Ligand Effects in the Rhodium(II)-Catalyzed Reactions of α-Diazoamides. Oxindole Formation is Promoted by the Use of Rhodium(II) Perfluorocarboxamide Catalysts

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An improved procedure for the preparation of ethyl 2-diazomalonyl chloride was developed which involves the reaction of ethyl diazoacetate with triphosgene. Using this diazo acid chloride, it was possible to prepare a variety of diazoamides from substituted amines. The rhodium(II)-catalyzed decomposition of these diazoamides was studied in order to probe the chemoselectivity of the carbenoid intermediates in intramolecular insertion reactions. Rhodium(II) acetate decomposition of *N*-benzyl-2-diazo-*N*-phenylmalonamic acid ethyl ester resulted in intramolecular C–H insertion to give ethyl 1,4-diphenyl-2-oxoazetidine-3-carboxylate. By changing the catalyst ligand to trifluoroacetamide, β-lactam formation was completely suppressed in favor of the aromatic C–H insertion which produces an oxindole as the only detectable product. The competition between aliphatic and aromatic carbon–hydrogen insertion of 2-diazo-*N*-isobutyl-*N*-phenylmalonamic acid ethyl ester provides another example of ligand effectiveness in controlling chemoselectivity in dirhodium(II)-catalyzed metal carbene reactions. Thus, treatment of the *N*-isobutyldiazoanilide with rhodium(II) acetate results in exclusive aliphatic C–H insertion giving 4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxylic acid ethyl ester, while the perfluorobutyramide ligand promotes oxindole formation by aromatic C–H insertion. Several other rhodium(II)-catalyzed reactions were studied and were found to be highly catalyst dependent, rhodium(II) perfluorocarboxamides promoting aromatic C–H insertion, and hence oxindole formation, over O–H insertion, cyclization onto adjacent triple bonds, or cyclization to generate 1,3-dipolar intermediates.

The transition-metal catalyzed decomposition of diazo compounds, discovered over 80 years ago, continues to find wide application in organic synthesis.[1] Although the historically important copper-based catalysts are still widely used, rhodium(II) acetate, introduced by Teyssié and co-workers in the early 1970s,[2] is often the catalyst of choice for the decomposition of diazocarbonyl compounds. Rhodium(II) carboxylates mediate a wide range of synthetic transformations such as cyclopropanation, C–H and X–H insertion, and ylide formation, the intermediate rhodium carbenoids often showing high levels of stereoselectivity despite their high reactivity. While many of the recent reports deal with controlling the stereoselectivity, and in particular with chiral catalysts the enantioselectivity, of metal-catalyzed diazocarbonyl reactions, there are a growing number of examples which also address the question of chemoselectivity. Site selectivity has been found not only to depend on the type of diazocarbonyl utilized, but is also governed by steric,[3-6] conformational,[7] as well as electronic factors.[8-12] The question of chemoselectivity of rhodium carbenoids has been addressed by the preparation of diazocarbonyl compounds containing two different reaction sites and studying the competition between the two carbenoid processes.[12] These studies have revealed some dramatic ligand effects; for example, carboxylate and carboxamide ligands in rhodium(II) catalysts can effectively control chemoselectivity in competitive carbenoid transformations of diazocarbonyl compounds. Our own interest in rhodium carbenoid-mediated processes has centered on X–H insertion reactions[13] and on ylide formation,[14] and we have recently described the results of experiments designed to probe the efficiency of

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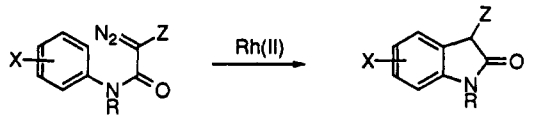
such processes in competition with aliphatic and aromatic C–H insertion and cyclopropanation.[15] In this paper we describe some remarkable ligand effects in the rhodium(II)-catalyzed decomposition of diazoamides and demonstrate that the synthesis of oxindoles (by aromatic C–H insertion) can be greatly enhanced by the appropriate choice of catalyst.

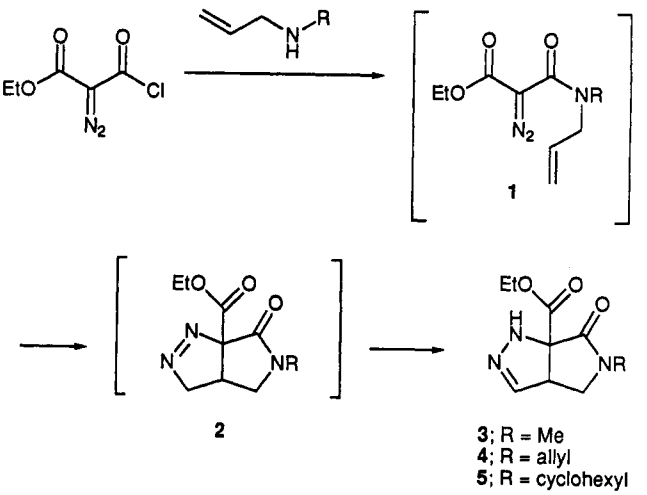
Results and Discussion

The preparation and rhodium(II)-catalyzed decomposition of diazoamides has been previously investigated by three groups of workers,[16–18] the most common starting materials being diazoanilides. Intramolecular aromatic C–H insertion leads to oxindoles,[16,17] although reactions such as C–H insertion at the nonaromatic N-substituent have also been observed.[18] Interestingly, in the case of diazomalonamic derivatives (Z=CO_2Et), no oxindoles were observed, the ester group apparently preventing aromatic C–H insertion by the carbenoid.[17,18] We now report the results of a much more detailed study of the chemoselectivity of such carbenoid reactions which reveals some dramatic catalyst effects.



(R=Me, Et, Bu, CH_2Ph; Z= H, Ac, SO_2Ph)

The starting material for all the compounds used in this study was ethyl 2-diazomalonyl chloride. Although this compound has been described in the literature previously,[19] we developed an improved procedure for its preparation involving the reaction of ethyl diazoacetate with triphosgene.[20] This gave the diazo acid chloride in 53% yield on a 40-g scale. The acid chloride was used to acylate a range of amines leading to the desired diazoamide substrates. Our initial experiments involved the use of simple allylamine derivatives, and confirmed the earlier observations of Sturm and co-workers that the resulting diazoamides are thermally unstable.[21] Thus, reaction of ethyl diazomalonyl chloride with *N*-methylallylamine in dichloromethane at room temperature for 15 h led, after chromatography, to a high yield of the pyrrolopyrazole **3**. This results from an intramolecular dipolar cycloaddition to give **2** (R = Me), followed by a 1,3-hydrogen shift.[21] The cycloaddition is rapid, so that if the reaction is quenched after 5 min, the only product obtained is the initial cycloadduct **2** (R = Me). The same rapid dipolar cycloaddition reaction was also observed in the diazoamides derived from diallylamine and *N*-allylcyclohexylamine; this resulted in the formation of pyrrolopyrazoles **4** and **5**, respectively.



