times. The extracts were washed with brine, dried, and evaporated to give a crude aldehyde (12). To a suspension of methyltriphenylphosphonium bromide (161 mg, 0.452 mmo) in THF (600 μL) was added 1 M lithium bis(trimethylsilyl)amide in THF (434 μL, 0.434 mmol) at -20 °C. After being stirred for 15 min, the mixture was gradually warmed to room temperature. After being stirred for 15 min, the mixture was cooled to -20 °C, and a solution of 12 (0.328 mmol) in THF (360 μL) was added. The reaction mixture was warmed to room temperature, stirred for 2 h, and quenched with saturated NH_4Cl. The mixture was extracted with ether three times. The extracts were washed with brine, dried, and evaporated to give an oil, which was chromatographed on alumina to yield 2 (47 mg, 58%) as an oil: bp 75 °C/0.4 mmHg (Kugelrohr); $[\alpha]^{24}_D$ +11.3° (c 2.255, $CHCl_3$); IR (neat) 2925, 2855 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (3 H, d, J = 6.4 Hz), 1.29-1.63 (16 H, m), 1.88-2.02 (6 H, m), 2.56-2.67 (1 H, m), 2.71-2.83 (1 H, m), 3.54-3.65 (1 H, m), 4.89-5.03 (2 H, m), 5.72-5.89 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 22.00 (CH_3), 27.27 (CH_2), 28.97 (CH_2), 29.14 (CH_2), 29.55 (CH_2), 29.89 (CH_2), 31.76 (CH_2), 32.14 (CH_2), 32.45 (CH_2), 33.84 (CH_2), 34.50 (CH_2), 37.18 (CH_2), 61.71 (CH), 64.99 (CH), 66.64 (CH), 114.12 (=CH_2), 139.23 (CH=); MS 249, 248, 234, 220, 180, 166, 152, 138, 125, 124; HRMS calcd for $C_{17}H_{31}N$ 249.2457, found 249.2462. Anal. Calcd for $C_{17}H_{31}N$: C, 81.86; H, 12.53; N, 5.62. Found: C, 81.62; H, 12.66; N, 5.80.

Acknowledgment. We are grateful for Dr. T. H. Jones, National Institutes of Health, for spectral data for 2.

Supplementary Material Available: ^1H and ^{13}C NMR spectra for compounds 1, 2, 9, and 10 (8 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Dirhodium Tetraacetate Catalyzed Carbon-Hydrogen Insertion Reaction in N-Substituted α-Carbomethoxy-α-diazoacetanilides and Structural Analogues. Substituent and Conformational Effects[1]

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A series of acyclic α-carbomethoxy-α-diazoacetanilides with different N-substituents, **5a-k**, was prepared and the rhodium(II) acetate catalyzed reactions studied. It was found that the rhodium carbenoid reaction with these compounds occurred only at the N-substituent; when the N-substituent is a propargyl group, rhodium carbenoid addition to the triple bond is favored, resulting, ultimately, in the formation of a bicyclic furan derivative **8**. With an *N*-(*tert*-butyloxycarbonyl)methyl substituent, interception of the rhodium carbenoid by the ester carbonyl oxygen occurred preferentially to give, eventually, 1,4-oxazine derivatives **9** and **9'**. For *N*-alkyl substituents, rhodium carbenoid carbon-hydrogen (C-H) insertion into the alkyl group to give 2-azetidinone and/or 2-pyrrolidinone derivatives was observed. The chemoselectivity of the rhodium carbenoid C-H insertion can be altered by the use of the α-acetyl and α-phenylsulfonyl substituents. In these cases, exclusive C-H insertion at the *N*-aryl moiety resulted to give 2(3*H*)-indolinone products. However, the α-substituent effect on the chemoselectivity of the insertion reaction is easily overridden by conformational effects about the amide N-C(O) bond as revealed by the insertion reactions of the conformationally rigid compounds **20a-c**. The α-substituent effects are reestablished when conformational rigidity is removed, as exemplified by the rhodium carbenoid insertion reactions of compounds **29a,b**.

Introduction

Reactions caused by the dirhodium tetraacetate catalyzed reaction of α-diazo carbonyl compounds are facile, efficient processes that have been the subject of extensive investigations recently.[2] A synthetically useful reaction is the intramolecular rhodium carbenoid mediated carbon-hydrogen (C-H) insertion reaction, and its use in carbocyclic[3] and heterocyclic[4] ring synthesis is well documented.[2a,c] Some characteristics of the reaction are evident, particularly in the area of carbocyclic ring formation. It has been shown that the intramolecular reaction exhibits a strong preference for five-membered ring formation,[3a,i] and more importantly, electronic[3c,f,4c,g] as well as steric and conformational factors[3b,f] can influence the site selectivity of the reaction.

The rhodium(II) acetate catalyzed intramolecular C-H insertion reaction in diazo amides has been shown to be an effective method for the preparation of 2-azetidi-

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0022-3263/92/1957-4404$03.00/0

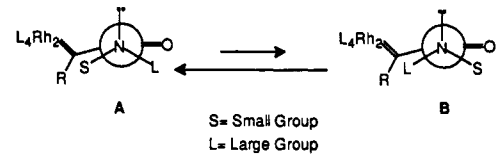
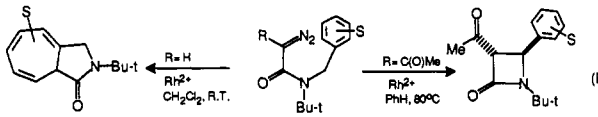


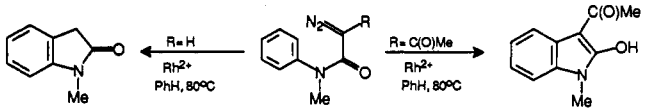
Figure 1.

nones.[4k,n] However, recent studies[4c] have revealed that conformational preferences about the amide N–C(O) bond of the reactive rhodium carbenoid intermediate can influence the site selectivity of the intramolecular rhodium carbenoid mediated C–H insertion in diazoamides. Thus, the preferred reactive conformer is represented by **A** in Figure 1, where the larger N-substituent is placed syn to the sterically less demanding amide carbonyl group. Consequently, the smaller N-substituent is located close to the reactive rhodium carbenoid center for facile C–H insertion. When such a conformational bias is absent, site selectivity is lost and a mixture of products arising from carbon–hydrogen insertion at both N-substituents is obtained.[5]

In addition to conformational effects, the α-substituent on the carbenoid carbon can affect the chemoselectivity of the rhodium carbenoid[5b,6] as exemplified by the example shown in eq 1. This difference was ascribed to the presence of the acetyl group,[5b] which inhibited carbenoid addition to the aromatic ring.

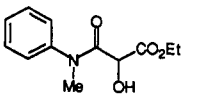


However, in the case of the diazoanilides typified by **1a** (R = H) and **1b** (R = C(O)Me), rhodium(II) acetate catalysis resulted in efficient C–H insertion into the aromatic ring to give 2(3*H*)-indolinone products.[7] No 2-azetidinone



1a; R = H
b; R = C(O)Me
c; R = CO_2Et

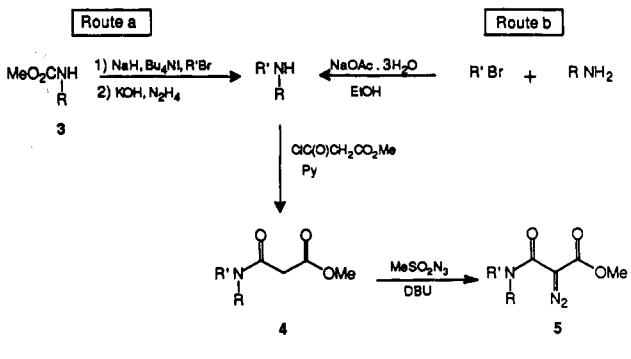
product arising from carbenoid insertion into a *N*-methyl C–H bond was detected. Interestingly, the presence of an α-ester group such as in compound **1c** (R = CO_2Et) resulted in the complete inhibition of the cyclization process. Also, no 2-azetidinone product was observed. The only product isolated from the complex reaction mixture was the hydroxylated compound (**2**, 12%), whose formation was ascribed to the interception of the reactive rhodium carbenoid by trace amounts of water during the reaction.[4e]



2

In contrast to this latter observation, we now show that the rhodium(II) acetate catalyzed reaction of diazoanilides, such as **1** (R = CO_2Me), results in preferential C–H insertion at the nonaromatic N-substituent. 2(3*H*)-Indolinone products arising from formal aryl C–H insertion were not detected. Further studies were conducted to assess the scope and generality of this reaction and to ascertain whether conformational factors, electronic factors, or a combination of factors influence the selectivity of the rhodium carbenoid reaction. These studies show that (i) reaction occurred only at the N-substituent, (ii) the nature of the α-substituent on the rhodium carbenoid carbon can influence the chemoselectivity of the C–H insertion reaction, and (iii) the subtle substituent effects are readily overridden by conformational preferences about the amide N–C(O) bond in the reactive rhodium carbenoid in conformationally rigid systems.

Scheme I



	R	R¹		R	R¹
a	Ph	Me	g	PMP	$(CH_2)_2CO_2Bu$-t
b	Ph	Et	h	PMP	n-Bu
c	PMP	CH_2Ph	i	PMP	$(CH_2)_2Ph$
d	Ph	$CH_2CH{=}CH_2$	j	PMP	$(CH_2)_2CH{=}CH_2$
e	PMP	$CH_2CH{=}CH_2$	k	PMP	$(CH_2)_3CH{=}CH_2$
f	PMP	CH_2CO_2Bu-t			

Results and Discussion

The secondary amines required for the preparation of the diazoanilides **5** were made following either routes a or b in Scheme I. For more reactive alkyl bromides, route a was used. Alkylation of the appropriate carbamate anion with the alkyl bromide, in the presence of tetrabutylammonium iodide and followed by decarbamoylation under basic conditions (KOH, N_2H_4, $(CH_2OH)_2$), gave the secondary amines in good yields. In the preparation of *N*-(*p*-methoxyphenyl)propargylamine, decarbamoylation of the methyl carbamate precursor resulted also in the removal of the propargyl group. This problem was circumvented by alkylation of the *tert*-butyl *N*-(*p*-methoxyphenyl)carbamate anion with propargyl bromide followed, subsequently, by treatment with trimethylsilyl iodide[8] to remove the *tert*-butoxycarbonyl group. For alkyl bromides that did not react under the carbamate alkylation reaction conditions, route b[9] was used to give the secondary amines directly. Since the secondary amines are unstable to light and air, they are immediately reacted with carbomethoxyacetyl chloride to give the anilides **4a–k**. Treatment of the compounds **4** with methanesulfonyl azide[10] in the presence of DBU[4j] (3 to 6 h, 0 °C → rt) efficiently provided the diazoanilides **5a–k**. Also, we found that when dry triethylamine or anhydrous potassium carbonate[11] was

(5) (a) Reference 3c. (b) Doyle, M. P.; Shanklin, M. S.; Oon, S.-M.; Pho, H. Q.; van der Heide, F. R.; Veal, W. R. *J. Org. Chem.* **1988**, *53*, 3384.
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(7) (a) Reference 4c. (b) Doyle, M. P.; Shanklin, M. S.; Pho, H.-Q.; Mahapatro, S. N. *J. Org. Chem.* **1988**, *53*, 1017.
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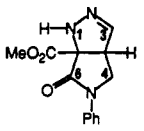
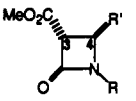
(10) Taber, D. F.; Ruckle, R. E. Jr.; Hennesy, M. J. *J. Org. Chem.* **1986**, *51*, 4077.
(11) Kosikinen, A. M. P.; Munoz, L. *J. Chem. Soc., Chem. Commun.* **1990**, 652.

used as the base, the diazo transfer reaction of these anilides was inefficient. All the diazoanilides are stable compounds except for **5d,e**. Compound **5d** was highly reactive and could not be isolated. During the diazo transfer reaction, the diazo unit underwent facile intramolecular 1,3-dipolar cycloaddition onto the allylic double bond to give the fused pyrazoline **6**[12] in 71% yield. The diazo compound **5e** decomposed slowly on storage and was used immediately once it was prepared.



