzed reactions were carried out in the aromatic solvents benzene and toluene, solvation effects may also be important. Benzene is known to form a 2:1 adduct with dirhodium(II) tetracarboxylates.[45a] Since the role of solvent has not been included in our calculations, some of the energy relationships might vary if aromatic π solvation were taken into account. Finally, the energy surfaces reflected by Figure 6 are certain to be modified by variations in the ligands bridging the Rh(II) atoms of the catalyst.[43] In future contributions we will address this issue as well as questions of stereochemical control.

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 flame-dried glassware under an atmosphere of 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.

3-[1-(Methylphenylcarbamoyl)cyclopropyl]-3-oxopropionic Acid Ethyl Ester. To a solution containing 9.5 g (60 mmol) of 1,1-cyclopropanecarboxylic acid monoethyl ester[51] in 150 mL of CH_2Cl_2 and a catalytic amount of DMF was added 15.7 mL (180 mmol) of oxalyl chloride dropwise at room temperature. The mixture was stirred for 3 h at room temperature, and the excess oxalyl chloride and the solvent were removed under reduced pressure. The crude residue was dissolved in 100 mL of CH_2Cl_2. To this solution was added a solution containing 7.7 g (72 mmol) of *N*-methylaniline, and the mixture was stirred for 4 h at room temperature. The solution was washed with a saturated aqueous $NaHCO_3$ solution followed by brine. The organic layer was separated and dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography to give 8.0 g (54%) of ethyl 1-(methylphenylcarbamoyl)cyclopropane carboxylate as a white solid: mp 44−45 °C; IR (neat) 1716, 1638, 1303, and 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.13 (t, 3H, J = 6.9 Hz), 1.20 (s, 2H), 1.34 (s, 2H), 3.31 (s, 3H), 3.82 (q, 2H, J = 6.9 Hz), 7.21 (m, 3H), and 7.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.1, 17.3, 30.0, 38.3, 61.1, 127.3, 127.4, 129.1, 143.2, 168.2, and 170.7. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.98; H, 6.93; N, 5.67. Found: C, 67.81; H, 6.92; N, 5.53.

A solution containing 8.0 g (32 mmol) of the above ester in 60 mL of ethanol was treated with 32 mL (97 mmol) of an aqueous 3 M KOH solution, and the resulting mixture was stirred at room temperature for 4 h. The solution was concentrated under reduced pressure, water was added, and the mixture was acidified with an aqueous 1 N HCl solution and extracted with ether. The combined ether extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 6.0 g (85%) of 1-(methylphenylcarbamoyl)cyclopropanecarboxylic acid as a white solid: mp 140−141 °C; IR (neat) 3000, 1716, 1645, 1381, and 1175 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (m, 4H), 3.31 (s, 3H), 7.30 (m, 2H), 7.35 (m, 3H), and 10.27 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 18.1, 29.8, 38.5, 127.4, 127.6, 129.3, 143.0, 167.8, and 176.7. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.73; H, 5.98; N, 6.39. Found: C, 65.46; H, 5.81; N, 6.27.

To a solution containing 4.4 g (34 mmol) of 2-carboethoxyacetic acid in 50 mL of CH_2Cl_2 at 0 °C was slowly added 34 mL (67 mmol) of isopropylmagnesium chloride, and the reaction mixture was stirred at 0 °C for 30 min. The solution was heated at 40 °C for an additional 30 min. In a separate flask, 4.0 mL (46 mmol) of oxalyl chloride and 2 drops of DMF were slowly added to a solution of 4.48 g (30 mmol) of 1-(methylphenylcarbamoyl)cyclopropanecarboxylic acid in 50 mL of CH_2Cl_2. The solution was allowed to stir for 2 h at room temperature and was concentrated under reduced pressure. The residue was taken up in 5 mL of CH_2Cl_2, and the mixture was added to the magnesium dianion solution. The resulting solution was stirred at 0 °C for 1 h and was then quenched with 50 mL of 50% HCl. The solution was extracted with CH_2Cl_2 and dried over $MgSO_4$. Purification of the crude residue by silica gel chromatography afforded 3.94 g (47%) of 3-[1-(methylphenylcarbamoyl)cyclopropyl]-3-oxopropionic acid ethyl ester as a clear oil: IR (neat) 1737, 1694, 1645, and 1374 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.2−1.5 (m, 7H), 3.33 (s, 3H), 3.36 (s, 2H), 4.10 (q, 2H, J = 7.1 Hz), and 7.2−7.4 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.0, 14.1, 18.1, 38.6, 40.6, 46.0, 127.2, 127.3, 127.4, 127.5, 127.8, 129.6, 142.5, 166.6, and 184.8. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.32; H, 6.39; N, 4.73.

2-Diazo-3-[1-(methylphenylcarbamoyl)cyclopropyl]-3-oxopropionic Acid Ethyl Ester (10). To a stirred solution of 1.3 g (4.5 mmol) of the above amide in 10 mL of CH_3CN at 0 °C was added 1.5 mL (10.8 mmol) of Et_3N. The reaction mixture was stirred for 30 min at 0 °C, and then 1.1 g (5.4 mmol) of tosyl azide was added in one portion and stirring was continued for an additional 12 h. The solvent was removed under reduced pressure, and the crude oil was purified by silica gel chromatography to give 1.0 g (73%) of **10** as a yellow solid, mp 64−65 °C: IR (neat) 2128, 1723, 1687, and 1367 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (m, 5H), 1.71 (m, 2H), 3.30 (s, 3H), 4.31 (q, 2H, J = 7.1 Hz), 7.14 (d, 2H, J = 7.4 Hz), 7.35 (d, 2H, J = 7.4 Hz), and 7.3−7.4 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 14.5, 17.6, 35.9, 38.6, 61.8, 76.3, 126.4, 127.5, 127.8, 129.1, 129.6, 142.7, 161.1, 169.3, and 185.4. Anal. Calcd for $C_{16}H_{17}N_3O_4$: C, 60.93; H, 5.44; N, 13.33. Found: C, 60.85; H, 5.28; N, 13.17.