The *N*-phenyldiazoamide **6** was also found to undergo the same cycloaddition, but at a much slower rate (days as opposed to minutes). The initial cycloadduct **7**, formed by heating the diazoamide **6** in benzene for 2 h or by stirring in CH_2Cl_2 at room temperature for 3 days, is relatively stable, but loses nitrogen on prolonged heating or attempted recrystallization to give the pyrrolone **8**. Treatment of the initial cycloadduct **7** with *p*-toluenesulfonic acid in CH_2Cl_2 results in hydrogen migration to the pyrrolopyrazole **9**; this rearranged cycloadduct is also formed upon prolonged heating of the crude diazoamide **6**. Nevertheless, the diazoamide **6** was sufficiently stable to study its rhodium-catalyzed decomposition. Thus, treatment of **6** with rhodium(II) acetate in CH_2Cl_2 resulted in intramolecular cyclopropanation to give the azabicyclohexane **10**, albeit in only 6% yield. The same cyclopropane was formed in slightly higher yield (23%) by photolysis of the cycloadduct **7**. However, when rhodium(II) trifluoroacetamide[13,22] was used as catalyst, the only product isolated was the oxindole **11**, thereby providing the first indication that intramolecular aromatic C–H insertion could be enhanced by appropriate choice of ligand. As previously noted, such diazomalonamic derivatives are reported not to give oxindoles.[17,18]

In order to investigate this catalyst dependence further, we prepared the diazoanilides **12**, **16**,[17] **20**, **24**, **28**, and **32** by reaction of the corresponding *N*-substituted aniline with ethyl diazomalonyl chloride. These diazoamides are stable oils or crystalline solids; indeed the *N*-benzyl-*N*-phenyl derivative **12** formed crystals suitable for X-ray crystallography. The crystal structure showed that diazo group adopts an orientation in which it is *syn* to the amide carbonyl (Figure 1).[23]

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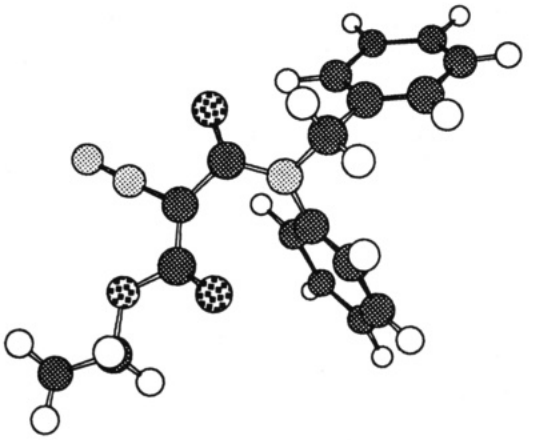
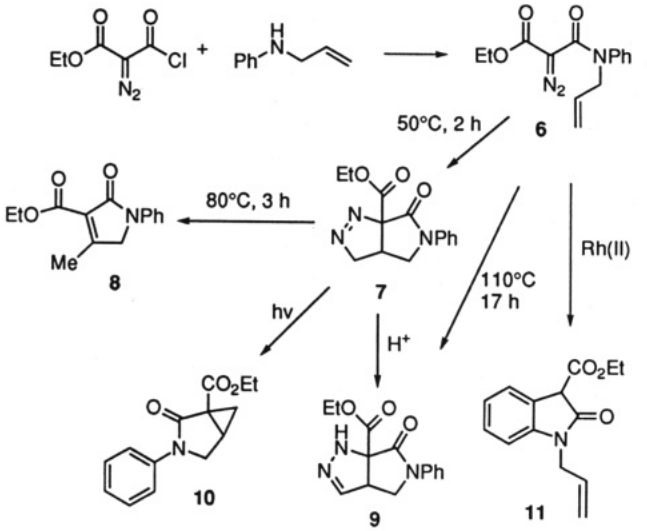
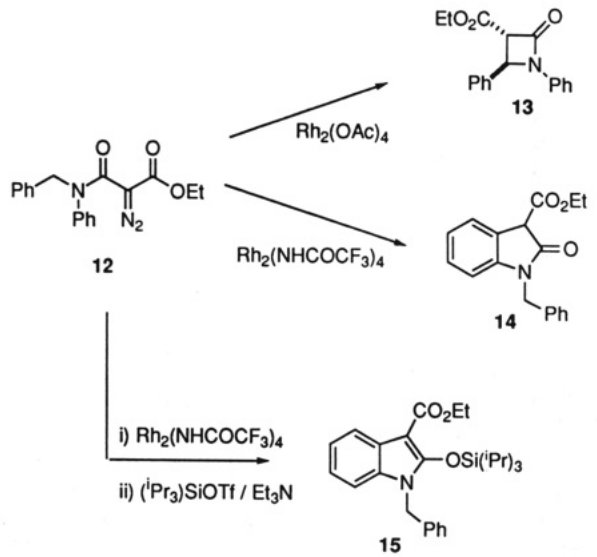


Figure 1. X-ray crystal structure of diazoamide **12**.



Rhodium(II) acetate-catalyzed decomposition of diazoamide **12** resulted in intramolecular C–H insertion to give the *trans*-β-lactam **13** as the major product in 61% isolated yield in line with previously reported results,[18] together with oxindole **14** (28% by NMR, Table 1).



However, by changing the catalyst ligand to trifluoroacetamide, β-lactam formation is completely suppressed in favor of the aromatic C–H insertion to give the oxindole **14** as the only detectable product. As a consequence of its hydrolytic lability, **14** was immediately reacted with TIPS-triflate to give the indole **15**. Typically, the oxindoles synthesized were converted to 2-silyl ether indoles for characterization purposes.

Table 1. Ligand Effects in the Rhodium(II)-Catalyzed Decomposition of Diazoamide 12

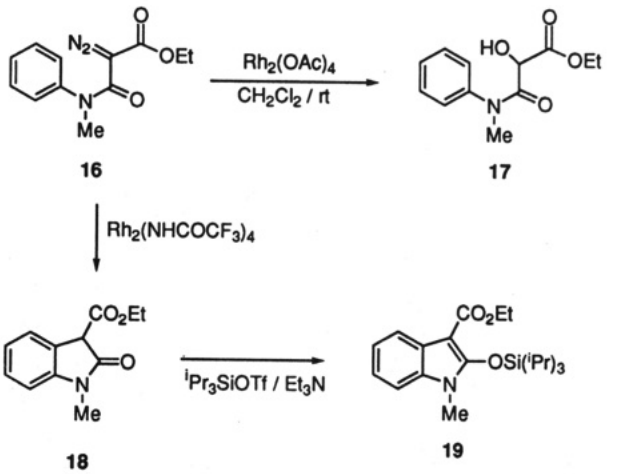
catalyst	reaction time	ratio β-lactam/oxindole[a] (13/14)
rhodium(II) acetate	9 days	72:28
rhodium(II) trifluoroacetate	61 h	0:100 (trace β-lactam)
rhodium(II) perfluorobutyrate	121 h	7:93
rhodium(II) acetamide	145 h	19:81
rhodium(II) trifluoroacetamide	10 min	0:100
rhodium(II) perfluorobutyramide	10 min	0:100

[a] Yields (±5%) measured by ^{1}H NMR, and although other minor (<5%) products were present, the ratios are normalized to β-lactam + oxindole = 100%.

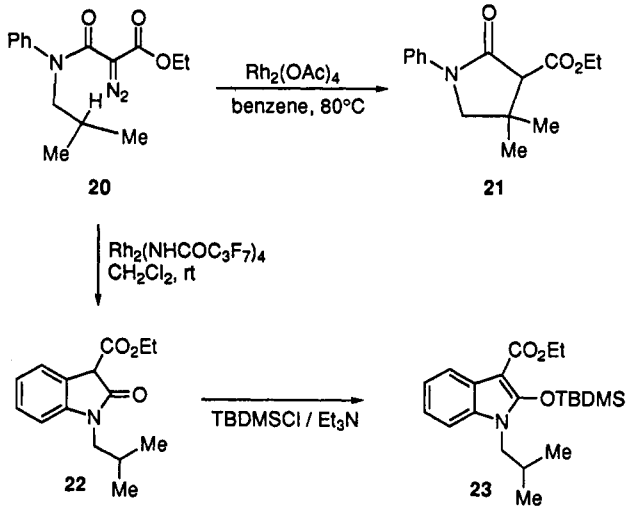
Having established that aliphatic or aromatic C–H insertion can be promoted by appropriate choice of ligand, we investigated other rhodium catalysts for the decomposition of diazoamide **12**. The results which are shown in Table 1 clearly establish that rhodium perfluorocarboxamides are the best catalysts for effecting the intramolecular aromatic C–H insertion reaction and also are the most "*catalytically active*" in terms of time taken for the reaction, as measured by consumption of diazoanilide starting material, which was carefully monitored by TLC.