6



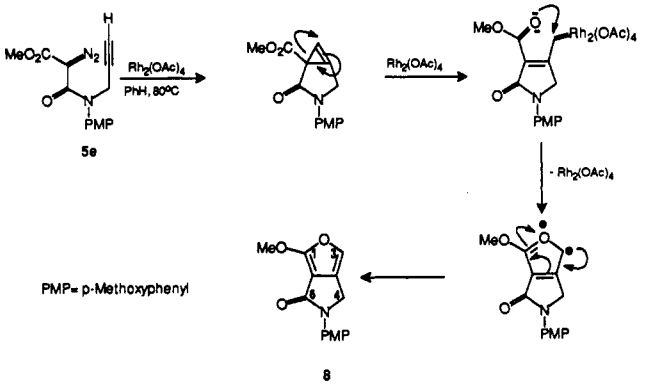
7	R	R'
a	Ph	H
b	Ph	Me
c	PMP	Ph

PMP= p-methoxyphenyl

Dirhodium Tetraacetate Catalyzed Reaction of Acyclic Diazoanilides 5. The rhodium(II) acetate catalyzed reaction of the diazoanilide **5a**, at room temperature, was first investigated. The reaction gave a product (51%) assigned as the 2-azetidinone derivative **7a** based on spectroscopic data. The salient features in its infrared spectrum showed an absorption at 1762 cm^{-1} characteristic of a 2-azetidinone carbonyl function,[13] and an absorption at 1735 cm^{-1} due to the ester carbonyl function. Its ^1H NMR spectrum showed a triplet centered at δ 3.77 (J = 4.9 Hz) due to H-4 and two double doublets (J = 4.9, 2.8 Hz), one centered at δ 3.95 due to H-3 and the other at δ 4.18 ascribed to H-4′. The 2(3*H*)-indolinone product, which could have arisen from formal C–H insertion at the phenyl ring was not detected. Identical results were obtained when the reaction was conducted in refluxing methylene chloride. We were surprised by this result since Durst and co-workers[4e] had found that a similar compound (**1c**) did not undergo any carbon–hydrogen insertion reaction (vide supra). We decided to examine the behavior of the *N*-ethyl analogue **5b**. The rhodium carbenoid mediated insertion reaction provided the *trans*-2-azetidinone compound **7b** ($J_{3,4}$ = 2.4 Hz[14]) in 51% yield. The infrared spectrum of the crude reaction mixture showed only characteristic adsorption bands at 1758 and 1731 cm^{-1}. There were no absorption bands in the range 1660–1690 cm^{-1}, corresponding to the carbonyl absorption for the 2-pyrrolidinone and 2(3*H*)-indolinone derivatives. These products would be generated if C–H insertion occurred at the methyl group of the ethyl unit and at the phenyl ring, respectively.

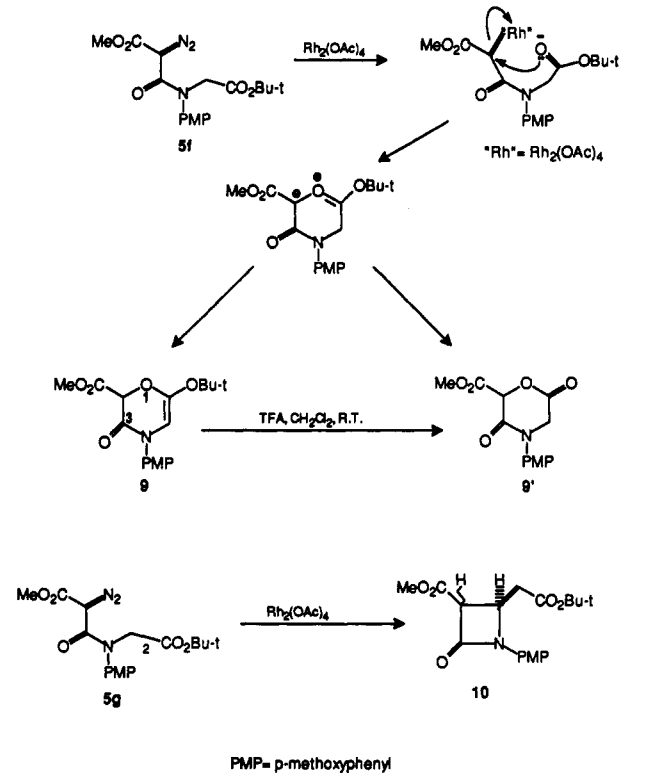
It was reasoned that since rhodium carbenoids behave like electrophiles,[7b] the placement of an electron-donating substituent in the phenyl ring to make it more electron-rich would promote aromatic C–H insertion. Compound **5c** was prepared and subjected to rhodium(II) acetate catalyzed reaction in dry dichloromethane at room temperature and at reflux. The only product isolated was the *trans*-2-azetidinone **7c**[15] ($J_{3,4}$ = 2.8 Hz). The above results encouraged us to study the scope and generality of this reaction.

Scheme II



PMP= p-Methoxyphenyl

Scheme III



PMP= p-methoxyphenyl

We first examined the reaction of ester–diazoanilides **5e–g** to see whether 2-azetidinone formation is still the preferred pathway. Treatment of compound **5e** with rhodium(II) acetate in refluxing benzene led to the formation of the crystalline bicyclic furan derivative **8** in 50% yield (Scheme II). Its formation involves initial addition of the rhodium carbenoid to the triple bond to generate a highly reactive cyclopropene intermediate. Such species have been proposed in the reaction of rhodium carbenoids with alkynes.[16] Rhodium(II) acetate mediated rearrangement of the cyclopropene gives the vinylic metallocarbenoid,[16,17] which is intercepted by the ester carbonyl oxygen to give a carbonyl ylide.[18] This ylide then un-

(12) Compounds are numbered according to the *Ring Systems Handbook*; Chemical Abstracts Service: Columbus, OH, 1984.

(13) Kronenthal, D. R.; Han, C. Y.; Taylor, M. K. *J. Org. Chem.* **1982**, *47*, 2765.

(14) (a) Barrow, K. D.; Spotswood, T. M. *Tetrahedron Lett.* **1965**, 3325. (b) Kagan, H. B.; Basselier, J. J.; Luche, J. L. *Tetrahedron Lett.* **1964**, 941. (c) See Experimental Section.

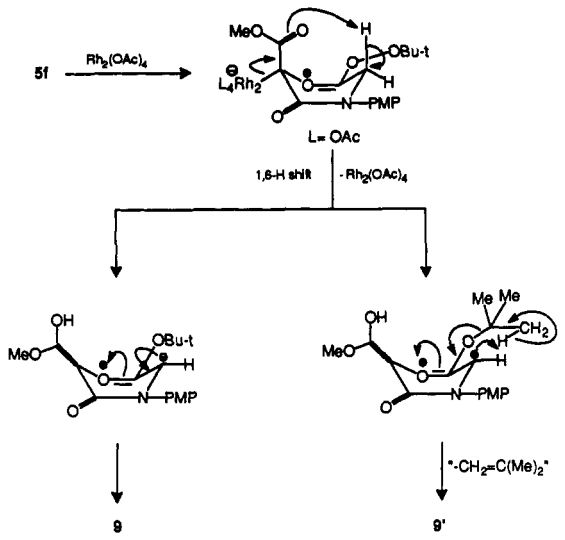
(15) Other analogues with *N*-(*o*- and *p*-methoxyphenyl)methyl, and *N*-(*p*-methylphenyl)methyl also gave the corresponding *trans*-2-azetidinone derivatives (45–50%). When the substituent is *N*-(2-furanyl)methyl, the reaction gave an intractable mixture of products.

(16) (a) Padwa, A.; Chiacchio, U.; Garreau, Y.; Kassir, J. M.; Krumpe, K. E.; Schoffstall, A. M. *J. Org. Chem.* **1990**, *55*, 414. (b) Hoye, T. R.; Dinsmore, C. J.; Johnson, D. S.; KorKowski, P. F. *J. Org. Chem.* **1990**, *55*, 4518. (c) Padwa, A.; Krumpe, K. E.; Gareau, Y.; Chiacchio, U. *J. Org. Chem.* **1991**, *56*, 2523. (d) Hoye, T. R.; Dismore, C. *J. Tetrahedron Lett.* **1991**, *32*, 3755. *J. Am. Chem. Soc.* **1991**, *113*, 4343. (e) Padwa, A.; Kassir, J. M.; Xu, S. L. *J. Org. Chem.* **1991**, *56*, 6971.

(17) Muller, P.; Pautex, N.; Doyle, M. P.; Bagheri, V. *Helv. Chim. Acta* **1990**, *73*, 1233.

(18) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22 and references cited. (b) Chen, C. W.; Beak, P. W. *J. Org. Chem.* **1986**, *51*, 3325 and references cited.

Chart I



dergoes electron rearrangement to give the observed product 8.

The reaction of compounds **5f,g** proved interesting (Scheme III). For **5f**, rhodium carbenoid mediated reaction gave only the readily separable, 1,4-oxazine derivatives **9** (42%) and **9'** (39%) when conducted either in refluxing dichloromethane or in benzene. Further corroboration of the structural assignment was provided by the efficient conversion (89%) of the enol–ether **9** to compound **9'** by treatment with trifluoroacetic acid in dichloromethane.

The formation of compound **9** is envisaged to occur via a metal-stabilized, six-membered-ring carbonyl ylide[18] (Chart I) formed from the interception of the transient rhodium carbenoid by the carbonyl oxygen of the ester function.[19] This ylide reacts via a precedented 1,6-hydrogen shift[20] to give a new transient ylide, which then undergoes electron rearrangement to produce the enol–ether **9** and loss of the *tert*-butyl group to yield the 1,4-oxazine derivative **9'**. A plausible mechanistic rationalization for the latter process entails the transient ylide to undergo an E_i-type[21a] elimination of 2-methylpropene as shown in Chart I.[21b] The absence of the 2-azetidinone product indicates that carbonyl ylide formation is the kinetically favored pathway in this system, despite the presence of the bulky ester *tert*-butyl group that has been shown to inhibit carbonyl ylide formation.[22]

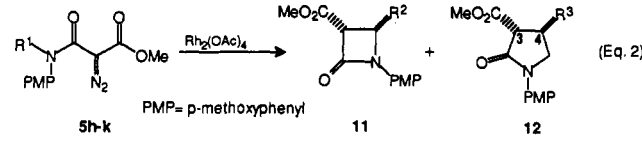
The rhodium carbenoid reaction of the homologous diazo ester **5g** (Scheme III) in either refluxing dichloromethane or benzene gave the 2-azetidinone derivative **10** (53%) as the only detectable product. Compound **10** was obtained as an inseparable mixture of cis and trans stereoisomers in a ratio of 1.0:1.5. This ratio is based on the integration of the H-3 doublet of the cis isomer centered at δ 4.35 ($J_{3,4}$ = 5.7 Hz) and of the trans isomer centered at δ 4.02 ($J_{3,4}$ = 2.3 Hz). The absence of the 2-pyrrolidinone derivative arising from metallocarbenoid insertion into the methylene C–H bond α to the *tert*-butyl ester group is consistent with the literature[3c,4c] that, in this type of compound, the ester function deactivates the α C–H bonds to rhodium carbenoid insertion; the β C–H bonds are not deactivated due to the activating effect of the amide nitrogen.[4c]

Table I. Dirhodium Tetraacetate Catalyzed Decomposition of Compounds 5h–k

compd 5	reaction conditions[a] (h)	2-azetidinone[b] 11, R^2	2-pyrrolidinone[b] 12, R^3
h	A (18)	$CH_2CH_3CH_3$ (6%)	CH_2CH_3 (70%)
i	B (2.5)	CH_2Ph (0%)	Ph (84%)
i	C (2.0)	CH_2Ph (5%)	Ph (73%)
j	B (2.5)	not detected	$CH{=}CH_2$ (81%)
k	A (18)	$(CH_2)_2CH{=}CH_2$ (13%)	$CH_2CH{=}CH_2$ (54%)
k	B (1.5)	$(CH_2)_2CH{=}CH_2$ (17%)	$CH_2CH{=}CH_2$ (59%)

[a] All reactions were conducted with ester–diazoanilide concentrations of 0.02–0.05 M. [b] All yields refer to isolated, chromatographically pure compounds.

Further investigations into the rhodium(II) acetate catalyzed decomposition of the diazoanilides **5h–k** (eq 2) were carried out in dichloromethane either at room temperature (26 °C, A) or at reflux (B), and in refluxing dry benzene (C). The results are collected in Table I.



It is clear from Table I that the diazoanilides with longer-chained alkyl substituents, R^1, show a strong kinetic preference for 2-pyrrolidinone (**12**) over 2-azetidinone (**11**) ring formation. In the case of compound **5j**, the 2-azetidinone derivative, **11j**, was not detected. Furthermore, the azabicyclo[4.1.0]heptane derivative, which would be formed via the intramolecular addition of the rhodium carbenoid to the double bond, was not observed. As expected, the rhodium carbenoid reaction in the diazoanilide **5k** did not result in the formation of a six-membered-ring product. The reaction temperature was found to have no effect on the course of the C–H insertion reaction except to decrease the reaction time. The reactions also did not give 2(3*H*)-indolinone products resulting from formal C–H insertion into the electron-rich *p*-methoxyphenyl (PMP) group. This result is synthetically useful because the *p*-methoxyphenyl group is a practical nitrogen protecting group.[13,24]

The stereochemistry of the 2-azetidinone products was assigned as trans, again based on the observed vicinal coupling constant[14c] of $J_{3,4}$ = 2.1–2.8 Hz.[14] The 2-pyrrolidinone derivatives were assigned the trans stereochemistry based on the experimental H-3 vicinal coupling constant, which falls in the range $J_{3,4}$ = 7.8–9.4 Hz.[25] This stereochemical assignment was substantiated by difference NOE measurements[26] on the representative compound **12h** ($J_{3,4}$ = 7.8 Hz).