Dimethyl 5-Carboethoxy-5,8-epoxy-8-(methylphenylcarbamoyl)-4-oxo-6-spiro[2.5]octene-6,7-dicarboxylate (11). To a solution containing 0.7 mL (5.9 mmol) of dimethyl acetylenedicarboxylate and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.35 g (1.2 mmol) of diazo amide **10**. The reaction mixture was heated at reflux for 30 min, and the solution was concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to give 0.45 g (87%) of **11** as a yellow solid: mp 134−135 °C; IR (neat) 1773, 1723, 1488, and 1282 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.04 (m, 2H), 1.32 (t, 3H, J = 7.2 Hz), 1.35 (m, 2H), 3.26 (s, 3H), 3.41 (s, 3H), 3.81 (s, 3H), 4.28 (q, 2H, J = 7.2 Hz), 6.9−7.1 (m, 3H), and 7.2−7.3 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 29.4, 41.5, 51.6, 52.8, 62.4, 77.4, 77.5, 116.9, 120.8, 124.0, 126.6, 128.9, 129.2, 129.3, 129.4, 145.9, 155.8, 161.5, and 168.9. Anal. Calcd for $C_{22}H_{23}NO_8$: C, 61.53; H, 5.40; N, 3.26. Found: C, 61.49; H, 5.43; N, 3.25.

(51) Singh, R. K.; Danishefsky, S. *J. Org. Chem.* **1975**, *40*, 2969.

Spiro[7-carboethoxy-4,7-epoxy-4-(methylphenylcarbamoyl)-2-phenyl-1,3,6-trioxopseudoisoindole-5,1′-cyclopropane] (12). To a solution containing 1.0 g (5.9 mmol) of *N*-phenylmaleimide and 2 mg of rhodium(II) acetate in 5 mL of refluxing benzene was added dropwise 0.35 g (1.2 mmol) of diazo amide **10**. The reaction mixture was heated at reflux for 30 min, and the solution was concentrated under reduced pressure. The mixture was purified by silica gel chromatography to give 0.23 g (42%) of **12** as a yellow solid: mp 162−163 °C; IR (neat) 1744, 1701, and 1495 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.1−1.3 (m, 2H), 1.36 (t, 3H, J = 7.2 Hz), 1.68 (m, 2H), 3.49 (s, 3H), 3.72 (d, 1H, J = 7.4 Hz), 3.95 (d, 1H, J = 7.4 Hz), 4.43 (q, 2H, J = 7.2 Hz), 6.8−6.9 (m, 3H), and 7.2−7.4 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 14.2, 20.0, 28.4, 33.7, 43.2, 60.4, 63.7, 76.6, 112.3, 116.2, 116.9, 121.1, 126.6, 128.4, 128.9, 129.2, 131.8, 163.7, 170.1, 170.8, and 200.0. Anal. Calcd for $C_{26}H_{24}N_2O_6$: C, 67.82; H, 5.25; N, 6.08. Found: C, 67.74; H, 5.30; N, 6.01.

2-Diazo-3-[1-methylphenylcarbamoyl)cyclopropyl]-3-oxopropionic Acid Methyl Ester (13). To a 1.0 g (4.6 mmol) sample of 1-(methylphenylcarbamoyl)-cyclopropanecarboxylic acid in 25 mL of CH_2Cl_2 were added 0.7 g (7.0 mmol) of oxalyl chloride and 1 drop of DMF. The solution was allowed to stir at room temperature for 30 min and was concentrated under reduced pressure to remove the excess oxalyl chloride. The residue was taken up in 1 mL of CH_2Cl_2, and this solution was added slowly to 10 mL of a 0.5 M THF solution of the magnesium dianion of hydrogen ethyl malonate at 0 °C. The solution was allowed to stir for 1 h and was then quenched with a 1 N HCl solution. The reaction was extracted with ether, and the ether extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.96 g (76%) of 3-[1-methylphenylcarbamoyl]-3-oxopropionic acid methyl ester as a yellow oil: IR (neat) 2960, 1720, 1637, and 1340 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20−1.36 (m, 4H), 3.31 (s, 3H), 3.36 (s, 2H), 3.63 (s, 3H), and 7.14−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 18.1, 38.5, 38.6, 45.7, 52.3, 127.3, 127.8, 129.6, 142.5, 167.0, and 168.5. Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.31; H, 6.13; N, 5.17.

Standard diazo transfer afforded **13** (91%) as a labile yellow oil which was immediately subjected to the rhodium(II)-catalyzed reaction: IR (neat) 2135, 1723, 1637, and 1368 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.20−1.40 (m, 2H), 1.61−1.68 (m, 2H), 3.26 (s, 3H), 3.81 (s, 3H), and 7.09−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.6, 35.9, 38.5, 52.4, 125.8, 127.6, 129.1, 142.6, 161.5, 169.2, and 185.2.

4,7-Epoxy-4-(methylphenylamino)-8-oxospiro[2.5]oct-5-ene-5,6,7-tricarboxylic Acid Trimethyl Ester (14). To a mixture of 2 mg of rhodium(II) acetate and 40 μL (0.35 mmol) of dimethyl acetylenedicarboxylate in 2 mL of benzene at 80 °C was added 0.05 g (0.17 mmol) of diazo amide **13** in 0.5 mL of benzene over a period of 5 min. The solution was heated at 80 °C for 1 h and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.6 g (87%) of **14** as a yellow oil: IR (neat) 2940, 1737, 1694, 1467, and 1374 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.03 (dd, 2H, J = 7.1 and 5.3 Hz), 1.35 (dd, 2H, J = 7.1 and 5.3 Hz), 3.26 (s, 3H), 3.42 (s, 3H), 3.82 (s, 3H), 3.83 (s, 3H), and 6.96−7.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.4, 41.7, 51.6, 52.9, 53.0, 109.8, 121.0, 124.2, 128.4, 129.3, 129.4, 138.4, 145.8, 155.8, 161.9, 164.3, 166.1, and 168.9. Anal. Calcd for $C_{21}H_{21}NO_8$: C, 60.72; H, 5.10; N, 3.37. Found: C, 60.58; H, 5.05; N, 3.24.