Since rhodium(II) trifluoroacetamide is somewhat tedious to prepare and purify (the novel catalyst rhodium perfluorobutyramide is somewhat easier to generate), we investigated its *in situ* preparation. As described in the Experimental Section, rhodium(II) acetate was pretreated with trifluoroacetamide, and the resulting "*catalyst*" was used for the decomposition of **12**. The result in terms of chemoselectivity was identical with that obtained by use of rhodium(II) trifluoroacetamide, *i.e.* exclusive oxindole formation, although the reaction times were slightly longer.

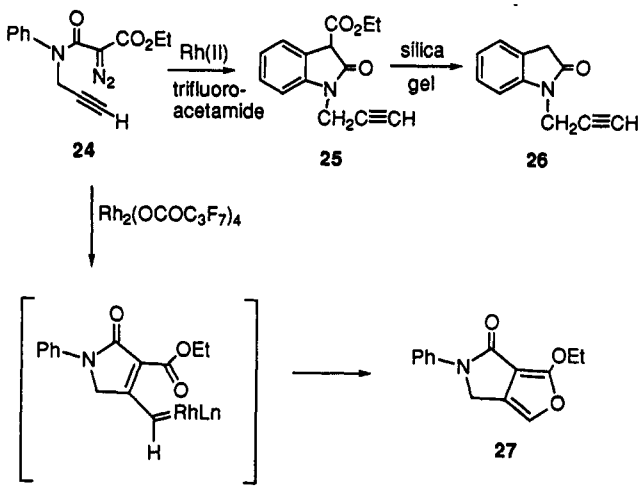
Since there are conflicting reports in the literature on the rhodium-catalyzed decomposition of the *N*-methyldiazoanilide **16**,[17,18] we decided to reinvestigate its decomposition with a different rhodium catalyst. Using rhodium(II) acetate as the catalyst, we confirmed Durst's observation that the only identifiable product is **17** which is presumably derived from insertion of the carbenoid into adventitious water.[17] Rhodium(II) trifluoroacetamide, however, promotes oxindole formation to give, after silylation, the indole 3-ester **19** in 79% yield.



The intramolecular C–H insertion reaction of a rhodium carbenoid generally exhibits an overwhelming preference for five-membered ring formation.[7,24,25] Exceptions are known,[5,26] but they can be attributed to steric factors or to electronic stabilization of the center at which four- or six-membered ring formation occurs. The competition between aliphatic and aromatic carbon–hydrogen insertion of *N*-isobutyldiazoanilide **20** provides another example of ligand effectiveness in controlling chemoselectivity in dirhodium(II)-catalyzed metal carbene reactions. Thus, treatment of **20** with rhodium(II) acetate results in exclusive aliphatic C–H insertion giving pyrrolone **21**, while the perfluorobutyramide ligand promotes oxindole formation by aromatic C–H insertion. Again, as a consequence of its hydrolytic lability, oxindole **22** was immediately reacted with *tert*-butyldimethylsilyl chloride (TBDMSCl) producing indole **23** in excellent yield.



The metal-catalyzed reactions of α-diazocarbonyl compounds with alkenes and alkynes have been extensively employed in organic synthesis.[27,28] Indeed, the rhodium(II)-catalyzed reaction of α-diazo ketones bearing tethered alkyne units represents a powerful method for the construction of a variety of polycyclic skeletons.[29,30] Exposure of an α-diazocarbonyl compound containing a tethered alkynyl group to a rhodium(II) catalyst generally results in cyclization of the α-keto carbenoid to an intermediate in which carbene-like reactivity has appeared on one of the original alkyne carbon atoms. A neighboring functional group present on the backbone then traps the cyclized intermediate *via* known carbene chemistry to give various products. With this in mind, we prepared *N*-propargyldiazoanilide **24** and investigated its behavior toward several Rh(II) catalysts. Interestingly, we found that rhodium(II) trifluoroacetamide promotes exclusive oxindole formation from **24**. The resulting oxindole **25** readily hydrolyzes and decarboxylates upon silica gel chromatography to give *N*-propargyloxindole **26** (87%). When rhodium(II) perfluorobutyrate was used as the catalyst, however, the only product obtained corresponded to furopyrrolone **27** in line with previous results.[18,29] Its



formation can be explained in terms of insertion of the initially formed rhodium carbenoid onto the neighboring acetylenic π-bond with formation of a cyclized vinyl rhodium carbenoid that is subsequently intercepted by the adjacent carbonyl oxygen.[29,30] Formation of furans by 6π-electrocyclization of acyl vinylcarbenes is a well-precedented reaction in heterocyclic chemistry.[31–34]

Bimolecular insertion of rhodium carbenoids into heteroatom hydrogen bonds are facile processes.[1] Intramolecular insertion into OH, NH, and SH bonds also occurs readily and results in the formation of novel heterocycles from various diazo precursors.[35–38] The reaction is not subject to steric hindrance at the oxygen center since tertiary alcohols cyclize just as easily as primary alcohols.[39] The rhodium carbenoid cyclization to both six and seven-membered ring ethers occur easily in good yield.[40] Although O–H bonds are thermodynamically stronger than C–H bonds, competing C–H insertion processes were not encountered thereby providing good evidence that the reaction proceeds by nucleophilic attack of the oxygen atom on a metallocarbenoid intermediate which retains highly electrophilic properties. In order to probe the

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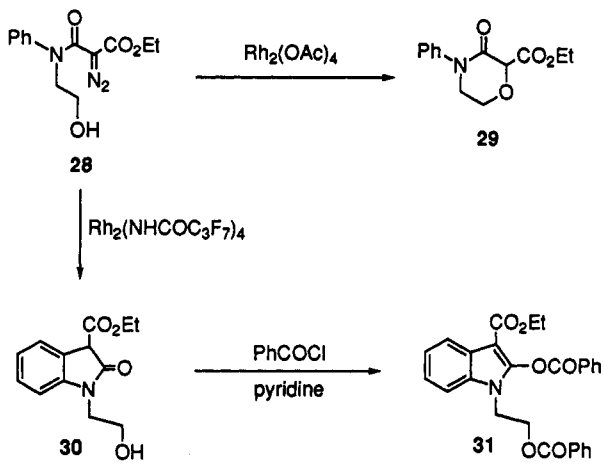
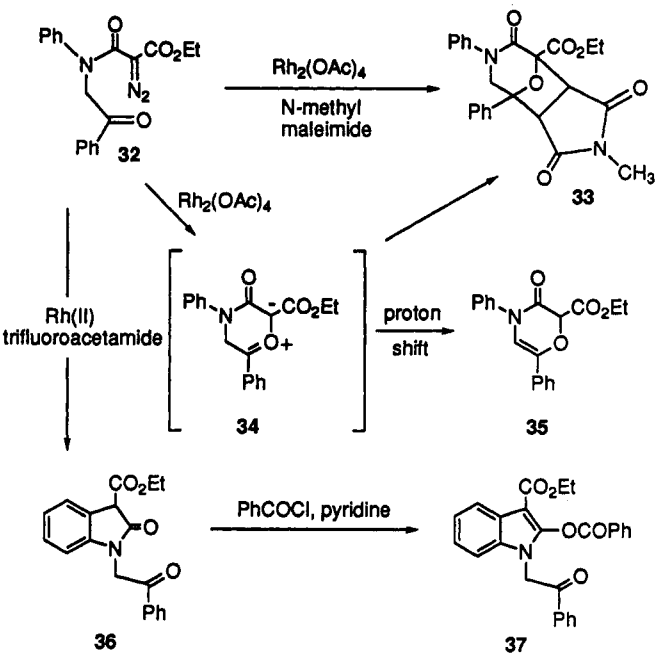
competition between aromatic C–H insertion and O–H insertion, we investigated the rhodium(II)-catalyzed behavior of diazo-*N*-(2-hydroxyethyl)-*N*-phenylmalonamic ester **28**. Once again, remarkable levels of chemoselectivity were observed; diazoanilide **28** is cleanly converted into the morpholine derivative **29**, the product of intramolecular O–H insertion, by treatment with rhodium(II) acetate. A perfluorocarboxamide ligand, however, promotes aromatic C–H insertion to give, after O-benzoylation, the indole 3-ester **31** in high yield.