Previous reports of the rhodium(II) acetate catalyzed reaction of α-diazo- and α-acetyl-α-diazoacetanilides,[4e,7b]

(19) Doyle, M. P.; Taunton, J.; Pho, H.-Q. *Tetrahedron Lett.* **1989**, *30*, 5397.

(20) (a) Lottes, A. C.; Landgrebe, J. A.; Larsen, K. *Tetrahedron Lett.* **1989**, *30*, 4089. (b) Reference 4c.

(21) (a) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley-Interscience: New York, 1985; Chapter 17, pp 899–905. Statistical factors generally favor such a process; there are nine β-hydrogens available for abstraction by the carbanion. (b) The thermal or intermolecular mediated elimination of the *tert*-butyl group cannot be ruled out.

(22) Cf. ref 19. It has been shown that the success of the interception of the rhodium carbenoid by the ester carbonyl oxygen is also dependent on the nature of the ligands on the rhodium catalyst. See also ref 4c.

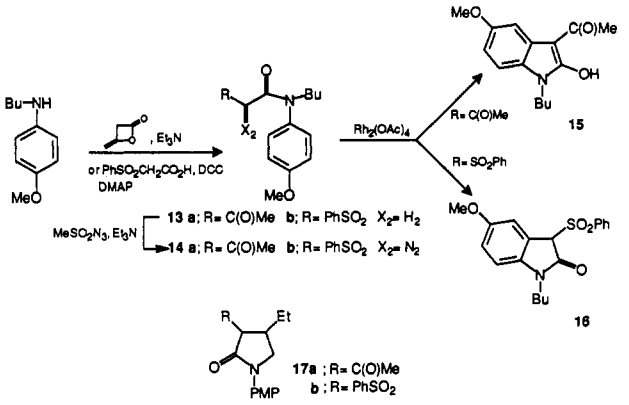
(23) Cf. ref 4f. In the carbocyclic area, the formation of the bicyclo[3.1.0]hexane system is a favored process.

(24) The *N*-(*p*-methoxyphenyl) group can be efficiently removed from the 2-pyrrolidinone using CAN in aqueous acetonitrile. Wee, A. G. H. Unpublished observations.

(25) Cf. Byers, J. H.; Gleason, T. G.; Knight, K. S. *J. Chem. Soc., Chem. Commun.* **1991**, 354 and references cited. For 2-pyrrolidinone derivatives, $J_{3,4}$(trans) = 6.9 Hz. Cooper, J.; Knight, D. W.; Gallagher, P. T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 705 and references cited. For a 3,4-disubstituted pyrrolidine, $J_{3,4}$(trans) = 8.1 Hz.

(26) See the supplementary material.

Scheme IV



Scheme V

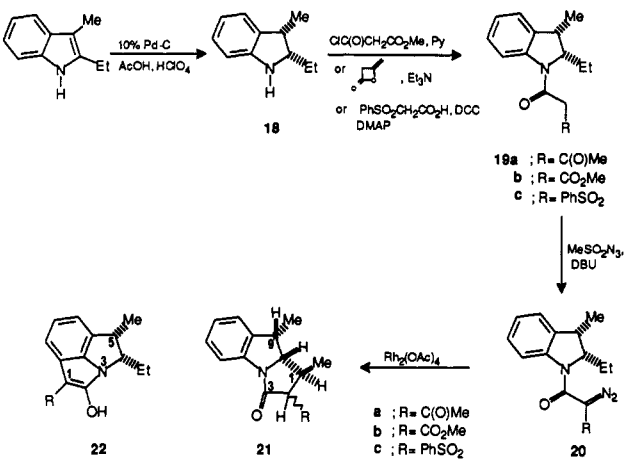
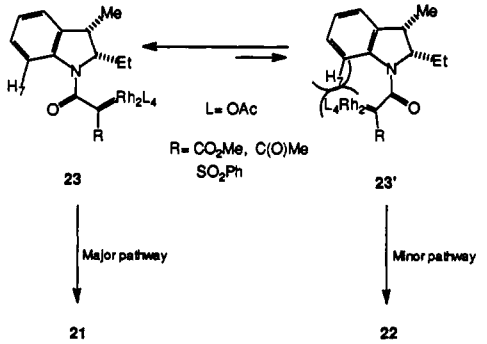


Chart II



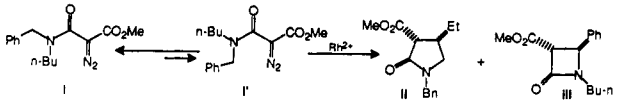
such as **1a** and **b** (vide supra), have shown that these compounds invariably give 2(3*H*)-indolinone derivatives resulting from formal aromatic C–H insertion. However, in these studies, the N-substituents were either benzyl, ethyl, or methyl groups. Since our results show that there is a preference for 2-pyrrolidinone formation with longer-chained *N*-alkyl substituents, we decided to compare the outcome of the rhodium(II) acetate catalyzed reaction of the *N*-butyldiazoanilides **14a,b** to that of **5h** under identical reaction conditions. It was anticipated that the *N*-butyl substituent would serve to compete with the aromatic ring for the reactive rhodium carbenoid resulting in the formation of 2(3*H*)-indolinone and 2-pyrrolidinone (**17**) derivatives. The requisite diazoanilides were readily prepared from *N*-butyl-*p*-methoxyanisidine (Scheme I, route a). Thus, acylation of the aniline with diketene[27] provided **13a**, which was treated with methanesulfonyl azide[10] to give **14a** (Scheme IV). Reaction of the same amine with α-(phenylsulfonyl)acetic acid[28]–DCC under Steglich conditions[29] yielded **13b**. Subsequent diazo transfer[10] reaction provided compound **14b**. The rhodium carbenoid mediated reaction of **14a,b** in methylene chloride at room temperature[30] produced only the 2-hydroxyindole, **15**, and 2(3*H*)-indolinone, **16**, respectively.

Taking the above results together suggests that the nature of the substituent on the rhodium carbenoid dictates the chemoselectivity of the insertion reaction of the diazoanilides, **5**, and conformational effects may not be important.[31,32] A plausible explanation is that the substituent on the metallocarbenoid carbon modifies the electrophilic character of the carbenoid center; the metallocarbenoid carrying an acetyl or the phenylsulfonyl group is more electrophilic than an ester-substituted one and, therefore, participates efficiently in an electrophilic aromatic substitution[7b]-type reaction to give the observed products. For the ester-substituted rhodium carbenoid, a C–H insertion route involving a two-electron, three-centered species such as that proposed by Taber[33] is envisaged.

Rhodium Carbenoid C–H Insertion in Geometrically Constrained Systems. The unexpected and important influence of the carbenoid substituent on the chemoselectivity of rhodium carbenoid C–H insertion in acyclic diazo compounds led us to examine the C–H insertion reaction of some geometrically constrained systems exemplified by the 2,3-dihydroindole diazo amides **20** and the tetrahydroquinoline diazo amides **28**. In these systems, the phenyl and alkyl units would be held in proximity to the reactive rhodium carbenoid center, and we were interested to see whether their C–H insertion reactions would still show chemoselectivities that are dependent on the nature of the carbenoid substituent.

2,3-Dihydroindole Diazo Amides. The known 2-ethyl-3-methylindole[34] was hydrogenated over 10% palladized charcoal at room temperature to give the corresponding 2,3-dihydroindole **18** (Scheme V). The vicinal coupling constant of $J_{2,3}$ = 7.7 Hz observed for H-3, in **18**, after decoupling of the C-3 methyl doublet centered at δ 1.11 indicates[35] that the relative stereochemistry at C-2 and C-3 is cis. The amides **19a–c** were obtained, from **18**, using the previously mentioned conditions for acylation and

(27) Clemens, R. J. *Chem. Rev.* **1986**, *86*, 241.
(28) Pasto, D. J.; McMillan, D.; Murphy, T. *J. Org. Chem.* **1965**, *30*, 2688.
(29) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.
(30) The reactions were also conducted in dry refluxing dichloromethane. Identical results were obtained, but in shorter reaction times.
(31) The rhodium carbenoid species derived from the diazoanilides **5** may have low amide N–C(O) rotational barriers, which would result in free rotation about the N–C(O) bond axis and at a rate far greater than rhodium carbenoid C–H insertion. The chemoselectivity of the rhodium carbenoid ultimately determines the site of C–H insertion. We thank a reviewer for this suggestion.
(32) We also prepared the diazo compound (i). Unlike the compounds studied above, the phenyl moiety in (i) is now separated from the nitrogen by a methylene unit. The rhodium(II) acetate catalyzed C–H insertion reaction in dichloromethane (rt and reflux) gave a mixture (73%) of the 2-pyrrolidinone (ii) and the 2-azetidinone (iii) in a ratio of 1.7:1.0. This suggests that in this system, the conformational preferences about the amide N–C(O) bond in the reactive rhodium carbenoid determines the site of C–H insertion.



(33) Reference 3f, footnote 31.
(34) Naruse, Y.; Ito, Y.; Inagaki, S. *J. Org. Chem.* **1991**, *56*, 2256. (b) Noyce, D. S.; Vergilio, J. A. *J. Org. Chem.* **1972**, *37*, 2643.
(35) Lanzilotti, A. E.; Littell, R.; Fanshawe, W. J.; McKenzie, T. C.; Lovell, F. M. *J. Org. Chem.* **1979**, *44*, 4809 and references cited.

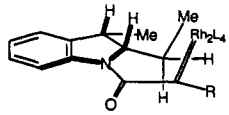
followed subsequently by diazo transfer to provide the diazo substrates **20a–c**.

The rhodium(II) acetate catalyzed reaction of **20a**, in methylene chloride at room temperature or at reflux, gave two products, *trans*-**21a** and **22a** (87%), in a ratio of 2.4:1.0; compound **21a**[36] was formed by rhodium carbenoid insertion into a methylene C–H bond of the ethyl unit and **22a** was formed via C–H insertion into the phenyl moiety. On the other hand, compounds **20b,c** only gave high yields (99%) of only crystalline **21b,c**[37] under the same reaction conditions, and as inseparable mixture of cis and trans isomers. The ratio of the isomers was determined by integration of the H-9a signals in **21b** (trans:cis, 95:5) and **21c** (trans:cis, 96:4).

A notable resonance in the ^{1}H NMR of **21a–c** is the low-field doublet due to H-5. This proton is coplanar to and is deshielded by the amide carbonyl,[38] serving to further corroborate our structural assignment for these compounds. The same doublet was not observed in **21c** since it resonated in the region δ 7.41–7.70 where the phenyl protons of the phenylsulfonyl moiety also occurred.

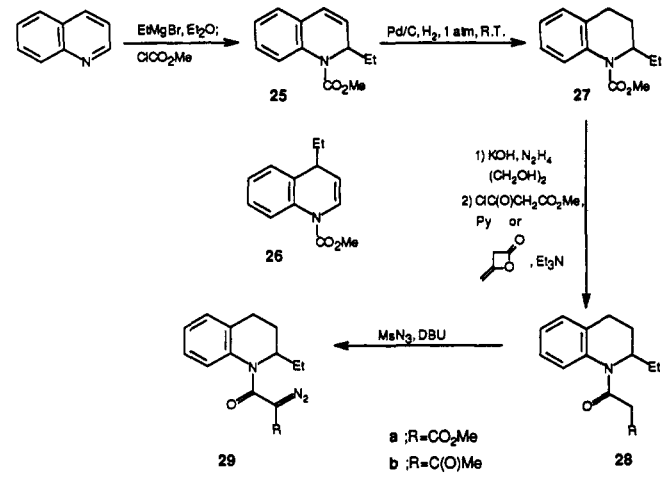
It is interesting to note the reversal of the chemoselectivity exhibited by the acetyl- and phenylsulfonyl-substituted rhodium carbenoids. This unexpected outcome can be rationalized by considering the reactions as proceeding via two reactive conformers **23** and **23′** (Chart II). The 2,3-dihydroindole nucleus is inherently planar. The rhodium carbenoid/amide unit is coplanar to the 2,3-dihydroindole nucleus because of the interaction of the nitrogen lone pair of electrons with the amide carbonyl π-system. This results in a destabilizing steric interaction between the rhodium carbenoid moiety and H-7 of the phenyl unit in confomer **23′**. In conformer **23**, the interaction between the rhodium carbenoid unit and the C-2 ethyl group is minimal because the ethyl group does not intrude into the steric region of the rhodium carbenoid. Therefore, rhodium carbenoid C–H insertion occurs via the preferred conformer **23** leading to products of type **21**. Interestingly, the 2-azetidinone derivative, which would be formed from C–H insertion into the C_2–H bond, was not observed. This may due to electronic factors, whereby placement of the rhodium carbenoid in proximity to the C_2–H bond would result in the disruption of the overlap of the nitrogen lone pair of electrons and the amide carbonyl π-system.

The preference for the formation of the trans stereochemistry at C-1/C-2 ($J_{1,2} \geq 10.0$ Hz) in these reactions is noteworthy. This suggests that the rhodium carbenoid moiety interacts with the methylene C–H bond in a chair-like transition state,[39] such as **24**, wherein the methyl group of the ethyl moiety occupies a pseudoequatorial position.