4′,7′-Epoxy-7′-carbomethoxy-4′-(methylphenylamino)-2′-phenyl-1′,3′,6′-trioxospiro[1,5′-cyclopropane-1′,3′,3a′,4′,5′,6′,7′,7a′-octahydroisoindole (15). To a solution of 0.06 g (0.35 mmol) of *N*-phenylmaleimide and 2 mg of rhodium(II) acetate in 1 mL of benzene at 80 °C was added 0.05 g (0.17 mmol) of diazo amide **13** in 0.5 mL of benzene over a period of 10 min. The reaction was allowed to stir at 80 °C for 2 h, cooled to room temperature, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.06 g (80%) of **15** as a white solid: mp 203−204 °C; IR (KBr) 1751, 1698, 1591, and 1490 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25−1.76 (m, 4H), 3.50 (s, 3H), 3.97 (s, 3H), 4.19 (s, 1H), 4.40 (s, 1H), 6.83−7.43 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.1, 28.5, 33.7, 43.3, 46.7, 54.0, 112.1, 116.9, 117.0, 121.2, 126.5, 128.4, 128.9, 129.3, 131.8, 146.3, 154.6, 163.6, 170.6, 170.8, and 199.9. Anal. Calcd for $C_{25}H_{22}N_2O_6$: C, 67.24; H, 4.97; N, 6.28. Found: C, 67.14; H, 4.83; N, 6.17.

4-(Methylphenylamino)-5,7-dioxo-6-phenyl-3,5,6,7-tetrahydro-2*H*-1-oxa-5-indacene-8-carboxylic Acid Methyl Ester (17). To a solution of 0.04 g (0.1 mmol) of cycloadduct **15** in 2 mL of CH_2Cl_2 was added 2 equiv of $BF_3{\cdot}OEt_2$, and the solution was allowed to stir at room temperature for 12 h. The mixture was poured into 2 mL of a saturated NaCl solution and extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.04 g (85%) of **17** as a colorless oil: IR (neat) 3434, 1735, 1591, and 1490 and 997 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.74 (t, 2H, J = 8.9 Hz), 3.45 (s, 3H), 3.97 (s, 3H), 4.68 (t, 2H, J = 8.9 Hz), 6.77−6.91 (m, 3H), and 7.22−7.44 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.9, 40.4, 53.1, 73.6, 116.4, 120.4, 126.6, 127.9, 129.0, 129.3, 130.9, 131.6, 133.1, 143.7, 146.0, 163.5, 164.3, 164.6, and 164.9. Anal. Calcd for $C_{25}H_{20}N_2O_5$: C, 70.07; H, 4.71; N, 6.54. Found: C, 69.86; H, 4.59; N, 6.43.

6-Phenyl-5-methyl-4,7-dioxo-5-azaspiro[2.4]heptane-6-carboxylic Acid Ethyl Ester (19). To a suspension containing 2 mg of rhodium(II) acetate in 10 mL of benzene was added 0.5 g (1.6 mmol) of diazoamide **10**. The reaction was heated at reflux for 4 h, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography to give 0.3 g (62%) of **19** as a clear oil: IR (neat) 2980, 1767, 1707, 1450, and 1390 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.92 (m, 1H), 1.13 (m, 1H), 1.35 (t, 3H, J = 7.1 Hz), 1.53 (m, 1H), 1.70 (m, 1H), 3.05 (s, 3H), 4.22 (q, 2H, J = 7.1 Hz), 7.00 (m, 2H), and 7.23 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 20.3, 21.6, 26.8, 30.9, 36.2, 62.7, 78.0, 127.5, 128.4, 128.6, 129.9, 133.3, 166.6, 172.3, 204.0. Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.87; H, 5.97; N, 4.88. Found: C, 66.81; H, 5.77; N, 4.61.

1-(Benzylmethylcarbamoyl)cyclopropanecarboxylic Acid Ethyl Ester. To a solution containing 10.0 g (63 mmol) of 1,1-cyclopropanecarboxylic acid monoethyl ester in 250 mL of CH_2Cl_2 and a catalytic amount of DMF was added 16.5 mL (190 mmol) of oxalyl chloride dropwise at room temperature. The mixture was stirred for 3 h at room temperature, and the excess oxalyl chloride and CH_2Cl_2 were removed under reduced pressure. The crude residue was dissolved in 250 mL of CH_2Cl_2, 19.2 g (158 mmol) of *N*-benzylmethylamine was added, and the mixture was stirred for 24 h at room temperature. The reaction mixture was washed with a saturated aqueous $NaHCO_3$ solution and brine and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 16.1 g (98%) of 1-(benzylmethylcarbamoyl)-cyclopropanecarboxylic acid ethyl ester as a yellow oil: IR (neat) 1732, 1651, 1304, 1178, and 1028 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.15 (t, 3H, J = 7.1 Hz), 1.34 (m, 2H), 1.47 (m, 2H), 2.89 (s, 3H), 4.11 (q, 2H, J = 7.1 Hz), 4.58 (s, 2H), and 7.30 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 16.1, 18.7, 28.7, 34.4, 50.8, 61.3, 127.0, 127.6, 128.2, 136.6, 168.2, and 171.1; HRMS calcd for $C_{15}H_{19}NO_3$ 261.1365, found 261.1368.