Ylide formation as a result of carbene interaction with the unshared electron pair of heteroatoms has been extensively studied.[41] In earlier papers we described the formation of bridged oxabicyclo[3.2.1]heptanes from the rhodium(II)-catalyzed reactions of 1-diazopentanediones.[42] The reaction involves the formation of a rhodium carbenoid and subsequent transannular cyclization of the electrophilic carbon onto the adjacent carbonyl group to generate a cyclic carbonyl ylide, followed by 1,3-dipolar cycloaddition. In order to determine whether aromatic C–H insertion can compete with carbonyl ylide formation we studied the Rh(II)-catalyzed behavior of diazoanilide **32**. Rhodium(II) acetate-catalyzed decomposition of **32** in the presence of *N*-methylmaleimide gives the tricycle **33**, as a result of carbonyl ylide formation and interception in a 1,3-dipolar cycloaddition. In the absence of the dipolarophile, the initial ylide rearranges by hydrogen shift to give the oxazinone **35**. In contrast, rhodium(II) perfluorobutyramide catalyzes the conversion of diazoanilide **32** into oxindole **36**, isolated as its benzoate **37**.

In conclusion, the above experiments involving the rhodium(II)-catalyzed decomposition of diazoamides have demonstrated a dramatic catalyst effect. Rhodium(II) perfluorocarboxamides exclusively promote intramolecular aromatic C–H insertion reactions to give oxindoles in good yield, thereby significantly extending this route to oxindoles.[16–18,43] The aromatic C–H insertion occurs in preference to aliphatic C–H insertion, addition to C=C and C≡C bonds, O–H insertion, and ylide formation, all of which are observed simply by switching to a carboxylate-based rhodium catalyst. This remarkable chemoselectivity presumably reflects the differences in electrophilicity



between the various rhodium carbenoid intermediates, implying involvement of the metal and its ligands during the electrophilic substitution reaction at the aromatic ring.[16] Work is in progress to delineate further ligand effects in rhodium-catalyzed reactions of diazocarbonyl compounds.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator. Reaction mixtures were purified by silica gel chromatography. The *in-situ* generation and use of Rh(II) trifluoroacetamide was carried out in the following manner. A solution containing 10 mg (0.0226 mmol) of rhodium(II) acetate and 50 mg (0.44 mmol) of 2,2,2-trifluoroacetamide in 5 mL of 1,2-dichloroethane was heated at reflux overnight under N_2. The solution was cooled to rt and a solution of the diazoamide in 10 mL of CH_2Cl_2 was added dropwise. After stirring at rt for 4 h all the diazo compound had been consumed. The solvent was removed *in vacuo* and the reaction mixture was examined by ^1H NMR.

Preparation of Rhodium(II) Perfluorobutyramide ($Rh_2(NHCOC_3F_7)_4$) from Rhodium(II) Acetate ($Rh_2(OAc)_4$). To a solution containing 0.5 g (1.1 mmol) of rhodium(II) acetate in 30 mL of chlorobenzene was added 12 g (57 mmol) of perfluorobutyramide. The mixture was refluxed for 60 h under a Soxhlet extractor equipped with a thimble, containing a 1:1 Na_2CO_3: sand mixture, which was changed daily. The solution was concentrated under reduced pressure and the excess perfluorobutyramide removed by sublimation. The resulting solid was chromatographed on a neutral alumina column using a 1:1 hexane: ethyl acetate mixture as the eluent. Concentration of the purple fraction followed by drying in a vacuum oven at rt yielded 0.89 g (74%) of rhodium(II) perfluorobutyramide ($Rh_2(NHCOC_3F_7)_4$) as a navy blue solid: HPLC (Zorbax CN (9.4 mm × 25 cm) column; 1.0 mL/min; isocratic methanol) t_R 13.9 min.

Ethyl 2-Diazomalonyl Chloride. To a three-necked flask equipped with a cold-finger and thermometer was added 16.8 g (56.6 mmol) of triphosgene and 75 mL of anhydrous benzene. This mixture is cooled to 0 °C and 0.5 g (0.51 mL, 6.0 mmol) of anhydrous pyridine was added causing the formation of a white precipitate. To this solution was added 16.1 g (14.8 mL, 0.14 mol) of ethyl diazoacetate at such a rate that the internal temperature did not rise above 10 °C. This mixture was warmed to rt and stirred for 4–6 h. The red solution was filtered through

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(42) Padwa, A. *Acc. Chem. Res.* **1991**, *24*, 22.
(43) For some other recent approaches to oxindoles, see: Clark, R. D.; Muchowski, J. M.; Fisher, L. E.; Flippin, L. A.; Repke, D. B.; Souchet, M. *Synthesis* **1991**, 871. Karp, G. M. *J. Org. Chem.* **1992**, *57*, 4765. Quallich, G. J.; Morrissey, P. M. *Synthesis* **1993**, 51. Karp, G. M. *Org. Prep. Proc. Int.* **1993**, *25*, 481.

a pad of Celite and concentrated. Trituration with cold pentane precipitated unreacted triphosgene, the mixture was filtered through Celite, and the solution was then concentrated under reduced pressure. Purification of the red residue by vacuum distillation provided 11.0 g (44%) of ethyl-2-diazomalonyl chloride as a yellow liquid: bp 60–62 °C (1.5 torr) (lit.[19] 63–64 °C at 0.02 torr); IR (neat) 2120, 1750, and 1690 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.35 (t, J = 5.0 Hz, 3H), and 4.33 (q, J = 5.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 62.7, 64.1, 153.4, and 158.4.

Ethyl 5-Methyl-1,3a,4,5,6,6a-hexahydro-6-oxopyrrolo[3,4-*c*]pyrazole-6a-carboxylate (3). A 353-mg (2 mmol) sample of ethyl 2-diazomalonyl chloride was added to a solution containing 355 mg (5 mmol) of *N*-methylallylamine in 10 mL of CH_2Cl_2. After stirring at rt for 15 h the solution was washed with 2 N HCl, water, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash silica gel chromatography using ethyl acetate as the eluent to give 390 mg (93%) of **3** as a colorless oil: IR (film) 1747, 1697, 1235, and 735 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.42 (t, 3H, J = 7.1 Hz), 3.03 (s, 3H), 3.50 (dd, 1H, J = 10.0 and 1.9 Hz), 3.91 (dd, 1H, J = 10.0 and 8.2 Hz), 4.06 (brd, 1H, J = 7.7 Hz), 4.40 (q, 2H, J = 7.2 Hz), 6.68 (brs, 1H), and 6.81 (d, 1H, J = 0.6 Hz); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.1, 30.1, 48.9, 50.9, 62.6, 74.9, 143.2, 168.3, and 169.0; *m/z* (EI) 211 (M^+, 7%), 182 (32), 137 (18), 95 (100), 81 (30), 43 (54), and 42 (38); HRMS calcd for $C_9H_{13}N_3O_3$ 211.0956, found 211.0957.