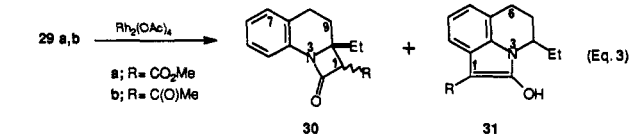
24

Scheme VI



Tetrahydroquinoline Diazo Amides. We next examined the rhodium(II) acetate catalyzed reaction of the tetrahydroquinoline diazoamides **29a,b**. These compounds were prepared from quinoline as depicted in Scheme VI. The reaction of ethylmagnesium bromide with quinoline[40] followed by quenching with methyl chloroformate was the most reliable and direct way to introduce the ethyl moiety into the C-2 position of quinoline. However, the reaction was not completely regiospecific, and a mixture of regioisomeric dihydroquinolines **25** and **26** was formed in a combined yield of 69%. Careful chromatographic separation afforded the desired compound **25** (57%) and the regioisomer **26** (11%). Compound **25** was hydrogenated over 5% palladized charcoal to give **27**, which was then decarbamoylated and acylated (α-carbomethoxyacetyl chloride or diketene) in the usual way to give the diazo precursors **28a** (71%) and **28b** (92%). Subsequent diazo transfer reaction[10] furnished the diazo amides **29a** (66%) and **29b** (72%).

Treatment of **29a** with rhodium(II) acetate (eq 3) gave the 2-azetidinone derivative **30a** (IR ν_{max} 1768 and 1734 cm^{-1}) in 85%. Its ^{1}H NMR showed it to be a 1:1 mixture of diastereoisomers based on the integration of the H-1 singlets at δ 3.88 and 4.05. There was no aromatic C–H



insertion product detected in this reaction. Attempted epimerization of the ester function using a catalytic quantity of sodium methoxide in dry methanol at room temperature or Krapcho decarboxylation[41] only led to an intractable mixture of products. The acetyl-substituted compound **29b**, however, gave the aromatic C–H insertion compound **31b** as the major product (88%). A very small amount (<2%) of a compound, tentatively assigned the 2-azetidinone structure **30b** (IR ν_{max} 1768 cm^{-1} and ^{1}H NMR similar to that of **30a**), was also isolated.

The above results suggest that substituent effects, as observed in the acyclic systems, again determine the chemoselectivity of the C–H insertion reaction. This outcome can be understood when the two reactive conformers **32** and **32′** (Chart III) are considered. It is well documented that the piperidine moiety of the tetra-

(36) *cis*-**21a** was not observed. There may be facile epimerization to the thermodynamically stable *trans*-**21a** under the reaction conditions due to the acidity of H-2.

(37) The success of this cyclization is noteworthy in light of a recent report (Jones, G.; Moody, C. J.; Padwa, A.; Kassir, J. M. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1721) on the unsuccessful attempts in effecting rhodium carbenoid cyclization in *N*-substituted indolyl diazo ketones.

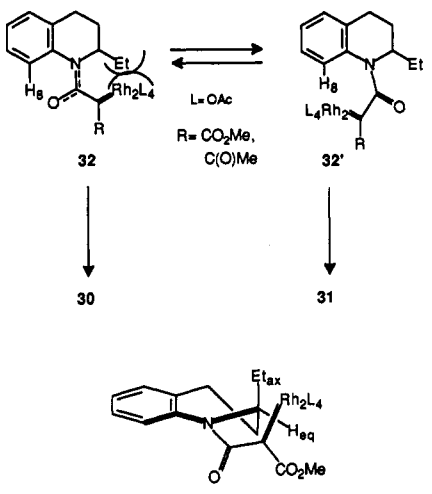
(38) Mclean, S.; Trotz, U. O.; Macdonald, C. J.; Reynolds, W. F.; Wood, D. J. *Can. J. Chem.* **1971**, *49*, 1638.

(39) Taber, D. F.; Raman, K.; Gaul, M. D. *J. Org. Chem.* **1987**, *52*, 28. (b) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5953.

(40) Otsuji, Y.; Yutani, K.; Imoto, E. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 520.

(41) For a review: Krapcho, A. P. *Synthesis* **1982**, *805*, 893.

Chart III



hydroquinoline nucleus adopts a half-chair conformation that is also conformationally mobile.[42] In conformer **32**, the planar amide functionality would bring the rhodium carbenoid unit close to an equatorially oriented ethyl group. This results in a destabilizing $A^{1,3}$-type[43] interaction. A relief of this steric strain is possible when the ethyl group adopts a pseudoaxial position. For conformer **32'**, the rhodium carbenoid unit is held either above or below the plane of the phenyl moiety due to the conformational flexibility of the piperidine ring. This means that the destabilizing steric interaction between the rhodium carbenoid and H-8 of the phenyl ring is avoided. The two conformers may be comparable in energy and present in equal amounts. The results suggest that it is the substituent on the rhodium carbenoid carbon that ultimately determines the chemoselectivity of the metallocarbenoid. The formation of the 2-azetidinone **30a** is envisioned to proceed via conformer **32** (R = CO_2Me) with a pseudoaxial ethyl group; insertion occurs into the well-positioned pseudoequatorial C–H bond.[3b,44]

Conclusions

Our results reveal that acyclic N-substituted α-carbomethoxy-α-diazoacetanilides of type **5** undergo rhodium(II) acetate catalyzed reaction preferentially at the nonaromatic N-substituent. With a *N*-propargyl substituent, the rhodium carbenoid is found to add to the triple bond resulting in the formation of a bicyclic furan **8**. In the case of an *N*-(*tert*-butyloxycarbonyl)methyl group, interception of the rhodium carbenoid by the ester carbonyl oxygen is the favored pathway, resulting in the production of 1,4-oxazine derivatives. When the N-substituent is an alkyl group, rhodium carbenoid C–H insertion results in the formation of 2-azetidinone and/or 2-pyrrolidinone derivatives, and as the chain length increases, there is a greater preference for the formation of 2-pyrrolidinone derivatives.

It is also found that the α-substituent in the rhodium carbenoid can determine the chemoselectivity of the C–H insertion reaction. The α-carbomethoxy group promotes C–H insertion at the nonaromatic N-substituent, whereas the α-acetyl and α-phenylsulfonyl substituents direct C–H insertion to the *N*-aryl moiety. However, this substituent effect is readily overridden by conformational effects about the amide N–C(O) bond as exemplified in the reactions of the conformationally rigid indoline diazo amides **20**. When conformational mobility is reintroduced, as in the tetrahydroquinoline diazo amides **29**, the α-substituent on the rhodium carbenoid is found to control the chemoselectivity of the C–H insertion reaction.

Since these results are of synthetic utility, further studies in this area and applications of these techniques to alkaloid synthesis are in progress.

Experimental Section

General. Melting points were determined on a Kofler hot-stage melting point apparatus and are uncorrected. Infrared spectra were recorded using a Perkin-Elmer 1600FT infrared spectrophotometer. NMR spectra were obtained at 200.00 MHz on a Bruker AC200 QNP at the University of Regina; chemical shifts are reported in parts per million (δ) relative to the appropriate reference signals. ^1H NMR (200 MHz) spectra were recorded in deuteriochloroform ($CDCl_3$) using tetramethylsilane (δ_H 0.0) or residual chloroform (δ_H 7.24) as reference; multiplicities of signals are given as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad, and coupling constants are given in hertz. Proton assignments were based on homonuclear decoupling experiments and, where appropriate, supported by homonuclear 2D-COSY experiments. ^{13}C and ^{13}C DEPT-135 NMR (50.32 MHz) were recorded in $CDCl_3$ using the $CDCl_3$ signal at δ 77.0 as reference. The ^{13}C DEPT-135 pulse sequence[45] inverted only the CH_2s (designated –); the CHs and CH_3s remained upright. Quaternary carbons are not seen. Microanalyses were performed at the Microanalytical Department, University of Alberta, and at the University of Regina, Canada. Low-resolution electron-impact (70 eV) mass spectra were recorded at the University of Saskatchewan on an VG-MS-12 spectrometer. Reaction progress was monitored by thin-layer chromatography on Merck silica gel 60_{F254} precoated (0.25 mm) on aluminum-backed sheets. Petroleum ether used is the fraction with bp 35–60 °C. Chromatographic purification means flash chromatography[46] performed on Merck silica gel 60 (230–400 mesh). Air- and moisture-sensitive reactions were conducted under a static pressure of argon. Dirhodium tetraacetate was prepared from rhodium trichloride.[47] Methanesulfonyl azide was prepared from methanesulfonyl chloride and sodium azide.[10] DBU, dichloromethane, benzene, and acetonitrile were dried by distillation from calcium hydride, and methanol was dried by distillation from magnesium methoxide.

Dirhodium Tetracetate Catalyzed Reaction of the Diazo Compounds 5. The appropriate diazoanilide **5** (1 mmol) was dissolved either in dry CH_2Cl_2 or PhH, under N_2. $Rh_2(OAc)_4$ (5 mol %) was added to the solutions, and the mixture was stirred at rt or immediately immersed in an oil bath set at 50 °C (CH_2Cl_2) or at 90 °C (PhH). There was evolution of N_2 gas before the mixture started refluxing, and the color of the mixture changed from yellow to green (sometimes brown). The mixture was refluxed for 3–4 h, cooled to rt, filtered, and evaporated. The residue was flash chromatographed.

3-Carbomethoxy-1-phenyl-2-azetidinone (7a). Yield: 51%. Mp (ether–petroleum ether): 67–69 °C. IR: ν_{max} (Nujol) 1762, 1735, 1599, 1501 cm^{-1}. ^1H NMR: δ_H 3.77 (t, 1 H, J = 4.9 Hz, H-4), 3.80 (s, 3 H, OMe), 3.95 (dd, 1 H, J = 4.9, 2.8 Hz, H-3), 4.18 (dd, 1 H, J = 4.9, 2.8 Hz, H-4'), 7.06–7.18 (m, 1 H, PhH), 7.28–7.38 (m, 4 H, PhH). ^{13}C NMR: δ_C 41.38 (–), 52.82, 116.43, 124.48, 129.22, 137.78, 158.78, 167.28. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.36; H, 5.41; N, 6.83. Found: C, 64.49; H, 5.41; N, 6.78.

***trans*-3-Carbomethoxy-4-methyl-1-phenyl-2-azetidinone (7b).** Yield: 51%. Mp (ether–petroleum ether): 87–89 °C. IR: ν_{max} (Nujol) 2997, 2943, 1758, 1735, 1599, 1501 cm^{-1}. ^1H NMR: δ_H 1.45 (d, 3 H, J = 6.1 Hz, Me), 3.63 (d, 1 H, J = 2.6 Hz, H-3),

(42) Nagarajan, K.; Nair, M. D.; Pillai, P. M. *Tetrahedron* **1967**, *23*, 1683.
(43) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.
(44) The preference for the formation of the 2-azetidinone product is also in accord with a similar observation by Doyle and co-workers.[5b] They reported that the rhodium(II) acetate catalyzed reaction of *N*-(α-diazoacetyl)-*trans*-2,6-dimethylpiperidine gave mainly the 2-azetidinone product.
(45) Doddrell, D. M.; Pegg, D. T.; Bendall, M. R. *J. Magn. Reson.* **1982**, *48*, 323.
(46) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(47) Legzdins, P.; Mitchell, R. W.; Rempel, G. L.; Ruddick, J. D.; Wilkinson, G. *J. Chem. Soc. A* **1970**, 3322.

3.67 (s, 3 H, OMe), 4.34 (dq, 1 H, J = 6.1, 2.6 Hz, H-4), 6.95–7.10 (m, 1 H, PhH), 7.20–7.30 (m, 4 H, PhH). ^{13}C NMR: δ_C 17.68, 50.86, 52.66, 60.68, 117.08, 124.32, 129.18, 136.90, 158.70, 167.00. Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.73; H, 5.98; N, 6.39. Found: C, 65.80; H, 5.98; N, 6.51.

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-phenyl-2-azetidinone (7c).** Yield: 41%. IR: ν_{max} (film) 2954, 1760, 1736, 1513 cm^{-1}. ^{1}H NMR: δ_H 3.72 (s, 3 H, OMe), 3.80 (s, 3 H, OMe), 3.98 (d, 1 H, J = 3.4 Hz, H-3), 5.30 (d, 1 H, J = 3.4 Hz, H-4), 6.79 (d, 2 H, J = 8.5 Hz, Ar H), 7.22 (d, 2 H, J = 8.5 Hz, Ar H), 7.37 (s, 5 H, PhH). ^{13}C NMR: δ_C 52.50, 55.00, 57.50, 63.30, 114.33, 118.55, 126.19, 129.03, 129.28, 136.20, 156.00, 167.00. Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.43; H, 5.51; N, 4.50. Found: C, 69.72; H, 5.60; N, 4.43.