1-(Benzylmethylcarbamoyl)cyclopropanecarboxylic Acid. A solution containing 16 g (61 mmol) of the above ester in 150 mL of ethanol was treated with 3.4 g (61 mmol) of KOH, and the resulting mixture was stirred at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure, and water was added. The solution was acidified with an aqueous 1 N HCl solution and was extracted with ether. The combined organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 5.8 g (41%) of 1-(benzylmethylcarbamoyl)cyclopropanecarboxylic acid as a yellow oil: IR (neat) 3473, 1732, 1644, 1321, 1206, and 1162 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.72 (m, 2H), 1.78 (m, 2H), 3.10 (s, 3H), 4.58 (s, 2H), 7.28 (m, 5H), and 11.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.5, 21.9, 24.3, 62.6, 127.3, 127.8, 128.5, 138.0, 171.7, and 175.3; HRMS calcd for $C_{13}H_{15}NO_3$ 233.1052, found 233.1049.

3-[1-Benzylmethylcarbamoyl)cyclopropyl]-3-oxopropionic Acid Ethyl Ester. To a solution containing 2.5 g (19 mmol) of 2-carboethoxyacetic acid in 160 mL of THF at 0 °C was slowly added 19 mL (38 mmol) of isopropylmagnesium chloride, and the reaction mixture was stirred at 0 °C for 30 min. In a separate flask, a mixture containing 2.8 mL (32 mmol) of oxalyl chloride and 2 drops of DMF was slowly

added to a solution of 3.7 g (16 mmol) of 1-(benzylmethylcarbamoyl)-cyclopropane carboxylic acid in 160 mL of CH_2Cl_2. The solution was allowed to stir for 2 h at room temperature and was then concentrated under reduced pressure, the residue was taken up in 5 mL of THF, and the mixture was added to the above magnesium dianion solution. The resulting mixture was stirred at 0 °C for 1 h and was then quenched with 50 mL of 50% HCl. The solution was extracted with ether, dried over $MgSO_4$, and chromatographed on a silica gel column to give 1.9 g (42%) of 3-[1-benzylmethylcarbamoyl)cyclopropyl]-3-oxopropionic acid ethyl ester as a clear oil: IR (neat) 1743, 1694, 1650, 1243, and 1029 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.18 (t, 3H, $J = 7.1$ Hz), 1.40 (m, 2H), 1.52 (m, 2H), 2.88 (s, 3H), 3.41 (s, 2H), 4.10 (m, 2H), 4.56 (s, 2H), and 7.24 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 17.2, 34.6, 37.7, 45.3, 51.2, 53.3, 61.3, 127.5, 128.0, 128.5, 136.3, 166.5, 168.5, and 198.4. Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.29; H, 6.98; N, 4.62. Found: C, 67.05; H, 6.87; N, 4.60.

3-[1-(Benzylmethylcarbamoyl)cyclopropyl]-2-diazo-3-oxopropionic Acid Ethyl Ester (20). To a solution containing 1.3 g (4.2 mmol) of the above ester in 25 mL of CH_2Cl_2 was added 1.17 mL (8.4 mmol) of triethylamine, and the resultant mixture was stirred for 30 min at 0 °C. At the end of this time, 0.63 mL (5 mmol) of mesyl azide was added dropwise over a period of 15 min and the mixture was stirred for an additional 24 h. The reaction was quenched with 10% NaOH and extracted with CH_2Cl_2. Silica gel chromatography of the crude reaction mixture afforded 1.2 g (92%) of **20** as a yellow oil which decomposed on standing and was immediately subjected to the rhodium(II)-catalyzed reaction: IR (neat) 3064, 2135, 1729, 1695, 1647, and 1308 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 3H, $J = 7.2$ Hz), 1.44 (m, 4H), 2.80 (s, 3H), 4.21 (q, 2H, $J = 7.2$ Hz), 4.45 (s, 2H), and (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 13.9, 14.7, 34.6, 35.4, 51.6, 61.3, 77.2, 127.0, 127.8, 128.2, 136.5, 160.0, 168.5, and 186.2.

Dimethyl 5-Carboethoxy-5,8-epoxy-8-(benzylmethylcarbamoyl)-4-oxo-6-spiro[2,5]octene-6,7-dicarboxylate (21). To a solution containing 0.06 mL (0.46 mmol) of dimethyl acetylenedicarboxylate and 2 mg of rhodium(II) acetate in 10 mL of refluxing benzene was added 0.1 g (0.30 mmol) of diazo amide **20** dropwise over 20 min. The reaction mixture was heated for an additional 1 h, and the solvent was removed under reduced pressure. The crude mixture was purified by silica gel chromatography to give 0.8 g (57%) of **21** as a yellow solid: mp 108−109 °C; IR (KBr) 3062, 1772, 1726, 1693, 1600, 1270, 1243, and 1045 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.91 (m, 1H), 1.07 (m, 1H), 1.31 (t, 3H, $J = 7.1$ Hz), 1.50 (m, 1H), 1.73 (m, 1H), 2.92 (s, 3H), 3.66 (s, 3H), 3.79 (s, 3H), 4.26 (m, 2H), 4.37 (d, 1H, $J = 16$ Hz), 5.21 (d, 1H, $J = 16$ Hz), 7.16 (m, 2H), and 7.32 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 14.4, 15.0, 28.6, 30.8, 43.7, 51.6, 52.7, 53.4, 58.8, 62.0, 104.9, 126.6, 127.8, 129.0, 135.7, 156.9, 165.1, 167.2, 168.3, and 206.8. Anal. Calcd for $C_{23}H_{25}NO_8$: C, 62.30; H, 5.68; N, 3.16. Found: C, 62.29; H, 5.66; N, 3.15.