Ethyl 5-Allyl-1,3a,4,5,6,6a-hexahydro-6-oxopyrrolo[3,4-*c*]pyrazole-6a-carboxylate (4). A solution containing 353 mg (2 mmol) of ethyl 2-diazomalonyl chloride in 2 mL of CH_2Cl_2 was added to a 388-mg (4 mmol) solution of diallylamine in 15 mL of CH_2Cl_2. After stirring at rt for 5 min the solution was washed with 2 N HCl and then with 20 mL of brine and dried over $MgSO_4$. Filtration and concentration *in vacuo* gave a colorless oil which was shown by infrared spectroscopy to contain only a trace of the diazo compound. Purification by flash column chromatography (eluent ether) gave 340 mg (72%) of **4** as a colorless oil: IR (film) 1751, 1697, and 1237 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.31 (t, 3H, J = 7.2 Hz), 3.39 (dd, 1H, J = 10.1 and 1.9 Hz), 3.78 (dd, 1H, J = 10.1 and 7.7 Hz), 3.95 (m, 3H), 4.24 (q, 2H, J = 7.2 Hz), 5.21 (m, 2H), 5.70 (m, 1H), 6.60 (brs, 1H), and 6.70 (d, 1H, J = 1.4 Hz); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.2, 45.4, 48.4, 49.0, 62.5, 75.0, 118.3, 131.1, 143.3, and 168.3 and 169.2; *m/z* (EI) 237 (M^+, 3.6%), 208 (33), 135 (19), 95 (100), 68 (30), 43 (62), 41 (69), 39 (43), 29 (36), and 27 (36); HRMS calcd for $C_{11}H_{15}N_3O_3$ 237.1108, found 237.1113.

Ethyl 5-Cyclohexyl-1,3a,4,5,6,6a-hexahydro-6-oxopyrrolo-[3,4-*c*]pyrazole-6a-carboxylate (5). To a solution containing 278 mg (2 mmol) of *N*-allylcyclohexylamine and 202 mg (2 mmol) of triethylamine in 10 mL of CH_2Cl_2 was added 353 mg (2 mmol) of ethyl 2-diazomalonyl chloride. After stirring at rt for 5 min, the solution was washed with 2 M HCl, water, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography (eluent ether/petroleum ether) to give 458 mg (82%) of **5** as a viscous clear oil: IR (film) 1754, 1689, and 1262 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.05–1.20 (m, 1H), 1.30 (t, 3H, J = 7.2 Hz), 1.27–1.43 (m, 4H), 1.66–1.83 (m, 5H), 3.42 (dd, 1H, J = 10.0 and 1.6 Hz), 3.72 (dd, 1H, J = 9.9 and 7.5 Hz), 3.88 (m, 2H), 4.26 (q, 2H, J = 7.1 Hz), 6.53 (brs, 1H), and 6.66 (s, 1H); ^{13}C-NMR (C_6D_6, 62.9 MHz) δ 14.0, 25.5, 25.6, 25.7, 30.0, 30.1, 44.8, 48.7, 51.7, 62.3, 75.3, 143.3, 168.1, and 168.7; *m/z* (EI) 279 (M^+, 2.3%), 250 (21), 168 (11), 153 (13), 95 (18), 55 (27), 45 (44), 41 (21), 31 (100), and 27 (34); HRMS calcd for $C_{14}H_{21}N_3O_3$ 279.1583, found 279.1585.

Preparation and Rhodium(II)-Catalyzed Reaction of *N*-Allyl-2-diazo-*N*-phenylmalonamic Acid Ethyl Ester (6). A solution containing 1.0 g (7.51 mmol) of *N*-allylaniline in 45 mL of THF at 0 °C was treated with 1.33 g (7.51 mmol) of ethyl 2-diazomalonyl chloride for 20 min. The reaction mixture was warmed to rt and stirred for 1.5 h. The yellow solution was taken up in ether and washed with a saturated aqueous $NaHCO_3$ solution and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 1.14 g (56%) of *N*-allyl-2-diazo-*N*-phenylmalonamic acid ethyl ester (**6**) as a yellow oil: IR (neat) 2121, 1716, and 691 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.09 (t, 3H, J = 6.9 Hz), 3.97 (q, 2H, J = 6.9 Hz), 4.39 (d, 2H, J = 5.4 Hz), 5.12 (m, 2H), 5.87 (m, 1H), 7.18 (m, 3H), and 7.33 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.8, 53.1, 53.5, 60.9, 117.3, 125.9, 126.5, 128.9, 132.7, 142.4, 160.1, and 161.3.

A solution containing 111 mg (0.406 mmol) of the above *N*-allyldiazoamide in 25 mL of benzene was heated at 50 °C for 2 h. The solution was then concentrated under reduced pressure and the residue was subjected to flash silica gel chromatography. The major product obtained (66%) corresponded to 6-oxo-5-phenyl-3a,4,5,6-tetrahydro-3*H*-pyrrolo[3,4-*c*]pyrazole-6a-carboxylic acid ethyl ester (**7**): mp 102–103 °C; IR (neat) 1747, 1693, and 1292 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.38 (t, 3H, J = 8.0 Hz), 3.17 (m, 1H), 3.48 (dd, 1H, J = 10.3 and 2.6 Hz), 4.24 (dd, 1H, J = 10.3 and 8.6 Hz), 4.38 (m, 2H), 4.66 (dd, 1H, J = 18.4 and 4.4 Hz), 5.12 (dd, 1H, J = 18.4 and 8.6 Hz), 7.20 (t, 1H, J = 7.3 Hz), 7.38 (t, 2H, J = 7.3 Hz), and 7.57 (d, 2H, J = 7.3 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.9, 31.2, 51.9, 62.7, 86.5, 106.4, 120.2, 125.6, 128.9, 137.8, 162.3, and 165.7. Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.54; H, 5.61; N, 15.23.

The second product isolated from the column was assigned as 4-methyl-2-oxo-1-phenyl-2,5-dihydro-1*H*-pyrrole-3-carboxylic acid ethyl ester (**8**) (33%): mp 141–142 °C; IR (neat) 1731, 1061, and 755 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.36 (t, 3H, J = 7.2 Hz), 2.39 (s, 3H), 4.24 (s, 2H), 4.30 (q, 2H, J = 7.2 Hz), 7.10 (t, 1H, J = 7.5 Hz), 7.34 (t, 2H, J = 7.5 Hz), and 7.66 (d, 2H, J = 7.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 15.1, 54.5, 60.7, 118.5, 123.9, 125.7, 128.9, 138.6, 162.1, 162.5, and 165.7. Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.18; N, 5.71. Found: C, 68.41; H, 6.17; N, 5.65. This same compound was obtained in quantitative yield by heating a sample of **7** at reflux in benzene for 3 h.