1-Methoxy-5-(*p*-methoxyphenyl)-6-oxopyrrolidino[3,4-*b*]furan (8). Yield: 50%. Mp (ether–petroleum ether): 128–130 °C. IR: ν_{max} (Nujol) 1686, 1678, 1636, 1610, 1560, 1542, 1508 cm^{-1}. ^{1}H NMR: δ_H 3.81 (s, 3 H, OMe), 4.33 (s, 3 H, OMe), 4.66 (s, 2 H, NCH_2), 6.73 (s, 1 H, furan-H), 6.91 (d, 2 H, J = 7.2 Hz, Ar H), 7.54 (d, 2 H, J = 7.2 Hz, Ar H). ^{13}C NMR: δ_C 46.09 (–), 55.47, 60.53, 96.56, 114.17, 117.00, 122.72, 125.18, 133.10, 156.25, 156.54, 161.60. Anal. Calcd for $C_{14}H_{13}NO_4$: C, 64.84; H, 5.06; N, 5.41. Found: C, 64.99; H, 5.25; N, 5.27.

6-*tert*-Butoxy-2-carbomethoxy-4-(*p*-methoxyphenyl)-3-oxo-2*H*-1,4-oxazine (9). Yield: 42%. Mp (EtOAc–petroleum ether): 88–89.5 °C. IR: ν_{max} (Nujol) 3118, 1761, 1703, 1676, 1607, 1511 cm^{-1}. ^{1}H NMR: δ_H 1.41 (s, 9 H, t-Bu), 3.80 (s, 3 H, CO_2Me), 3.89 (s, 3 H, OMe), 5.19 (s, 1 H, H-5), 5.48 (s, 1 H, H-2), 6.90 (d, 2 H, J = 7.6 Hz, Ar H), 7.25 (d, 2 H, J = 7.6 Hz, Ar H). ^{13}C NMR: δ_C 28.41, 53.03, 55.42, 77.17, 82.47, 97.36, 114.27, 126.27, 131.67, 147.44, 157.13, 158.44, 166.32. Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.87; H, 6.31; N, 4.19. Found: C, 60.87; H, 6.34; N, 4.16. **2-Carbomethoxy-4-(*p*-methoxyphenyl)-3,6-dioxo-2,5-dihydro-1,4-oxazine (9′).** Yield: 39%. Mp (EtOAc–petroleum ether): 132–134 °C. IR: ν_{max} (Nujol) 3050, 1778, 1754, 1693, 1600, 1575, 1514 cm^{-1}. ^{1}H NMR: δ_H 3.80 (s, 3 H, CO_2Me), 3.90 (s, 3 H, OMe), 4.32 (d, 1 H, J = 18.0 Hz, H-5), 4.71 (d, 1 H, J = 18.0 Hz, H-5′), 5.45 (s, 1 H, H-2), 6.91 (d, 2 H, J = 7.6 Hz, Ar H), 7.20 (d, 2 H, J = 7.6 Hz, Ar H). ^{13}C NMR: δ_C 50.47 (–), 53.88, 55.37, 77.38, 114.51, 125.89, 131.35, 158.76, 159.19, 163.82, 165.60. Anal. Calcd for $C_{13}H_{13}NO_6$: C, 55.90; H, 4.69; N, 5.02. Found: C, 55.87; H, 4.85; N, 4.95.

3-Carbomethoxy-4-((*tert*-butoxycarbonyl)methyl)-1-(*p*-methoxyphenyl)-2-azetidinone (10). Yield: 53%. IR: ν_{max} (neat) 1763, 1733, 1654, 1627, 1513 cm^{-1}. ^{1}H NMR: δ_H 1.41 and 1.42 (s, 9 H, t-Bu), 2.58 (dd, J = 16.1, 9.3 Hz) and 2.92 (dd, J = 16.5, 8.6 Hz) (1 H, $CHCO_2$), 3.02 (dd, J = 16.1, 3.8 Hz) and 3.05 (dd, J = 16.5, 4.6 Hz) (1 H, $CHCO_2$), 3.77 and 3.80 (s, 3 H, CO_2Me), 3.82 (s, 3 H, OMe), 4.02 (d, J = 2.3 Hz) and 4.35 (d, J = 5.7 Hz) (1 H, H-3), 4.55–4.67 (m, 1 H, H-4), 6.85 (d, 2 H, J = 7.6 Hz, Ar H), 7.29 (d, 2 H, J = 7.6 Hz, Ar H). Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.86; H, 6.64; N, 4.01. Found: C, 62.05; H, 6.85; N, 4.08.

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-propyl-2-azetidinone (11h).** Yield: 5.6%. IR: ν_{max} (film) 2958, 2874, 1760, 1731, 1513 cm^{-1}. ^{1}H NMR: δ_H 1.00 (t, 3 H, J = 7.0 Hz, Me), 1.47–1.51 (m, 3 H, CH_2 and CH), 2.02–2.20 (m, 1 H, CH), 3.78 (d, 1 H, J = 2.6 Hz, H-3), 3.80 (s, 6 H, OMe), 4.32 (dt, 1 H, J = 8.8, 2.6, 2.6 Hz, H-4), 6.90 (d, 2 H, J = 7.2 Hz, Ar H), 7.35 (d, 2 H, J = 7.2 Hz, Ar H). ^{13}C NMR: δ_C 13.86, 18.23, 33.40, 52.71, 55.20, 55.50, 58.93, 114.45, 118.99, 129.41, 156.48, 158.70, 167.54. MS: m/z (rel intensity) 277 (M^+, 23.9), 149 ($M^+ - C_7H_{12}O_2$, 100), 134 ($M^+ - C_7H_{12}O_2 - CH_3$), 22.5), 128 ($C_7H_{12}O_2$, 0.9), 97 ($C_6H_9O$, 10.3). The coupling constant for H-3 was derived from the smaller of the coupling constants of the H-4 resonance. This was supported by double irridiation of the H-3 signal, which simplified the H-4 signal to a double doublet: J (H-4, $CHCH_2$) = 8.8 Hz, J (H-4, $CHCH_2$) = 2.6 Hz.

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-(phenylmethyl)-2-azetidinone (11i).** Yield: 4.8%. IR: ν_{max} (neat) 1760, 1731, 1604, 1585, 1513 cm^{-1}. ^{1}H NMR: δ_H 3.04 (dd, 1 H, J = 14.4, 6.9 Hz, PhCH), 3.31 (dd, 1 H, J = 14.4, 3.8 Hz, PhCH), 3.72 (s, 3 H, CO_2Me), 3.80 (d, 1 H, J = 2.5 Hz, H-3), 3.83 (s, 3 H, OMe), 4.65 (dq, 1 H, J = 6.9, 3.8, 2.5 Hz, H-4), 6.90 (d, 2 H, J = 7.6 Hz, Ar H), 7.10–7.40 (m, 7 H, Ar H, PhH). ^{13}C NMR: δ_C 36.77 (–), 52.70, 55.03, 55.51, 58.00, 114.59, 119.07, 127.25, 128.84, 129.24, 135.00, 156.60, 162.72. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.13; H, 5.89; N, 4.31. Found: C, 70.42; H, 6.31; N, 4.25.

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-(4-(1-butenyl))-2-azetidinone (11k).** Yield: 10%. IR: ν_{max} (neat) 1758, 1731, 1640, 1593, 1585, 1513 cm^{-1}. ^{1}H NMR: δ_H 1.61–1.88 (m, 1 H, CH_2CH_2CH=), 2.05–2.31 (m, 3 H, CH_2CH_2CH= and CH_2CH=), 3.77 (s, 6 H, OMe), 3.79 (d, 1 H, J = 2.8 Hz, H-3), 4.33 (dt, 1 H, J = 9.5, 2.8, 2.8 Hz, H-4), 4.96–5.10 (m, 2 H, $=CH_2$), 5.68–5.89 (m, 1 H, CH=), 6.83 (d, 2 H, J = 7.2 Hz, Ar H), 7.28 (d, 2 H, J = 7.2 Hz Ar H). ^{13}C NMR: δ_C 29.18 (–), 30.45 (–), 52.71, 54.93, 55.48, 59.06, 114.47, 116.15 (–), 118.99, 130.21, 136.43, 156.53, 158.31, 167.37. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.02; H, 6.73; N, 4.84.

***trans*-4-Ethyl-3-carbomethoxy-1-(*p*-methoxyphenyl)-2-pyrrolidinone (12h).** Yield: 70%. Mp (ether–petroleum ether): 74–75 °C. IR: ν_{max} (Nujol) 2959, 2876, 2838, 1738, 1694, 1611, 1586, 1513 cm^{-1}. ^{1}H NMR: δ_H (1.00 (t, 3 H, J = 7.4 Hz, Me), 1.55–1.70 (m, 2 H, CH_2), 2.78 (sextet, 1 H, J = 7.6 Hz, H-4), 3.34 (d, 1 H, J = 7.8 Hz, H-3), 3.46 (dd, 1 H, J = 9.7, 6.8 Hz, H-5), 3.79 (s, 3 H, OMe), 3.82 (s, 3 H, OMe), 3.96 (dd, 1 H, J = 9.7, 7.9 Hz, H-5), 6.90 (d, 2 H, J = 7.2 Hz, Ar H), 7.50 (d, 2 H, J = 7.2 Hz, Ar H). ^{13}C NMR: δ_C 11.44, 26.60 (–), 37.54, 52.70, 52.92 (–), 55.44, 55.06, 114.04, 121.84, 132.00, 156.90, 168.20, 170.38. Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.95; H, 6.91; N, 5.05. Found: C, 65.11; H, 6.96; N, 4.93.

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-phenyl-2-pyrrolidinone (12i).** Yield: 73%. Mp: 88–89 °C. IR: ν_{max} (neat) 1741, 1697, 1581, 1513 cm^{-1}. ^{1}H NMR: δ_H 3.75–3.95 (m, 2 H, H-3, H-5), 3.80 (s, 6 H, OMe), 4.05–4.20 (m, 2 H, H-4, H-5′), 6.80 (d, 2 H, J = 7.6 Hz, Ar H), 7.20–7.40 (m, 5 H, PhH), 7.50 (d, 2 H, J = 7.6 Hz, Ar H). ^{13}C NMR: δ_C 41.18, 52.72, 54.00 (–), 55.33, 56.77, 114.02, 121.75, 126.91, 127.64, 129.01, 131.46, 139.38, 156.73, 167.32, 169.57. Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.13; H, 5.89; N, 4.31. Found: C, 70.07; H, 6.05; N, 4.41.

3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-vinyl-2-pyrrolidinone (12j). Yield: 81%. Mp (EtOAc–petroleum ether): 101–103 °C. IR: ν_{max} (Nujol): 1742, 1697, 1658, 1575, 1513 cm^{-1}. ^{1}H NMR: δ_H 3.42–3.69 (m, 3 H, H-3, H-4, H-5), 3.80 (s, 3 H, CO_2Me), 3.81 (s, 3 H, OMe), 3.85–4.08 (m, 1 H, H-5′), 5.15–5.30 (m, 2 H, $=CH_2$), 5.76–5.95 (m, 1 H, CH=), 6.90 (d, 2 H, J = 7.6 Hz, Ar H), 7.48 (d, 2 H, J = 7.6 Hz, Ar H). ^{13}C NMR: δ_C 40.10, 52.18 (–), 52.76, 55.28, 55.41, 114.04, 117.88, 121.86, 131.70, 135.76, 156.88, 167.81, 169.48. Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.43; H, 6.23; N, 5.09. Found: C, 65.51; H, 6.50; N, 5.30. The coupling constant for H-3 was determined indirectly by double irridiation of the multiplet at δ 2.05–2.31, which caused the H-4 signal at δ 4.33 to collapse to a double doublet: J (H-4, $CHCH_2$) = 9.5 and J (H-3, H-4) = 2.8 Hz).

***trans*-3-Carbomethoxy-1-(*p*-methoxyphenyl)-4-(3-(1-propenyl))-2-pyrrolidinone (12k).** Yield: 67%. Mp (ether–petroleum ether): 90–92 °C. IR: ν_{max} (Nujol) 1731, 1690, 1638, 1610, 1586, 1516 cm^{-1}. ^{1}H NMR: δ_H 2.20–2.43 (m, 2 H, CH_2CH=), 2.92 (sextet, 1 H, J = 7.2 Hz, H-4), 3.35 (d, 1 H, J = 9.0 Hz, H-3), 3.47 (dd, 1 H, J = 10.8, 7.8 Hz, H-5), 3.78 (s, 6 H, OMe), 3.94 (dd, 1 H, J = 10.8, 9.6 Hz, H-5′), 5.06–5.29 (m, 2 H, $=CH_2$), 5.64–5.86 (m, 1 H, CH=), 6.85 (d, 2 H, J = 7.2 Hz, Ar H), 7.25 (d, 2 H, J = 7.2 Hz, Ar H). ^{13}C NMR: δ_C 35.17, 37.59 (–), 52.53 (–), 52.72, 55.47, 114.05, 118.12 (–), 121.86, 131.97, 134.12, 156.88, 167.95, 170.05. Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.47; H, 6.72; N, 4.65.