6-Benzyl-5-methyl-4,7-dioxo-5-azaspiro[2.4]heptane-6-carboxylic Acid Ethyl Ester (22). To a solution containing 2 mg of rhodium(II) acetate in 25 mL of refluxing benzene was added 0.5 g (1.5 mmol) of diazo amide **20** dropwise over 20 min. The reaction mixture was heated for 6 h, and the solvent was removed under reduced pressure. The crude mixture was purified by silica gel chromatography to give 0.32 g (70%) of **22** as a clear oil: IR (neat) 3028, 1761, 1734, 1706, 1597, 1502, 1380, 1237, and 1087 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.86 (td, 1H, $J = 9.0$ and 3.3 Hz), 1.01 (td, 1H, $J = 9.0$ and 3.3 Hz), 1.26 (t, 3H, $J = 7.2$ Hz), 1.53 (m, 2H), 3.04 (s, 3H), 3.24 (d, 1H, $J = 14.4$ Hz), 3.54 (d, 1H, $J = 14.4$ Hz), 4.26 (m, 2H), 6.97 (m, 2H), and 7.21 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.4, 19.7, 21.0, 26.1, 30.3, 35.6, 62.0, 76.1, 126.8, 127.8, 129.3, 132.7, 166.0, 171.6, and 203.4. Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.74; H, 6.36; N, 4.65. Found: C, 67.62; H, 6.41; N, 4.51.

Spiro[4-(benzylmethylamino)-7-carboethoxy-7-hydroxy-1,3,6-trioxo-2-phenyl-2,3,5,6,7,7a-hexahydro-1*H*-isoindole-5,1′-cyclopropane] (23). To a solution containing 0.09 g (0.54 mmol) of *N*-phenylmaleimide and 2 mg of rhodium(II) acetate in 10 mL of refluxing benzene was added 0.1 g (0.3 mmol) of diazo amide **20** dropwise over 20 min. The reaction mixture was heated for an additional 1 h, and the solvent was removed under reduced pressure. The crude mixture was purified by silica gel chromatography to give 0.9 g (60%) of **23** as a clear oil: IR (neat) 1756, 1716, 1689, 1372, and 1123 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.24 (m, 1H), 1.34 (t, 3H, $J = 7.1$ Hz), 1.56 (m, 2H), 1.71 (m, 1H), 2.83 (s, 3H), 4.05 (s, 1H), 4.37 (m, 3H), 4.49 (d, 1H, $J = 15$ Hz), 4.63 (d, 1H, $J = 15$ Hz), 7.16 (m, 2H), 7.30 (m, 6H), and 7.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 14.5, 27.5, 34.5, 40.2, 47.8, 60.1, 63.5, 76.5, 100.8, 126.7, 127.6, 127.9, 128.2, 128.7, 128.9, 132.2, 137.3, 157.8, 164.5, 170.2, 171.2, and 200.2. Anal. Calcd for $C_{27}H_{26}N_2O_6$: C, 68.33; H, 5.53; N, 5.91. Found: C, 68.31; H, 5.42; N, 5.86.

1-Diethylcarbamoylcyclopropanecarboxylic Acid Ethyl Ester. To a solution containing 10 g (63 mmol) of 1,1-cyclopropanecarboxylic acid monoethyl ester in 250 mL of CH_2Cl_2 and a catalytic amount of DMF was added 16.5 mL (190 mmol) of oxalyl chloride dropwise at room temperature. The mixture was stirred for 3 h at room temperature, and the excess oxalyl chloride and solvent were removed under reduced pressure. The crude residue was dissolved in 250 mL of CH_2Cl_2, 11.5 g (158 mmol) of diethylamine was added, and the mixture was stirred for 24 h at room temperature. The reaction mixture was washed with saturated aqueous $NaHCO_3$ and brine and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 13 g (96%) of 1-diethylcarbamoylcyclopropanecarboxylic acid ethyl ester as a yellow oil: IR (neat) 1725, 1643, 1307, and 1182 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.02 (m, 11H), 1.22 (m, 2H), 3.19 (t, 4H, $J = 6.9$ Hz), and 3.94 (q, 2H, $J = 7.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.1, 11.6, 12.4, 13.1, 14.8, 28.0, 38.3, 40.8, 60.5, 166.5, and 170.6; HRMS calcd for $C_{11}H_{19}NO_3$ 213.1364, found 213.1362.

1-Diethylcarbamoylcyclopropanecarboxylic Acid. A solution containing 13 g (60 mmol) of the above oil in 125 mL of ethanol was treated with 3.3 g (60 mmol) of KOH, and the resulting mixture was stirred at room temperature for 24 h. The reaction mixture was concentrated under reduced pressure, water was added, and the solution was acidified with an aqueous 1 N HCl solution and extracted with ether. The combined organic extracts were dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 4.9 g (45%) of 1-diethylcarbamoylcyclopropanecarboxylic acid as a yellow oil: IR (neat) 3427, 1727, 1614, 1305, and 1179 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 6H, $J = 7.2$ Hz), 1.33 (m, 2H), 1.48 (m, 2H), 3.40 (q, 4H, $J = 7.1$ Hz), and 9.65 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.2, 13.6, 16.2, 21.9, 28.6, 38.3, 42.3, 168.1, and 174.9; HRMS calcd for [$C_9H_{15}NO_3$ + Li] 192.1211, found 192.1208.