A solution containing 30.5 mg (0.11 mmol) of **6** in 4 mL of benzene was treated with 2.7 mg (0.005 mmol) of $Rh_2(NHCOCF_3)_4$. The reaction mixture was stirred for 2 h at rt, concentrated under reduced pressure, and subjected to silica gel chromatography. The only product isolated in quantitative yield corresponded to 1-allyl-2-oxo-2,3-dihydro-1*H*-indole-3-carboxylic acid ethyl ester (**11**): IR (neat) 1764, 1672, and 696 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, 3H, J = 7.2 Hz), 4.15 (q, 2H, J = 7.2 Hz), 4.26 (t, 2H, J = 6.0 Hz), 4.72 (s, 1H), 5.05 (m, 2H), 5.79 (m, 1H), 7.21 (d, 2H, J = 7.5 Hz), and 7.37 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.8, 52.8, 53.7, 62.8, 118.6, 128.2, 128.8, 129.8, 131.6, 140.7, 164.0, and 164.7; HRMS calcd for $C_{14}H_{15}NO_3$ 245.1051, found 245.1044.

Ethyl 5-Phenyl-1,3a,4,5,6,6a-hexahydro-6-oxopyrrolo[3,4-*c*]pyrazole-6a-carboxylate (9). A 266-mg (2 mmol) sample of *N*-allylaniline and 202 mg (2 mmol) of triethylamine were dissolved in 20 mL of CH_2Cl_2. A solution containing 353 mg (2 mmol) of ethyl 2-diazomalonyl chloride was added dropwise and the solution was stirred for 5 min. The solution was then washed with 2 M HCl and water, dried over $MgSO_4$, and concentrated *in vacuo* to leave behind a yellow oil. To the residue was added 20 mL of toluene and the solution was heated at reflux for 17 h. The solution was cooled to rt, washed with water, dried over $MgSO_4$, and concentrated *in vacuo*. Purification by flash silica gel chromatography using petroleum ether/ether/ethyl acetate as the eluent gave 326 mg (60%) of the title compound as a buff-colored solid: mp 113–114 °C; IR (CH_2Cl_2) 1755, 1704, 1271, and 746 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.28 (t, 3H, J = 7.2 Hz), 3.87 (dd, 1H, J = 11.6 and 1.9 Hz), 3.99–4.03 (m, 1H), 4.21–4.31 (m, 3H), 6.74 (d, 1H, J = 0.6 Hz), 6.78 (brs, 1H), and 7.15–7.60 (m, 5H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.0, 48.1, 50.1, 62.6, 75.9, 120.5, 125.8, 129.0, 138.1, 143.2, 167.9, and 168.8; *m/z* (EI) 273 (M^+, 4%), 245 (M – N_2, 6.1), 244 (19), 105 (100), 104 (45), 95 (40), 77 (63), 44 (41), and 39 (35). Anal. Calcd for $C_{14}H_{15}N_3O_3$: C, 61.53; H, 5.53; N, 15.38. Found: C, 61.56; H, 5.55; N, 15.34. The same compound was formed in quantitative yield when a sample of **7** was allowed to stir with *p*-toluenesulfonic acid in CH_2Cl_2.

Ethyl 2-Oxo-1-phenyl-1-azabicyclo[3.1.0]hexane-3-carboxylate (10). A solution containing 511 mg (1.87 mmol) of ethyl 5-phenyl-1,3a,4,5,6,6a-hexahydro-6-oxopyrrolo[3,4-*c*]pyrazole-6a-carboxylate (**7**) in 50 mL of 1,4-dioxane was photolyzed for 24 h. The solvent was removed *in vacuo* and the residue purified by flash chromatography (1:1 petroleum ether:ether) followed by recrystallization from petroleum ether/ether to give

107 mg (23%) of the title compound as a colorless solid: mp 98–99 °C; IR (CH_2Cl_2) 1743, 1719, and 1396 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.27 (m, 1H), 1.33 (t, 3H, J = 7.1 Hz), 2.03 (dd, 1H, J = 8.0 and 4.5 Hz), 2.48 (m, 1H), 3.72 (d, 1H, J = 10.3 Hz), 4.10 (dd, 1H, J = 10.3 and 5.9 Hz), 4.27 (q, 2H, J = 7.1 Hz), 7.16 (m, 1H), 7.34 (m, 2H), and 7.57 (m, 2H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.2, 20.9, 22.1, 32.8, 48.4, 61.6, 120.0, 124.7, 128.9, 139.0, 168.4, and 168.5; m/z (EI) 245 (M^+, 100%), 200 (16), 172 (41), 144 (34), 104 (43), 77 (57), 53 (24), and 29 (12); HRMS calcd for $C_{14}H_{15}NO_3$ 245.1052, found 245.1047.

The same compound was also isolated (6% yield) when a solution containing 200 mg (0.73 mmol) of *N*-allyl-2-diazo-*N*-phenylmalonamic acid ethyl ester (**6**) in 10 mL of dry CH_2Cl_2 was treated with 10 mg of rhodium(II) acetate for 40 h.

N-Benzyl-2-diazo-N-phenylmalonamic Acid Ethyl Ester (12). A 706-mg (4 mmol) sample of ethyl 2-diazomalonyl chloride was added neat to a 1.5-g (8.2 mmol) solution containing *N*-benzylaniline in 50 mL of CH_2Cl_2. After stirring for 10 min at rt, the solution was washed with 2 N HCl, water, and brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash silica gel chromatography (3:1 petroleum ether:ether) gave 1.15 g of the title compound (89%) as a bright yellow oil which crystallized on standing to a yellow solid: mp 78–79 °C; IR (film) 2123, 1721, and 1633 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.12 (t, 3H, J = 7.1 Hz), 4.01 (q, 2H, J = 7.1 Hz), 5.01 (s, 2H), and 7.10–7.35 (m, 10H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.1, 54.2, 61.3, 126.3, 126.9, 127.4, 128.2, 128.4, 129.2, 136.9, 142.6, 161, and 162; m/z (EI) 295 ($M^+ - N_2$, 4.7%), 249 (10), 222 (10), 103 (20), 91 (100), 86 (28), 84 (43), 77 (36), 65 (19), 49 (88), 44 (29), and 36 (36); HRMS calcd for [$C_{18}H_{17}N_3O_3 - N_2$] 295.1208, Found 295.1195.

The structure of **12** and its and solid state conformation has been confirmed by single crystal X-ray diffraction analysis.[23]

Ethyl 1,4-Diphenyl-2-oxoazetidine-3-carboxylate (13). A 20-mg sample of rhodium(II) acetate was added to a solution containing 250 mg (0.77 mmol) of *N*-benzyl-2-diazo-*N*-phenylmalonamic acid ethyl ester in 40 mL of dry CH_2Cl_2. After stirring at rt for 6 days, the solution was concentrated *in vacuo* and purified by flash silica gel chromatography (9:1 pentane–ether) to give 140 mg (61%) of the title compound as a colorless oil which crystallized on standing to a colorless solid: mp 87–89 °C; IR (film) 1769, 1729, and 755 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.33 (t, 3H, J = 7.1 Hz), 3.98 (d, 1H, J = 2.6 Hz), 4.29 (q, 2H, J = 7.1 Hz), 5.33 (d, 1H, J = 2.6 Hz), and 7.05–7.40 (m, 10H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.2, 57.5, 62.1, 63.6, 117.2, 124.4, 126.2, 129.0, 129.1, 129.3, 136.3, 137.2, 159.3, and 166.3; m/z (EI) 295 (M^+, 20%), 176 (50), 131 (100), 115 (19), 103 (26), 91 (27), 77 (52), and 29 (29). Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.22; H, 5.76; N, 4.75. Found: C, 72.97; H, 5.77; N, 4.59.