***N*-Butyl-*N*-(*p*-methoxyphenyl)-3-oxobutanamide (13a).** Freshly distilled diketene (150 uL, 2.85 mmol) in dry CH_2Cl_2 (5.0 mL) was added via cannula to a solution of the *N*-butyl-*p*-methoxyaniline (340 mg, 1.90 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C, under N_2. Dry Et_3N (50 ul, 20 mmol %) was added dropwise via syringe, and the mixture was stirred briefly at 0 °C and then at rt for 2.5 h. The reaction mixture was concentrated and the residue chromatographed to give the desired amide. Yield: 476 mg (95%). IR: ν_{max} (neat) 1738, 1640, 1625, 1587, 1556, 1511 cm^{-1}. ^{1}H NMR: δ_H 0.90 (t, 3 H, J = 7.6 Hz, Me), 1.21–1.60 (m, 4 H, CH_2), 1.80 and 2.10 (s, 3 H, COMe), 3.30, 4.58 and 14.40 (s, 2 H, $CH_2(CO)$, =CH(OH)), 3.70 (t, 2 H, J = 7.6 Hz, NCH_2), 3.86 (s, 3 H, OMe), 6.92 (d, 2 H, J = 7.6 Hz, Ar H), 7.10 (d, 2 H, J = 7.6 Hz, Ar H). Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.46; H, 8.43; N, 5.32. Found: C, 68.13; H, 8.03; N, 5.17.

***N*-Butyl-*N*-(*p*-methoxyphenyl)-α-(phenylsulfonyl)acetamide (13b).** The *N*-butyl-*p*-methoxyaniline (695.1 mg, 3.88

mmol), α-(phenylsulfonyl)acetic acid[29] (776.9 mg, 3.88 mmol), and DMAP (47.0 mg, 10 mol %) in dry DMF (10.0 mL) were cooled to 0 °C, under N_2. DCC (856.6 mg, 4.15 mmol) was added to the reaction mixture, and after 5 min, the mixture was stirred for 22 h at rt. The precipitated urea was filtered off and the filtrate evaporated in vacuo. The residue was taken into ether (10.0 mL), and washed with water (10.0 mL), 0.5 N aqueous HCl (10.0 mL), water (10.0 mL), and saturated $NaHCO_3$. The ethereal layer was dried (Na_2SO_4), filtered, and evaporated to give the product. Yield: 1.362 g (97%). Mp (ether): 90.5–97 °C. IR: ν_{max} (Nujol) 1650, 1582, 1511, 1310, 1147 cm^{-1}. ^{1}H NMR: δ_H 0.87 (t, 3 H, J = 7.8 Hz, Me), 1.14–1.55 (m, 4 H, CH_2), 3.61 (s, 2 H, J = 7.8 Hz, NCH_2), 3.83 (s, 3 H, OMe), 3.97 (s, 2 H, CH_2SO_2), 6.92 (d, 2 H, J = 7.6 Hz, Ar H), 7.06 (d, 2 H, J = 7.6 Hz, Ar H), 7.49–7.75 (m, 3 H, PhH), 7.90 (d, 2 H, J = 6.6 Hz, PhH). ^{13}C NMR: δ_C 13.57, 19.60, 29.19, 49.27, 55.31, 59.03, 114.87, 128.47, 128.73, 129.28, 133.58, 133.66, 139.34, 159.25, 161.05. Anal. Calcd for $C_{19}H_{23}NO_4S$: C, 63.00; H, 6.41; N, 3.93. Found: C, 63.30; H, 6.48; N, 3.93.

***N*-Butyl-*N*-(*p*-methoxyphenyl)-2-diazo-3-oxobutanamide (14a).** Compound **13a** was diazotized folowing the procedure described for the preparation of compounds **5**. Yield: 80%. IR: ν_{max} (neat) 2107, 1656, 1644, 1625, 1568, 1511 cm^{-1}. ^{1}H NMR: δ_H 0.90 (t, 3 H, J = 7.6 Hz, Me), 1.20–1.42 (m, 2 H, CH_2), 1.45–1.64 (m, 2 H, CH_2), 2.51 (s, 3 H, COMe), 3.71 ("t", 3 H, J = 7.6 Hz, NCH_2), 3.82 (s, 3 H, OMe), 6.91 (d, 2 H, J = 7.6 Hz, Ar H), 7.09 (d, 2 H, J = 7.6 Hz, Ar H). ^{13}C NMR δ_C: 13.78, 20.06, 28.57, 29.73, 50.47, 55.53, 115.24, 128.88, 133.99, 159.31, 160.60, 192.12. MS: m/z (rel intensity) 289 (M^+, 9), 261 ($M^+ - N_2$, 63), 205 ($M^+ - N_2 - C_4H_8$, 13), 149 ($M^+ - C_3H_3N_2O$ - Bu, 38), 134 (100).

***N*-Butyl-*N*-(*p*-methoxyphenyl)-α-diazo-α-(phenylsulfonyl)acetamide (14b).** Compound **13b** was diazotized according to the procedure described for compounds **5**. Yield: 80%. Mp (ether): 107.5–109 °C. IR: ν_{max} (Nujol): 2101, 1628, 1582, 1509, 1338, 1149 cm^{-1}. ^{1}H NMR: δ_H 0.82 (t, 3 H, J = 7.2 Hz, Me), 1.12–1.32 (m, 2 H, CH_2), 1.35–1.55 (m, 2 H, CH_2), 3.59 (t, 2 H, J = 7.2 Hz, NCH_2), 3.82 (s, 3 H, OMe), 6.92 (d, 2 H, J = 7.6 Hz, Ar H), 7.10 (d, 2 H, J = 7.6 Hz, Ar H), 7.48–7.68 (m, 3 H, PhH), 8.02 (d, 2 H, J = 6.6 Hz, PhH). ^{13}C NMR: δ_C 13.62, 19.82, 29.41, 50.01, 55.50, 115.20, 128.00, 128.73, 129.27, 132.72, 133.40, 142.25, 157.76, 159.87. Anal. Calcd for $C_{19}H_{21}N_3O_4S$: C, 58.89; H, 5.47; N, 10.85. Found: C, 58.78; N, 5.43; H, 10.98.

3-Acetyl-1-butyl-2-hydroxy-5-methoxyindole (15). Compound **14a** was treated with $Rh_2(OAc)_4$ in CH_2Cl_2 at rt following the procedure described for **5**. Mp (ether–petroleum ether): 48–50 °C. IR: ν_{max} (Nujol) 1651, 1591, 1511 cm^{-1}. ^{1}H NMR: δ_H 0.97 (t, 3 H, J = 7.6 Hz, Me), 1.28–1.49 (m, 2 H, CH_2), 1.60–1.78 (m, 2 H, CH_2), 2.41 (s, 3 H, COMe), 3.80 ("t", 2 H, J = 7.6 Hz, NCH_2), 3.82 (s, 3 H, OMe), 6.75 (dd, 1 H, J = 7.6, 2.5 Hz, H-6), 6.85 (d, 1 H, J = 7.6 Hz, H-7), 6.94 (d, 1 H, J = 2.5 Hz, H-4), 13.20–13.80 (br hump, 1 H, OH). ^{13}C NMR: δ_C 13.72, 20.17 (–), 20.21, 30.04 (–), 39.34 (–), 55.81, 101.79, 107.20, 108.75, 109.53, 123.44, 132.21, 155.46, 170.75, 173.18. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.93; H, 7.33; N, 5.36. Found: C, 69.26; H, 7.35; N, 5.35.

1-Butyl-5-methoxy-3-(phenylsulfonyl)-2(3*H*)-indolinone (16). Yield: 98%. Mp ($CHCl_3$): 209–211.5 °C. IR: ν_{max} (Nujol) 1711, 1629, 1599, 1581 cm^{-1}. ^{1}H NMR: δ_H 0.85 (t, 3 H, J = 7.0 Hz, Me), 1.02–1.38 (m, 4 H, CH_2), 3.32 (dt, 1 H, J = 14.0, 7.8 Hz, NCH), 3.58 (dt, 1 H, J = 14.0, 7.8 Hz, NCH'), 3.86 (s, 3 H, OMe), 4.88 (s, 1 H, H-3), 6.60 (d, 1 H, J = 8.6 Hz, H-7), 6.90 (dd, 1 H, J = 8.6, 2.9 Hz, H-6), 7.36 (d, 1 H, J = 2.9 Hz, H-4), 7.38–7.50 (m, 2 H, PhH), 7.55–7.65 (m, 1 H, PhH), 7.70 (d, 2 H, J = 7.9 Hz, PhH). ^{13}C NMR: δ_C 13.64, 19.81, 29.02, 40.10, 55.91, 68.45, 109.14, 113.61, 115.93, 119.21, 128.62, 129.53, 134.20, 136.10, 137.60, 155.96, 165.96. Anal. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.43; H, 5.84; N, 3.82.

2-Ethyl-3-methyl-2,3-dihydroindole (18). The known 2-ethyl-3-methylindole[34] (4.00 g) was dissolved in acetic acid (100 mL) containing 70% aqueous $HClO_4$ (2.0 mL); 10% palladized charcoal (1.00 g) was added, and the mixture was hydrogenated (balloon, 1 atm) at rt. After the reaction was over, the mixture was filtered and basified with aqueous NaOH. The aqueous mixture was extracted with CH_2Cl_2 (3 × 15 mL), and the extracts were washed with water (2 × 15 mL), dried (Na_2SO_4), and filtered. The solution was evaporated to give the **18** as an oil (61%). IR: ν_{max} (neat) 3365, 3025, 2964, 2925, 2850, 1609 cm^{-1}. ^{1}H NMR: δ_H 0.99 (t, 3 H, J = 7.7 Hz, Me), 1.11 (d, 3 H, J = 7.7 Hz, Me), 1.41–1.70 (m, 2 H, CH_2), 3.22 (quin, 1 H, J = 7.7 Hz, CH_2), 3.65 (dt, 1 H, J = 8.0, 6.5 Hz, H-2), 6.13 (s, 1 H, NH), 6.60–6.79 (m, 2 H, Ar H), 6.98–7.08 (m, 2 H, Ar H).

1-Acetoacetyl-2-ethyl-3-methyl-2,3-dihydroindole (19a). **19a** was prepared by the reaction of **18** with diketene in an analogous manner to that described for **13a**. Yield: 89%. IR: ν_{max} (neat) 1720, 1638, 1577 cm^{-1}. ^{1}H NMR: δ_H 0.81 (d, 3 H, J = 7.2 Hz, Me), 1.38 (d, 3 H, J = 7.6 Hz, Me), 1.38–1.88 (m, 2 H, CH_2), 2.03 and 2.32 (s, 3 H, MeCO), 3.69, 5.20, and 14.70 (s, 2 H, CH_2CO), 3.40–3.98 (m, 1 H, H-3), 4.20–4.52 and 4.70–5.10 (br hump, 1 H, H-2), 6.91–7.30 (m, 3 H, Ar H), 7.70–8.20 (m, 1 H, Ar H). MS: m/z (rel intensity) 245 (M^+, 12), 161 ($M^+ - C_4H_4O_2$, 19), 132 ($M^+ - C_4H_4O_2$ - Et, 100), 117 ($M^+ - C_4H_4O_2$ - Et - Me, 15).

1-(α-Carbomethoxyacetyl)-2-ethyl-3-methyl-2,3-dihydroindole (19b). **19b** was prepared by reacting **18** with α-carbomethoxyacetyl chloride following the procedure described for compounds **4** (see the supplementary material). Yield: 75%. IR: ν_{max} (neat) 1740, 1656, 1599 cm^{-1}. ^{1}H NMR: δ_H 0.85 (br t, 3 H, J = 7.1 Hz, Me), 1.35 (br d, 3 H, J = 6.3 Hz, Me), 1.40–1.70 (m, 2 H, CH_2), 3.40–3.70 (m, 3 H, H-3, CH_2), 3.77 (s, 3 H, OMe), 4.25–4.45 and 4.82–5.02 (br hump, 1 H, H-2), 7.02–7.22 (m, 2 H Ar H), 7.96–8.10 (br hump, 2 H, Ar H). MS: m/z (rel intensity) 261 (M^+, 24), 232 (M^+ - Et, 10), 161 ($M^+ - C_4H_4O_3$, 5.8), 1.60 ($M^+ - C_4H_5O_3$, 15), 259 (M^+ - 2H, 2), 158 (M^+ - 2H - $C_4H_5O_3$, 38), 132 ($M^+ - C_4H_4O_3$ - Et, 100).

1-(α-(Phenylsulfonyl)acetyl)-2-ethyl-3-methyl-2,3-dihydroindole (19c). **19c** was prepared by treating **18** with α-(phenylsulfonyl)acetic acid–DCC in a similar manner to that described for **13b**. Yield: 73%. Mp (ether–petroleum ether): 116–117 °C. IR: ν_{max} (Nujol) 1653, 1597, 1311, 1153 cm^{-1}. ^{1}H NMR: δ_H 0.80 and 0.90 (br t, 3 H, J = 7.2 Hz, Me), 1.20–1.82 (m, 2 H, CH_2), 1.27 and 1.35 (d, 3 H, J = 7.4 Hz, Me), 3.29–3.50 (m) and 3.51–3.72 (m) (1 H, H-3), 4.15–4.40 (m, 1 H, CHC(O)), 4.43–4.92 (m, 2 H, H-2, CHC(O)), 7.12 (br s, 3 H, Ar H), 7.35–7.74 (m, 3 H, PhH), 7.81–8.10 (m, 3 H, PhH). ^{13}C NMR: δ_C (major rotamer) 10.11, 11.15, 22.82, 38.42, 61.64, 65.95, 117.82, 122.22, 124.82, 127.06, 128.35, 128.90, 133.96, 136.86, 138.68, 141.18, 158.60; (minor rotamer) 10.11, 11.15, 21.03, 37.69, 59.28, 66.92, 116.21, 123.60, 139.36, 140.15, 159.23. Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.17; N, 4.08. Found: C, 66.39; H, 6.21; N, 3.87.