3-(1-Diethylcarbamoylcyclopropyl)-3-oxopropionic Acid Ethyl Ester. To a solution containing 2.4 g (18.1 mmol) of 2-carboethoxyacetic acid in 100 mL of THF at 0 °C was slowly added 18.1 mL (36 mmol) of isopropylmagnesium chloride, and the reaction mixture was stirred at 0 °C for 30 min. In a separate flask, 2.6 mL (30 mmol) of oxalyl chloride and 2 drops of DMF were slowly added to a solution of 2.8 g (15 mmol) of 1-diethylcarbamoylcyclopropane carboxylic acid in 100 mL of CH_2Cl_2. The solution was allowed to stir for 2 h at room temperature and was then concentrated under reduced pressure. The residue was taken up in 5 mL of THF, and the solution was added to the above magnesium dianion solution. The resulting mixture was stirred at 0 °C for 1 h and was quenched with 50 mL of a 50% HCl solution. The mixture was extracted with ether and dried over $MgSO_4$. Purification of the crude residue by silica gel chromatography gave 2.5 g (65%) of 3-(1-diethylcarbamoylcyclopropyl)-3-oxopropionic acid ethyl ester as a yellow oil: IR (neat) 1746, 1699, 1640, 1327, 1248, and 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 6H, $J = 7.2$ Hz), 1.22 (t, 3H, $J = 7.2$ Hz), 1.34 (m, 2H), 1.47 (m, 2H), 3.37 (q, 4H, $J = 6.6$ Hz), 3.51 (s, 2H), and 4.14 (q, 2H, $J = 7.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 13.1, 13.8, 16.7, 37.6, 39.3, 41.6, 45.6, 61.1, 166.4, 167.6, and 198.6. Anal. Calcd for $C_{13}H_{21}NO_4$: C, 61.14; H, 8.29; N, 5.49. Found: C, 60.98; H, 8.15; N, 5.42.

2-Diazo-3-(1-diethylcarbamoylcyclopropyl)-3-oxopropionic Acid Ethyl Ester (24). To a solution containing 2.5 g (9.8 mmol) of the above ester in 50 mL of CH_2Cl_2 was added 2.7 mL (20 mmol) of triethylamine, and the resultant mixture was stirred for 30 min at 0 °C. At the end of this time, 1.5 mL (11.8 mmol) of mesyl azide was added dropwise over a period of 15 min and the mixture was stirred for an additional 24 h at room temperature. The mixture was quenched with 10% NaOH and extracted with CH_2Cl_2. Silica gel chromatography of

the crude mixture afforded 2.7 g (98%) of **24** as a labile yellow oil which was immediately used in the Rh(II)-catalyzed reaction: IR (neat) 2131, 1738, 1694, 1633, 1317, and 1127 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 6H, $J = 7.2$ Hz), 1.15 (t, 3H, $J = 7.2$ Hz), 1.26 (s, 4H), 3.24 (brs, 4H), and 4.13 (q, 2H, $J = 7.2$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.2, 12.9, 13.1, 13.9, 14.0, 35.6, 39.9, 41.5, 61.4, 75.5, 160.1, 167.2, and 185.8.

5-Ethyl-4,7-dioxo-5-azaspiro[2,4]heptane-6-carboxylic Acid Ethyl Ester (25). To a solution containing 2 mg of rhodium(II) acetate in 25 mL of refluxing benzene was added 0.5 g (1.8 mmol) of the diazo amide **24** dropwise over 20 min. The mixture was heated for an additional 5 h, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography to give 0.37 g (93%) of **25** as a clear oil: IR (neat) 1768, 1741, 1700, 1201, 1120, and 1019 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (t, 3H, $J =$ 7.2 Hz), 1.29 (t, 3H, $J = 7.2$ Hz), 1.61 (m, 2H), 1.72 (m, 2H), 3.19 (m, 1H), 3.95 (m, 1H), 4.26 (q, 2H, $J = 7.2$ Hz), and 4.64 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 13.8, 20.5, 21.8, 30.7, 36.3, 62.4, 67.7, 165.0, 171.5, and 200.2. Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N, 6.22. Found: C, 58.43; H, 6.69; N, 6.17.

Dimethyl 5-Carboethoxy-5,8-epoxy-8-(diethylcarbamoyl)-4-oxo-6-spiro[2.5]-octene-6,7-dicarboxylate (26). To a solution containing 0.07 mL (0.53 mmol) of dimethyl acetylenedicarboxylate and 2 mg of rhodium(II) acetate in 8 mL of refluxing benzene was added 0.1 g (0.36 mmol) of diazo amide **24** dropwise over a 20 min interval. The mixture was heated for an additional 1 h, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography to give 0.13 g (92%) of **26** as a yellow solid: mp 104−105 °C; IR (KBr) 1772, 1759, 1726, 1694, 1271, and 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (t, 6H, $J = 7.1$ Hz), 1.24 (m, 1H), 1.30 (t, 3H, $J = 7.1$ Hz), 1.35 (m, 1H), 1.67 (m, 2H), 3.34 (m, 4H), 3.65 (s, 3H), 3.78 (s, 3H), and 4.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.9, 13.6, 13.9, 16.2, 28.7, 45.8, 51.3, 52.5, 61.9, 101.4, 128.8, 137.8, 158.5, 161.7, 164.2, 166.9, and 168.2. Anal. Calcd for $C_{19}H_{25}NO_8$: C, 57.71; H, 6.37; N, 3.54. Found: C, 57.74; H, 6.36; N, 3.50.