Ethyl 1-Benzyl-2-(triisopropylsiloxy)indole-3-carboxylate (15). A 5-mg sample of rhodium(II) trifluoroacetamide was added to a solution containing 150 mg (0.46 mmol) of *N*-benzyl-2-diazo-*N*-phenylmalonamic acid ethyl ester (**12**) in 25 mL CH_2Cl_2. After stirring for 10 min, the solvent was removed *in vacuo* to leave behind 135 mg of the essentially pure (99%) ethyl 1-benzyl-2-oxoindole-3-carboxylate (**14**) as a crude solid: ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.30 (t, 3H, J = 7.1 Hz), 4.23 (m, 2H), 4.52 (s, 1H), 4.81 and 5.06 (AB, 2H, J = 15.7 Hz), 6.70 (d, 1H, J = 7.8 Hz), and 7.00–7.33 (m, 9H). However, this compound was very difficult to isolate in pure form so instead **14** was characterized as its triisopropylsilyl enol ether **15**. A 1.5-mg sample of rhodium(II) trifluoroacetamide was added to a solution containing 283 mg (0.88 mmol) of **12** in 10 mL of CH_2Cl_2. After stirring at rt for 10 min, 300 mg (0.98 mmol) of triisopropylsilyl trifluoromethanesulfonate and 100 mg (1 mmol) of triethylamine were added. After a further 5 min, the solution was diluted with 10 mL of CH_2Cl_2, washed with water, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash silica gel chromatography (eluent 99:1 petroleum ether:ether) gave 376 mg of ethyl 1-benzyl-2-(triisopropylsiloxy)indole-3-carboxylate (**15**) (94%) as a colorless solid: mp 77–78 °C; IR (CH_2Cl_2) 1702 and 773 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.08 (d, 18H, J = 7.5 Hz), 1.44 (t, 3H, J = 7.2 Hz), 1.50 (3H, heptet, J = 7.5 Hz), 4.37 (q, 2H, J = 7.2 Hz), 5.27 (s, 2H), 7.01–7.23 (m, 8H), and 8.00 (m, 1H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 14.7, 17.9, 44.7, 59.0, 89.1, 109.2, 120.8, 121.1, 121.7, 125.2, 126.1, 127.4, 128.6, 131.2, 136.3, 153.2, and 164.8; m/z (EI) 451 (M^+, 7.5%), 408 (100), 380 (15), 223 (10), 91 (96), and 59 (15); HRMS calcd for $C_{27}H_{37}NO_3Si$ 451.2543, found 451.2547.

2-Diazo-N-methyl-N-phenylmalonamic Acid Ethyl Ester (16). A solution containing 706 mg (4 mmol) of ethyl 2-diazomalonyl chloride in 5 mL of CH_2Cl_2 was added to an 856 mg (8 mmol) solution of *N*-methylaniline in 30 mL of CH_2Cl_2. After stirring at rt for 5 min, the solution was washed with 2 N HCl and water, dried over $MgSO_4$, filtered, and then concentrated *in vacuo* and purified by flash chromatography (eluent 4:1 to 1:1 petroleum ether:ether) to give 930 mg of the title compound (94%) as a yellow solid: mp 66–67 °C; IR (CH_2Cl_2 solution) 2127, 1722, 1629, and 766 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.13 (t, 3H, J = 7.1 Hz), 3.39 (s, 3H), 4.02 (q, 2H, J = 7.1 Hz), and 7.20–7.40 (m, 5H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.3, 38.7, 61.4, 125.8, 126.9, 129.5, 144.0, 161.1, and 162.0; m/z (EI) 247 (M^+, 1.8 %), 219 (21), 173 (60), 147 (55), 146 (72), 118 (53), 105 (34), 91 (35), 77 (100), and 29 (84). Anal. Calcd for $C_{12}H_{13}N_3O_3$: C, 58.30; H, 5.26; N, 17.00. Found: C, 58.18; H, 5.33; N, 16.94.

2-Hydroxy-N-methyl-N-phenylmalonamic Acid Ethyl Ester (17). A 2-mg sample of rhodium(II) acetate was added to a solution containing 56 mg (0.23 mmol) of 2-diazo-*N*-methyl-*N*-phenylmalonamic acid ethyl ester (**16**) in 5 mL of CH_2Cl_2. After stirring at rt for 8 days, the solvent was removed *in vacuo* and the residue purified to afford 8 mg (15%) 2-hydroxy-*N*-methyl-*N*-phenylmalonamic acid ethyl ester (**17**) as a colorless oil (lit.[17] oil); ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.21 (t, 3H, J = 7.1 Hz), 3.35 (s, 3H), 3.95 (d, 1H, J = 8.0 Hz), 4.09 (m, 2H), 4.60 (d, 1H), 7.20–7.55 (m, 5H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 13.9, 38.1, 62.1, 69.2, 127.8, 128.7, 129.9, 141.7, 168.2, and 169.5.

Ethyl 2-(triisopropylsiloxy)-1-methylindole-3-carboxylate (19). A 5-mg sample of rhodium(II) trifluoroacetamide was added to a solution containing 200 mg (0.81 mmol) of 2-diazo-*N*-methyl-*N*-phenylmalonamic acid ethyl ester (**16**) in 15 mL of CH_2Cl_2. After stirring at rt for 10 min, the solvent was removed *in vacuo* to afford 137 mg (77%) of essentially pure ethyl 1-methyl-2-oxoindole-3-carboxylate (**18**) as a pale green oil: ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.28 (t, 3H, J = 7.1 Hz), 3.23 (s, 3H), 4.26 (m, 2H), 4.42 (s, 1H), 6.80 (m, 1H), 7.08 (m, 1H), and 7.35 (m, 2H). This compound was very difficult to isolate in pure form so instead **18** was characterized as its triisopropylsilyl enol ether. A 1-mg sample of rhodium(II) trifluoroacetamide was added to a solution containing 83 mg (0.34 mmol) of **16** in 5 mL of CH_2Cl_2. After stirring at rt for 15 min, 107 mg (0.35 mmol) of triisopropylsilyl trifluoromethanesulfonate and 35 mg (0.35 mmol) of triethylamine were added. After 10 min, the solution was washed with water, dried over $MgSO_4$, concentrated *in vacuo*, and purified by flash silica gel chromatography (eluent petroleum ether) to afford 100 mg of ethyl 2-(triisopropylsiloxy)-1-methylindole-3-carboxylate (**19**) (79%) as a colorless solid: mp 56–57 °C; IR (CH_2Cl_2) 1693, 1533, and 1473 cm^{-1}; ^1H-NMR ($CDCl_3$, 250 MHz) δ 1.16 (d, 18H, J = 7.5 Hz), 1.42 (t, 3H, J = 7.1 Hz), 1.55 (3H, heptet, J = 7.5 Hz), 3.59 (s, 3H), 4.36 (q, 2H, J = 7.1 Hz), 7.16–7.22 (m, 3H), and 7.99–8.03 (m, 1H); ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 14.1, 14.7, 17.8, 27.8, 58.9, 89.3, 108.3, 120.8, 120.9, 121.5, 125.2, 131.3, 153.2, and 164.7; m/z (EI) 375 (M^+, 8.3%), 332 (100), 304 (27), 218 (8), 173 (11), 131 (17), 103 (19), 73 (18), and 59 (34); HRMS calcd for $C_{21}H_{33}NO_3Si$ 375.2230, found 375.2235.