1-(α-Diazoacetoacetyl)-2-ethyl-3-methyl-2,3-dihydroindole (20a). Compound **19a** was diazotized following the procedure for the preparation of **5**. Yield: 79%. IR: ν_{max} (neat) 2111, 1736, 1649 and 1594 cm^{-1}. ^{1}H NMR: δ_H 0.93 (t, 3 H, J = 7.2 Hz, Me), 1.38 (d, 3 H, J = 7.6 Hz, Me), 1.53–1.83 (m, 2 H, CH_2), 2.44 (s, 3 H, COMe), 3.62 (quintet, J = 7.6 Hz, H-3), 4.42–4.55 (m, 1 H, H-2), 7.02–7.28 (m, 3 H, Ar H), 7.39 (d, 1 H, J = 8.4 Hz, H-7). ^{13}C NMR: δ_C 10.54, 11.70, 22.05, 27.38, 38.19, 67.75, 114.89, 123.30, 124.42, 127.35, 137.25, 140.75, 157.67. Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.39; H, 6.32; N, 15.49. Found: C, 66.46; H, 6.48; N, 15.51.

1-(α-Carbomethoxy-α-diazoacetyl)-2-ethyl-3-methyl-2,3-dihydroindole (20b). Compound **19b** was diazotized as described above. Yield: 67%. IR: ν_{max} (CH_2Cl_2) 2127, 1713, 1633, 1594 cm^{-1}. ^{1}H NMR: δ_H 0.85 (t, 3 H, J = 7.8 Hz, Me), 1.31 (d, 2 H, J = 7.8 Hz, Me), 1.40–1.78 (m, 2 H, CH_2), 3.62 (quintet, 1 H, J = 7.8 Hz, H-3), 3.71 (s, 3 H, CO_2Me), 4.55 (dt, 1 H, J = 7.8, 4.9 Hz, H-2), 7.01–7.20 (m, 3 H, Ar H), 7.66 (d, 1 H, J = 8.4 Hz, H-7). ^{13}C NMR: δ_C 10.57, 11.47, 22.41 (–), 38.27, 52.20, 67.50, 115.63, 122.79, 124.25, 127.06, 137.13, 141.89, 157.97, 162.49. Anal. Calcd for $C_{15}H_{17}N_3O_3$: C, 62.69; H, 5.97; N, 14.63. Found: C, 62.75; H, 6.23; N, 14.84.

1-(α-Diazo-α-(phenylsulfonyl)acetyl)-2-ethyl-3-methyl-2,3-dihydroindole (20c). Compound **19c** was diazotized as described above. Yield: 80%. Mp (ether): 115.5–117 °C. IR: ν_{max} (Nujol) 2117, 1629, 1591, 1331, 1150 cm^{-1}. ^{1}H NMR: δ_H 0.82 (t, 3 H, J = 7.2 Hz, Me), 1.30 (d, 3 H, J = 7.4 Hz, Me), 1.40–1.85 (m, 2 H, CH_2), 3.49 (quintet, 1 H, H-3), 4.42 (dt, 1 H, J = 7.4, 5.0 Hz, H-2), 7.00–7.25 (m, 3 H, Ar H), 7.38–7.68 (m, 4 H, PhH, Ar H), 8.00–8.15 (m, 2 H, PhH). ^{13}C NMR: δ_C 10.28, 11.51, 22.09, 38.24, 67.76, 115.05, 123.13, 124.65, 127.38, 127.74, 128.94, 133.66, 137.07, 140.13, 141.98, 154.70. Anal. Calcd for $C_{19}H_{19}N_3O_3S$: C, 61.77; H, 5.19; N, 11.38. Found: C, 61.81; H, 5.21; N, 11.38.

Dirhodium Tetraacetate Reaction of 20a. Compound **20a** was treated with $Rh_2(OAc)_4$ in refluxing CH_2Cl_2 according to the procedure described for compounds **5** to give the readily separable

trans-**21a** and **22a**. ***trans*-2-Acetyl-1,9-dimethyl-3-oxo-1,2,9,9a-tetrahydropyrrolo[1,2-*a*]indole (21a).** Yield: 61%. Mp (ether–petroleum ether): 90.5–92 °C. IR: ν_{max} (Nujol) 1713, 1693, 1602 cm^{-1}. ^{1}H NMR: δ_H 1.19 (d, 6 H, J = 6.8 Hz, 2 Me), 2.49 (s, 3 H, COMe), 2.90–3.10 (m, 1 H, H-1), 3.34 (quintet, 1 H, H-9), 3.62 (d, 1 H, J = 10.6 Hz, H-2), 4.18 (dd, 1 H, J = 10.0, 8.2 Hz, H-9a), 7.00–7.13 (m, 3 H, Ar H), 7.58 (d, 1 H, J = 9.0 Hz, H-5). ^{13}C NMR: δ_C 10.50, 10.61, 30.76, 32.93, 35.98, 66.81, 68.76, 114.39, 124.69, 124.98, 127.88, 137.26, 140.13, 165.50, 202.75. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.03; H, 7.05; N, 5.76. Found: C, 74.27; H, 7.15; N, 5.75. **1-Acetyl-4-ethyl-2-hydroxy-5-methyl-4,5-dihydropyrrolo[3,2,1-*hi*]indole (22a).** Yield: 26%. Mp (petroleum ether): 55–57 °C. IR: ν_{max} (Nujol) 1660, 1620, 1581 cm^{-1}. ^{1}H NMR: δ_H 1.12 (t, 3 H, J = 7.2 Hz, Me), 1.39 (d, 3 H, J = 7.2 Hz, Me), 1.82–2.19 (m, 2 H, CH_2), 2.40 (s, 3 H, COMe), 4.01 (quintet, 1 H, H-5), 4.52 (dt, 1 H, J = 8.7, 7.2 Hz, H-4), 6.90–7.11 (m, 3 H, Ar H). ^{13}C NMR: δ_C 11.59, 14.83, 20.56, 22.41 (–), 45.18, 66.02, 107.62, 116.05, 117.92, 118.62, 123.26, 127.23, 145.63, 169,50, 172.38. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.03; H, 7.05; N, 5.76. Found: C, 74.34; H, 7.18; N, 5.72.

2-Carbomethoxy-1,9-dimethyl-3-oxo-1,2,9,9a-tetrahydropyrrolo[1,2-*a*]indole (21b). Compound **20b** was treated with $Rh_2(OAc)_4$ as described above to give an inseparable mixture of trans–cis (95:5) isomers. Yield: 99%. Mp (ether–petroleum ether): 125–126.5 °C. IR: ν_{max} (neat) 1740, 1698, 1602 cm^{-1}. ^{1}H NMR of the mixture is quoted with the signals of the minor cis isomer that occur in different chemical shifts in brackets: δ_H 1.19 (d, 3 H, J = 7.1 Hz, Me), 1.24 (d, 3 H, J = 7.1 Hz, Me), 2.85–3.08 (m, 1 H, H-1), 3.35 (quintet, 1 H, J = 7.1 Hz, H-9), 3.53 and [3.67, 3, J = 8.6 Hz] (d, 1 H, J = 10.9 Hz, H-2), [3.75] and 3.80 (s, 3 H, OMe), 4.20 and [4.60, dd, J = 10.5, 8.6 Hz] (dd, 1 H, J = 10.2, 7.1 Hz, H-9a), 7.00–7.25 (m, 3 H, Ar H), 7.52 (d, 1 H, J = 7.4 Hz, H-5). ^{13}C NMR: δ_C 16.25, 16.45, 35.93, 36.03, 52.49, 60.48, 69.12, 114.49, 124.59, 124.85, 127.84, 137.23, 139.87, 165.02, 169.06. Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.46; H, 6.61; N, 5.40. Found: C, 69.50; H, 6.68; N, 5.29.

1,9-Dimethyl-3-oxo-2-(phenylsulfonyl)-1,2,9,9a-tetrahydropyrrolo[1,2-*a*]indole (21c). Compound **20c** was treated with $Rh_2(OAc)_4$ as described above to give an inseparable mixture of trans–cis (96:4) isomers. Yield: 99%. Mp (ether): 197–199.5 °C. IR: ν_{max} (Nujol) 1708, 1653, 1605, 1302, 1145 cm^{-1}. ^{1}H NMR of the mixture is quoted with the signals of the minor cis isomer that occur in different chemical shifts in brackets: δ_H 1.09 (d, 3 H, J = 6.9 Hz, Me), 1.50 (d, 3 H, J = 6.9 Hz, Me), 3.01–3.21 (m, 1 H, H-1), 3.30 (quintet, 1 H, J = 6.9 Hz, H-9), 4.11 (d, 1 H, J = 10.2 Hz, H-2), 4.13 and [4.85, "t", J = 7.3 Hz] ("t", 1 H, J = 8.5 Hz, H-9a), 7.00–7.25 (m, 3 H, Ar H), 7.41–7.70 (m, 4 H, PhH, H-5), 8.02 (d, 2 H, J = 7.2 Hz, PhH). ^{13}C NMR: δ_C ($CDCl_3$) 16.21, 18.03, 32.40, 36.13, 68.89, 114.67, 124.95, 125.23, 127.91, 128.76, 129.52, 134.02, 136.72, 138.14, 139.87, 160.45. Anal. Calcd for $C_{19}H_{19}NO_3S$: C, 66.84; H, 5.61; N, 4.11. Found: C, 67.22; H, 5.59; N, 3.90.

1-Carbomethoxy-2-ethyl-1,2-dihydroquinoline (25). A solution of freshly distilled quinoline (15 mL, 0.13 mol) in dry ether (40.0 mL) was added dropwise via cannula, under N_2, to an ethereal solution of EtMgBr [prepared from the reaction of EtBr (22 mL, 0.37 mol) and Mg metal (6.20 g, 0.32 mol) in ether (80.0 mL)]. After addition was complete, the mixture was refluxed for 1 h and then methyl chloroformate (9.3 mL, 0.13 mol) in ether (60.0 mL) was added. The reaction mixture turned brown, and a precipitate was formed. After 2 h, the mixture was cooled in an ice bath to 0 °C, and saturated NH_4Cl solution (100.0 mL) was added. The ethereal layer was separated, washed with water (2 × 50 mL) and brine (100 mL), dried, filtered, and concentrated. Chromatographic separation of the residual oil using 1:20 v/v and then 1:16 v/v ether–petroleum ether, gave the regioisomeric carbamates **25** and **26** as oils. Compound **25**: Yield: 57%. IR: ν_{max} (neat) 1704, 1600, and 1562 cm^{-1}. ^{1}H NMR: δ_H 0.85 (t, 3 H, J = 7.5 Hz, Me), 1.25–1.60 (m, 2 H, CH_2), 3.75 (s, 3 H, OMe), 4.82–5.00 (m, 1 H, H-2), 6.05 (dd, 1 H, J = 9.6, 5.9 Hz, H-3), 6.45 (d, 1 H, J = 9.6 Hz, H-4), 7.05–7.18 (m) and 7.55 (d, J = 8.5 Hz) (4 H, Ar H). ^{13}C NMR: δ_C 9.41, 25.81, 52.52, 53.70, 123.88, 124.36, 125.77, 126.97, 127.08, 129.57, 134.24, 154.74. Anal. Calcd for $C_{13}H_{15}NO_2$: C, 71.85; H, 6.96; N, 6.45. Found: C, 72.04; H, 7.21; N, 6.30. **1-Carbomethoxy-4-ethyl-1,4-dihydroquinoline (26).** Yield: 11%. IR: ν_{max} (neat) 1704, 1600, 1562 cm^{-1}. ^{1}H NMR: δ_H 0.86 (t, 3 H, J = 7.3 Hz, Me), 1.45–1.69 (m, 2 H, CH_2), 3.22 (q, 1 H, J = 7.0 Hz, H-4), 3.82 (s, 3 H, OMe), 5.33 (dd, 1 H, J = 7.3, 7.0 Hz, H-3), 6.99 (d, 1 H, J = 7.3 Hz, H-2), 7.00–7.26 (m, 3 H, Ar H), 7.98 (d, 1 H, J = 8.2 Hz, H-8).