Spiro[7-carboethoxy-4-(diethylamino)-7-hydroxy-1,3,6-trioxo-2-phenyl-2,3,5,6,7,7a-hexahydro-1*H*-isoindole-5,1′-cyclopropane] (27). To a solution containing 0.09 g (0.54 mmol) of *N*-phenylmaleimide and 2 mg of rhodium(II) acetate in 8 mL refluxing benzene was added 0.1 g (0.36 mmol) of diazo amide **24** dropwise over 20 min. The mixture was heated at 80 °C for 2 h, and the solvent was removed under reduced pressure. The crude mixture was purified by silica gel chromatography to give 0.1 g (66%) of **27** as a yellow solid: mp 180−181 °C; IR (neat) 3453, 1752, 1706, 1693, 1594, 1371, and 1109 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.05 (t, 6H, $J = 7.2$ Hz), 1.33 (t, 3H, $J = 7.2$ Hz), 1.50 (m, 2H), 1.63 (m, 1H), 2.11 (m, 1H), 3.33 (m, 2H), 3.48 (m, 2H), 3.99 (s, 1H), 4.39 (m, 3H), 7.31 (m, 3H), and 7.42 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 13.9, 14.0, 27.7, 30.7, 34.2, 46.5, 47.7, 63.4, 76.5, 102.5, 126.6, 128.0, 128.7, 132.2, 156.8, 164.0, 170.2, 171.2, and 200.5. Anal. Calcd for $C_{23}H_{26}N_2O_6$: C, 64.78; H, 6.15; N, 6.57. Found: C, 64.55; H, 5.97; N, 6.40.

***N*′-(2-Diazo-2-methyloxycarbonylacetyl)-*N*,*N*,*N*′-trimethylurea (28).** A mixture of 2.0 g (20 mmol) of trimethylurea, 3.8 g (28 mmol) of distilled methyl malonyl chloride, and 50 mL of dry benzene was heated at reflux for 2 h. After all the starting material had been consumed, the solution was cooled to ambient temperature. The solvent was removed under reduced pressure, and the crude product was purified by silica gel chromatography to give 3.9 g (96%) of *N*′-(2-methyloxycarbonylacetyl)-*N*,*N*,*N*′-trimethylurea as a colorless oil: IR (neat) 3550, 2950, 1745, and 1670 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.97 (s, 3H), 3.05 (s, 3H), 3.58 (s, 2H), and 3.68 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.0, 39.3, 43.7, 54.2, 168.3, and 169.7.

A mixture of 2.0 g (10 mmol) of the above urea, 1.6 g (13 mmol) of mesyl azide, 2.6 g (26 mmol) of distilled triethylamine, and 50 mL of dry CH_2Cl_2 was stirred at room temperature for 48 h. After all starting material had been consumed, the reaction mixture was washed with ice-cold 5% aqueous KOH and brine. The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude diazo compound was purified by silica gel chromatography to give 1.8 g (81%) of diazo imide **28** (78% based on trimethylurea) as a yellow oil that crystallized on standing, mp 46−50 °C: IR (neat) 2130, 1725, 1685, and 1640 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.96 (s, 6H), 3.11 (s, 3H), and 3.74 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.9, 39.5, 54.0, 72.2, 161.4, 163.7, and 165.6. Anal. Calcd for $C_8H_{12}N_4O_4$: C, 42.11; H, 5.30; N, 24.55. Found: C, 41.91; H, 5.30; N, 24.34.

1,1,3-Trimethyl-5-methoxycarbonyl-2-oxo-2,3-dihydro-1*H*-imidazol-1-ium-4-olate (29). A solution of 0.23 g (1 mmol) of diazo imide **28** in 5 mL of dry toluene was added dropwise over 1 h to a solution of 2 mg of rhodium(II) acetate in 30 mL of toluene at reflux temperature. After the resulting mixture was kept at reflux for an additional 20 min, the solution was cooled in an ice bath. The precipitated solid was filtered to give 0.14 g (68%) of **29** as a colorless solid, mp 199−201 °C: IR (KBr) 1810, 1720, 1630, and 1440 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.15 (s, 3H), 3.46 (s, 6H), and 3.79 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.2, 49.2, 50.2, 93.1, 155.4, 156.0, and 161.0. Anal. Calcd for $C_8H_{12}N_2O_4$: C, 48.00; H, 6.04; N, 13.99. Found: C, 48.15; H, 6.14; N, 13.89.

The mother liquor of the above reaction was evaporated under reduced pressure, and the residue was purified by silica gel chromatography to give 0.02 g (10%) of the corresponding dimeric azine[22] as a yellow solid, mp 159−160 °C: IR (KBr) 1950, 1750, 1690, 1670, and 1500 cm^{-1};^1H NMR (200 MHz, $CDCl_3$) δ 2.96 (s, 12H), 3.18 (s, 6H), and 3.88 (s, 6H);^{13}C NMR (50 MHz, $CDCl_3$) δ 32.4, 37.5, 53.1, 153.0, 157.3, 159.6, and 162.4; FAB-MS: 429 (M + 1). Anal. Calcd for $C_{16}H_{24}N_6O_8$: C, 44.86; H, 5.65; N, 19.62. Found: C, 44.65; H, 5.63; N, 19.38.

Trimethyl 3-Dimethylamino-1-methyl-2,6-dioxo-1,2,3,6-tetrahydro-3,4,5-pyridinetricarboxylate (30). A solution of 0.23 g (1 mmol) of diazo imide **28** in 5 mL of dry toluene was added dropwise to a solution of 2 mg of rhodium(II) acetate and 0.28 g (2 mmol) of dimethyl acetylenedicarboxylate in 30 mL of toluene at reflux temperature. After the resulting mixture was kept at reflux for an additional 20 min, the solution was cooled in an ice bath. The precipitated solid was filtered to give 0.06 g (28%) of ylide **31** as a colorless solid, identical in all respects with a sample obtained above. Evaporation of the mother liquor and purification of the residue by careful silica gel chromatography provided 62 mg (18%) of trimethyl 3-dimethylamino-1-methyl-2,6-dioxo-1,2,3,6-tetra-hydro-3,4,5-pyridinetricarboxylate (**30**) as a yellow solid, mp 156−158 °C, and 0.07 g (25%) of trimethyl 5-dimethylamino-2,3,4-furan tricarboxylate (**33**) as a colorless solid, mp 107−108 °C. Compound **30** exhibited the following properties: IR (KBr) 1780, 1745, 1738, 1720, 1690, and 1660 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.45 (s, 6H), 3.27 (s, 3H), 3.77 (s, 3H), 3.82 (s, 3H), and 3.89 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 26.6, 40.7, 53.3, 53.6, 53.7, 71.0, 131.5, 141.4, 160.6, 162.9, 163.0, 165.0, and 165.8. Anal. Calcd for $C_{14}H_{18}N_2O_8$: C, 49.12; H, 5.30; N, 8.18. Found: C, 49.07; H, 5.36; N, 7.88.