2-Ethyl-1-(methoxycarbonyl)-1,2,3,4-tetrahydroquinoline (27). Compound **25** (2.78 gm, 12.75 mmol) was dissolved in methanol (100 mL) and hydrogenated over 10% Pd–C (678 mg, 5 mol %) at room temperature and atmospheric pressure. After 2 h, the mixture was filtered through Celite, the filtrate was concentrated, and the residue was purified by chromatography (1:5 v/v ether–petroleum ether). Yield: 92%. IR: ν_{max} (neat) 1701, 1603, 1581, and 1500 cm^{-1}. ^{1}H NMR: δ_H 0.85 (t, 3 H, J = 6.3 Hz, Me), 1.25–1.70 (m, 3 H, CH_2, H-3), 2.04–2.23 (m, 1 H, H-3′), 2.65 ("t", 2 H, J = 7.0 Hz, H-4), 3.70 (s, 3 H, OMe), 4.40–4.54 (m, 1 H, H-2), 6.92–7.18 (m, 3 H, Ar H), 7.49 (d, 1 H, J = 7.2 Hz, H-8). ^{13}C NMR: δ_C 9.90, 24.18, 25.33, 27.72, 52.26, 53.94, 123.68, 125.13, 125.50, 127.55, 130.93, 136.36, 155.08. MS: m/z (rel intensity) 220 (M^+ + 1, 3.6), 219 (M^+, 24.9), 190 (M^+ – Et, 100).

1-(α-Carbomethoxyacetyl)-2-ethyl-1,2,3,4-tetrahydroquinoline (28a). Compound **26** was decarbamoylated as described (supplementary material) to give 2-ethyl-1,2,3,4-tetrahydroisoquinoline. Yield: 100%. ^{1}H NMR: δ_H 0.95 (t, 3 H, J = 7.6 Hz, Me), 1.40–1.68 (m, 3 H, CH_2, H-3), 1.81–2.00 (m, 1 H, H-3′), 2.61–2.88 (m, 2 H, H-4), 3.05–3.21 (m, 1 H, H-2), 3.50–3.78 (br hump, 1 H, NH), 6.40–6.65 (m, 2 H, Ar H), 6.89–7.00 (m, 2 H, Ar H). Acylation with α-carbomethoxyacetyl chloride (supplementary material) gave **28a**. Yield: 71%. IR: ν_{max} (film) 1744, 1656, 1603, 1582 cm^{-1}. ^{1}H NMR: δ_H 0.80 (t, 3 H, J = 7.5 Hz, Me), 1.15–1.51 (m, 3 H, CH_2, H-3), 2.20–2.66 (m, 3 H, H-3′, H-4), 3.40 (d, 1 H, J = 12.6 Hz, $CH(CO)_2$), 3.51 (d, 1 H, J = 12.6 Hz, $CH(CO)_2$), 3.57 (s, 3 H, OMe), 4.60–4.85 (m, 1 H, H-2), 6.95–7.25 (br s, 4 H, Ar H). ^{13}C NMR: δ_C 10.01, 25.81, 27.61, 30.17, 41.66, 52.09, 53.40, 125.26, 126.34, 126.54, 127.52, 136.17, 137.19, 165.12, 168.25. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.93; H, 7.33; N, 5.36. Found: C, 68.81; H, 7.54; N, 5.62.

1-Acetoacetyl-2-ethyl-1,2,3,4-tetrahydroquinoline (28b). Compound **27** was decarbamoylated and acylated with diketene (see procedure for **13a**) to give **28b**. Yield: 92%. IR: ν_{max} (neat) 1720, 1638, 1588, 1500 cm^{-1}. ^{1}H NMR: δ_H 0.90 (t, 3 H, J = 7.3 Hz, Me), 1.25–1.62 (m, 3 H, CH_2, H-3), 1.85 and 2.15 (s, 3 H, COMe), 2.25–2.40 (m, 1 H, H-3′), 2.50–2.72 (m, 2 H, H-4), 3.60, 5.25, and 14.45 (s, 2 H, $CH_2(CO)_2$ ⇌CH(OH)), 4.65–4.80 (m, 1 H, H-2), 7.00–7.30 (m, 4 H, Ar H). MS: m/z (rel intensity) 246 (M^+ + 1, 0.7), 245 (M^+, 4.4), 216 (M^+ – Et, 5), 161 (M^+ – $C_4H_4O_2$, 11), 132 (M^+ – $C_4H_4O_2$ – Et, 100).

1-(α-Carbomethoxy-α-diazoacetyl)-2-ethyl-1,2,3,4-tetrahydroquinoline (29a). Compound **28a** was diazotized following the procedure described for the preparation of compounds **5**. Yield of **28a**: 66%. IR: ν_{max} (neat) 2122, 1723, 1696, 1618, 1581 cm^{-1}. ^{1}H NMR: δ_H 0.90 (t, 3 H, J = 6.9 Hz, Me), 1.28–1.82 (m, 3 H, CH_2, H-3), 2.22–2.42 (m, 1 H, H-3′), 2.56–2.80 (m, 2 H, H-4), 3.43 (s, 3 H, OMe), 4.41–4.60 (m, 1 H, H-2), 7.00–7.26 (m, 4 H, Ar H). ^{13}C NMR δ_C: 10.04, 24.98, 26.91, 29.06, 52.00, 55.13, 122.73, 125.37, 126.41, 127.79, 133.49, 138.07, 160.32, 162.49. Anal. Calcd for $C_{15}H_{17}N_3O_3$: C, 62.69; H, 5.97; N, 14.63. Found: C, 62.71; H, 6.23; N, 14.84.

1-(α-Diazoacetoacetyl)-2-ethyl-1,2,3,4-tetrahydroquinoline (29b). Compound **28b** was diazotized as described above. Yield of **29b**: 72%. Mp (ether–petroleum ether) 105–107.5 °C. IR: ν_{max} (Nujol) 2112, 1634, and 1581 cm^{-1}. ^{1}H NMR: δ_H 0.95 (t, 3 H, J = 7.3 Hz, Me), 1.30–1.81 (m, 3 H, CH_2, H-3), 2.25–2.40 (m, 4 H, COMe, H-3′), 2.50–2.80 (m, 2 H, CH_2), 4.52 (q, 1 H, J = 7.2 Hz, H-2), 7.05–7.25 (m, 4 H, Ar H). ^{13}C NMR: δ_C 9.99, 25.06, 27.09, 27.79, 29.43, 54.82, 123.27, 125.92, 127.15, 128.32, 133.35, 136.95, 160.09, 191.37. Anal. Calcd for $C_{15}H_{17}N_3O_2$: C, 66.39; H, 6.32; N, 15.49. Found: C, 66.32; H, 6.30; N, 15.32.

9a-Ethyl-1-carbomethoxy-2-oxo-3,8,9,9a-tetrahydroazeto-[1,2-*a*]quinoline (30a). Treatment of **29a** with $Rh_2(OAc)_4$ in refluxing CH_2Cl_2 according to the procedure described for compounds **5** gave **30a**. Yield: 61%. IR: ν_{max} (neat) 1768, 1734, 1700, 1650, 1618, 1588, 1500 cm^{-1}. ^{1}H NMR: δ_H 0.90 and 1.05 (t, 3 H, J = 7.3 Hz, Me), 1.51–2.05 (m, 3 H, H-9, CH_2), 2.15–2.25 (m) and 2.45–2.60 (m) (1 H, H-9′), 2.80–2.95 (m, 2 H, H-8), 3.76 and 3.81 (s, 3 H, OMe), 3.88 and 4.05 (s, 1 H, H-1), 6.98–7.27 (m, 3 H, Ar H), 7.48 (d, 1 H, J = 6.7 Hz, H-4). MS: m/z (rel intensity) 260 (M^+ + 1, 6.8), 259 (M^+, 37.6), 159 (M^+ – $C_4H_4O_3$, 100), 158 (M^+

- $C_4H_4O_3$ - H, 70.2), 144 (M^+ - $C_4H_4O_3$ - CH_3, 63), 130 (M^+ - $C_4H_4O_3$ - C_2H_5, 36).

1-Acetyl-2-hydroxy-4-ethyl-3,4,5,6-tetrahydropyrrolo[3,2,1-*ij*]quinoline (31b). Treatment of **29b** with $Rh_2(OAc)_4$ in refluxing CH_2Cl_2 as described above gave **31b**. Yield: 88%. IR: ν_{max} (neat) 1732, 1659, 1614, 1593 cm^{-1}. ^1H NMR: δ_H 1.01 (t, 3 H, J = 7.3 Hz, Me), 1.40-1.95 (m, 3 H, CH_2, H-5), 2.05-2.25 (m, 1 H, H-5'), 2.40 (s, 3 H, COMe), 2.65-2.90 (m, 2 H, H-6), 4.20-4.35 (m, 1 H, H-4), 6.92-7.02 (m, 2 H, Ar H), 7.16 (dd, 1 H, J = 6.3, 2.0 Hz, H-9), 12.90-13.40 (br hump, 1 H, OH). ^{13}C NMR: δ_C 10.51, 20.06, 20.56, 23.85, 25.68, 49.72, 102.50, 117.22, 119.98, 120.68, 121.33, 123.76, 134.40, 169.88, 172.70. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.03; H, 7.05; N, 5.76. Found: C, 74.24; H, 7.21; N, 5.69.

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Supplementary Material Available: Spectroscopic and analytical data for compounds **3**, N-substituted carbamates, secondary amines, and compounds **4**, **5**, and **6**, ^1H and ^{13}C NMR spectra for **11h,i,k**, **12h**, and **21a-c**, and NOE spectra for **12h** and **21b,c** (79 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Synthesis and Characterization of a New 26π-Aromatic Thiophene-Containing Macrocyclic Ligand

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A new porphyrin-like or "pentaplanar" macrocyclic ligand (**9**) has been synthesized by a McMurray coupling of 2,5-bis(5-formyl-4-propyl-2-pyrrolyl)thiophene, followed by air oxidation in chloroform. This highly stable macrocycle is aromatic, as evidenced by its UV-visible and ^1H NMR spectra. The pathway to **9** as well as the synthesis of two asymmetric dipyrrolylthiophenes is also described.

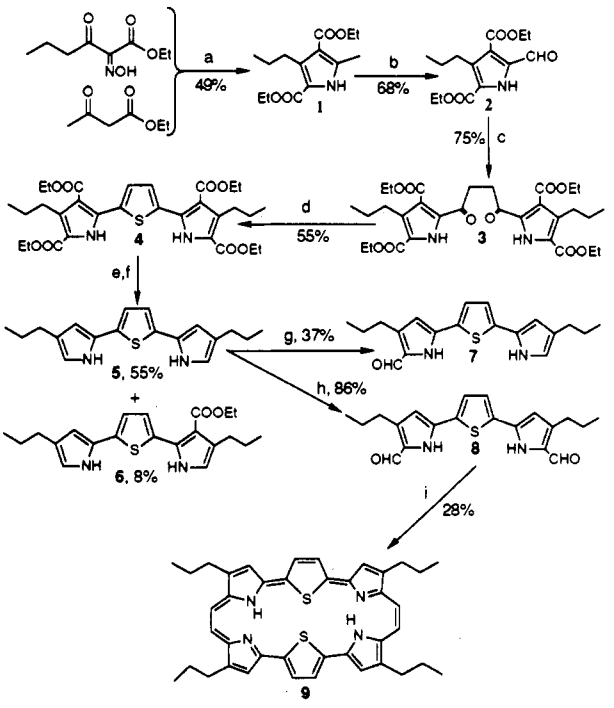
Introduction

Reports of new porphyrin-like, aromatic macrocyclic ligands have appeared in increasing number in the last few years.[1,2] These macrocyclic ligands generally consist of five-membered rings linked electronically by zero, one, or two sp-hybridized (methine) atoms to form a cyclic extended aromatic network. These and other unsaturated ligands have potential uses as one- and two-dimensional conductors,[3] as drugs for photodynamic therapy,[4] as multimetallic chelates for catalysis[5] and magnetic resonance imaging,[6] as media for chemical sensors,[7] and as anion chelands.[8] We report here the synthesis of the new macrocycle **9** and some of its spectroscopic features.

Results and Discussion

The precursor dialdehyde **8** for the synthesis of macrocycle **9** was made by modifications of the method of Merrill and LeGoff[9] (Scheme I). Pyrrole **1**[10] was treated with sulfuryl chloride in acetic acid at 70 °C to give aldehyde **2** in a 68% yield. This aldehyde was then coupled with divinyl sulfone by the method of Stetter[11] to give the 1,4-dipyrrolylbutane-1,4-dione **3**, which precipitated from the cooled reaction mixture in 75% yield and very high

Scheme I[a]



[a] (a) Zn^0/HOAc/H_2O; (b) (1) SO_2Cl_2/HOAc/70 °C, (2) H_2O; (c) divinyl sulfone, [3,4-dimethyl-5-(2-hydroxyethyl)thiazolium iodide], Et_3N, *p*-dioxane, 70 °C, 20 h; (d) Lawesson's reagent, toluene, reflux 1.5 h; (e) (1) NaOH/H_2O/EtOH/reflux, (2) hot HOAc/H_2O; (f) 240 °C/(0.2 Torr); (g) PhCOCl/DMF/0 °C; (h) PhCOCl/DMF/75 °C, 10 h; (i) (1) Ti^0/THF/reflux, (2) air oxidation in $CHCl_3$ 1 h.

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