Compound **33** exhibited the following properties: IR (KBr) 1750, 1700, 1610, and 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.20 (s, 6H), 3.73 (s, 3H), 3.82 (s, 3H), and 3.92 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 40.4, 51.5, 52.0, 52.8, 91.4, 129.5, 129.6, 157.7, 161.6, 161.8, and 164.3. Anal. Calcd for $C_{12}H_{15}NO_7$: C, 50.53; H, 5.30; N, 4.91. Found: C, 50.36; H, 5.25; N, 4.77.

A mixture of 0.1 g (0.5 mmol) of ylide **29**, 0.14 g (1 mmol) of dimethyl acetylenedicarboxylate, and 2 mL of dry toluene was heated at reflux for 2 h. After the solvent was removed under reduced pressure, the crude residue was purified by silica gel chromatography to give 0.1 g (61%) of pyridine **30**, identical in all respects with a sample obtained above.

Methyl 4-Dimethylamino-7-hydroxy-2,5,7-trimethyl-1,3,6-trioxo-2,3,5,−6,7,7a-hexahydro-1*H*-pyrrolo[3,4-c]pyridine-7-carboxylate (35). A solution of 0.23 g (1 mmol) of diazo imide **28** in 5 mL of dry toluene was added dropwise to a solution of 2 mg of rhodium(II) acetate and 0.21 g (2 mmol) of *N*-methylmaleimide in 30 mL of toluene at reflux temperature. After the resulting mixture was kept at reflux for an additional 20 min, the solution was cooled in an ice bath. The precipitated solid was filtered to give 0.09 g (46%) of ylide **29**. Evaporation of the mother liquor and purification of the residue by silica gel chromatography provided 0.08 g (24%) of **35** as a pale yellow solid, mp 178−180 °C: IR (KBr) 3400, 1750, 1690−1660, 1620, and

1500 cm^{-1};^{1}H NMR (200 MHz, $CDCl_3$) δ 2.97 (s, 3H), 3.07 (s, 6H), 3.13 (s, 3H), 3.98 (s, 3H), and 4.02 (s, 1H);^{13}C NMR (50 MHz, $CDCl_3$) δ 24.3, 32.7, 42.2, 46.1, 54.1, 75.3, 83.2, 152.5, 166.7, 168.1, 170.2, and 171.7. Anal. Calcd for $C_{13}H_{17}N_3O_6$: C, 50.16; H, 5.50; N, 13.50. Found: C, 50.44; H, 5.55; N, 13.45.

Reaction of Ammonium Ylide 29 with DMAD and Rhodium(II) Acetate. A mixture of 0.1 g (0.5 mmol) of ylide **29**, 0.14 g (1 mmol) of DMAD, 0.04 g (0.2 mmol) of Rh(II) acetate and 2 mL of dry toluene was heated at reflux for 30 min. After the solvent was removed under reduced pressure, the crude residue was purified by flash chromatography (ether/hexane 6:1) to yield 0.06 g (32%) of pyridine **30** and 0.02 g (10%) of furan **33** identical in all respects with the samples obtained above.

Computational Considerations All quantum mechanical calculations described were performed with Gaussian-94[52] and Gaussian-98[53] on IBM RS6000 workstations at the Emerson Center, Department of Chemistry, Emory University. In most cases, preliminary structures were generated by force field calculations using MacroModel[54] on local Silicon Graphics Workstations or derived from X-ray structure data.[55] Further preliminary structural manipulations were performed with Molecule (V. 1.2.2) on the Macintosh.[56] The latter platform was subsequently used for cross-network job submission, structure data retrieval, molecular viewing, and graphics generation (e.g., Figures 2, 3, and 5). Thus, all the structures in Scheme 1 were submitted to G-94 or G-98 for preliminary optimization: Becke3LYP/LANL2DZ/3-21G//Becke3LYP/ LANL2DZ/3-21G. Hay and Wadt effective core potentials (ECP2)[57] and the LANL2DZ basis set were placed on Rh atoms, the 3-21G basis set on all other atoms. In the case of the Rh(II) complexes, lack of convergence was initially a problem. With increasingly better start geometries, the structures were ultimately induced to converge to local minima. When optimization was achieved, a single point calculation along with NPA/NBO population analysis[47] was performed: Becke3LYP/LANL2DZ/6-31G*//Becke3LYP/LANL2DZ/3-21G. In a few cases, diffuse functions were also employed in the 3-21+G and 6-31+G* basis sets. Bond orders quoted in the text are those from the Wiberg formulation incorporated in the NPA population analysis.

Acknowledgment. A.P. gratefully acknowledges the National Institute of Health (GM59384-21) and the National Science Foundation (CHE-9806331) for generous support of this work. C.O.K. wishes to acknowledge support from the Austrian Academy of Sciences (ÖAW, APART 319) and the Austrian Science Fund (FWF, Project P-11994-CHE). J.P.S. is grateful to Professor Dennis Liotta (Emory University) for partial support of this work. C.O.K. wishes to thank Dr. Walter M. F. Fabian (Graz) for DFT calculations on ylides **29** and **31**.

Supporting Information Available: ^{1}H NMR spectra for new compounds lacking elemental analyses together with ORTEP drawings for structures **29** and **30** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA001088J

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