Preparation and Rhodium(II)-Catalyzed Reaction of 2-Diazo-N-isobutyl-N-phenylmalonamic Acid Ethyl Ester (20). A solution of 2.0 g (10.3 mmol) of t-BOC-aniline[44] in 50 mL of a 1:1 mixture of distilled DMF/THF at rt was treated with 620 mg (15.5 mmol) of NaH (60% dispersion in mineral oil). This solution was stirred at rt for 25 min. The mixture was then treated with 1.4 mL (12.4 mmol) of 1-bromo-2-methylpropane and was stirred at rt overnight. The excess NaH was quenched with a saturated aqueous NH_4Cl solution. The mixture was taken up in CH_2Cl_2 and washed with H_2O and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was dissolved in EtOAc and treated with 5% aqueous HCl. The mixture was heated at 50 °C for 5 h. The crude *N*-isobutylaniline was taken up in EtOAc and washed with 5% aqueous NaOH and brine. The organic extracts

(44) Hasan, I.; Marinelli, E.; Lin, L.; Fowler, F.; Levy, A. *J. Org. Chem.* **1981**, *46*, 157.

were dried over Na_2SO_4, filtered, and concentrated under pressure. The residue was subjected to flash silica gel chromatography to give 475 mg (32%) of *N*-isobutylaniline:[45] IR (neat) 3417, 2958, 1602, and 1505 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 0.92 (d, 6H, J = 6.6 Hz), 1.83 (m, 1H), 2.87 (d, 2H, J = 6.6 Hz), 3.72 (brs, 1H), 6.55 (d, 2H, J = 7.9 Hz), 6.62 (t, 1H, J = 7.2 Hz), and 7.11 (t, 2H, J = 7.9 Hz).

A solution of 300 mg (2.01 mmol) of *N*-isobutylaniline in 20 mL of CH_2Cl_2 at 0 °C was treated with 180 μL (2.21 mmol) of pyridine followed by 390 mg (2.21 mmol) of ethyl-2-diazomalonyl chloride. The solution was warmed to rt and was stirred for 2 h. The mixture was taken up in CH_2Cl_2, washed with a saturated aqueous $NaHCO_3$ solution and brine, and dried over Na_2SO_4. The organic extracts were filtered and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 0.561 g (96%) of 2-diazo-*N*-isobutyl-*N*-phenylmalonamic acid ethyl ester (**20**) as a crystalline yellow solid: mp 38–39 °C; IR (neat) 2117, 1720, and 1291 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 0.89 (d, 6H, J = 6.6 Hz), 1.09 (t, 3H, J = 7.0 Hz), 1.89 (m, 1H), 3.63 (d, 2H, J = 6.6 Hz), 3.98 (q, 2H, J = 7.0 Hz), 7.19 (m, 3H), and 7.32 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 20.1, 27.0, 57.5, 61.2, 126.3, 126.7, 129.2, 142.8, 160.9, and 161.9.

A solution containing 100 mg (0.35 mmol) of **20** in 4 mL of benzene was treated with 5 mg (0.011 mmol) of $Rh_2(OAc)_4$ and the mixture was heated at 80 °C for 6 h. The mixture was concentrated under reduced pressure and the residue was subjected to flash silica gel chromatography to give 54 mg (61%) of 4,4-dimethyl-2-oxo-1-phenylpyrrolidine-3-carboxylic acid ethyl ester (**21**) as a light yellow oil: IR (neat) 1734, 1699, and 1314 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 3H), 1.25 (t, 3H, J = 7.2 Hz), 1.29 (s, 3H), 3.21 (s, 1H), 3.45 (d, 1H, J = 9.2 Hz), 3.78 (d, 1H, J = 9.2 Hz), 4.18 (q, 2H, J = 7.2 Hz), 7.12 (t, 1H, J = 8.1 Hz), 7.33 (t, 2H, J = 8.1 Hz), and 7.56 (d, 2H, J = 8.1 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 22.7, 28.6, 36.2, 60.6, 61.2, 61.7, 120.3, 124.9, 128.8, 139.1, 168.5, and 169.2; HRMS calcd for $C_{15}H_{19}NO_3$ 261.1358, found 261.1357.

A solution of 100 mg (0.34 mmol) of **20** in 4 mL of CH_2Cl_2 was treated with 5 mg (0.011 mmol) of $Rh_2(NHCOC_3F_7)_4$ and the reaction was stirred at rt for 3 h. The mixture was then treated with 58 μL (0.41 mmol) of Et_3N and 63 mg (0.41 mmol) of TBDMSCl and was allowed to stir for an additional 2 h. The mixture was then taken up in CH_2Cl_2, washed with a saturated aqueous K_2CO_3 solution, and dried over Na_2SO_4. The organic extracts were filtered and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 105 mg (81%) of ethyl 1-isobutyl-2-(*tert*-butyldimethylsiloxy)indole-3-carboxylate (**23**) as a pale yellow oil: IR (neat) 2957, 1695, 1536, and 1464 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 0.37 (s, 6H), 0.90 (d, 6H, J = 7.0 Hz), 1.08 (s, 9H), 1.44 (t, 3H, J = 6.9 Hz), 2.23 (m, 1H), 3.86 (d, 2H, J = 7.0 Hz), 4.38 (q, 2H, J = 6.9 Hz), 7.18 (m, 3H), and 8.05 (d, 1H, J = 6.9 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.8, 18.8, 20.1, 25.9, 28.3, 48.8, 59.0, 89.4, 109.2, 120.9, 121.0, 121.4, 125.3, 131.1, 152.9, and 164.8; HRMS calcd for $C_{21}H_{33}NO_3Si$ 375.2229, found 375.2217.

Preparation and Rhodium(II)-Catalyzed Reaction of 2-Diazo-*N*-phenyl-*N*-prop-2-ynylmalonamic acid ethyl ester (24). A solution of 5.0 g (25.8 mmol) of t-BOC-aniline[44] in 80 mL of a 1:1 mixture of distilled DMF/THF at rt was treated with 2.07 g (51.8 mmol) of NaH (60% dispersion in mineral oil). This solution was stirred at rt for 30 min. The mixture was allowed to react with 3.0 g (33.6 mmol) of propargyl bromide and the mixture was stirred at rt for 8 h. The excess NaH was quenched with a saturated aqueous NH_4Cl solution. The mixture was taken up in ether and washed with H_2O and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude *N*-propargyl aniline was dissolved in EtOAc and treated with 5% aqueous HCl. The mixture was heated at 50 °C for 24 h. The deprotected product was taken up in EtOAc, and washed with 5% aqueous NaOH and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 2.76 g (81%) of *N*-propargylaniline:[46] IR (neat) 3400, 3280, 1602, 1502, and 748 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 2.22 (s, 1H), 3.88 (brs, 1H), 3.94 (s, 2H), 6.85 (d, 2H, J = 7.5 Hz), 6.79 (t, 1H, J = 7.5 Hz), and 7.22 (m, 2H).

A solution of 1.0 g (7.6 mmol) of the above *N*-propargylaniline in 30 mL of THF at 0 °C was treated with 0.90 g (5.1 mmol) of ethyl 2-diazomalonyl chloride. The solution was warmed to rt and was stirred for 3 h. The mixture was taken up in ether, washed with a saturated aqueous $NaHCO_3$ solution and brine, and dried over Na_2SO_4. The organic extracts were filtered and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 1.10 g (78%) of 2-diazo-*N*-phenyl-*N*-prop-2-ynylmalonamic acid ethyl ester (**24**) as a yellow oil: IR (neat) 3247, 2121, 1716, and 1630 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.10 (t, 3H, J = 7.2 Hz), 2.20 (s, 1H), 4.00 (q, 2H, J = 7.2 Hz), 4.52 (s, 2H), 7.27 (t, 3H, J = 7.2 Hz), and 7.37 (t, 2H, J = 7.2 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 39.9, 53.5, 61.2, 72.5, 78.4, 126.5, 127.4, 129.2, 141.6, 160.7, and 161.2.

A mixture of 0.18 g (0.66 mmol) of **24** in 20 mL of benzene and 20 mg (0.045 mmol) of the rhodium(II) catalyst was stirred at rt for 8 h. The solution was concentrated under reduced pressure and purified by flash silica gel chromatography. When $Rh_2(NHCOCF_3)_4$) was used as the catalyst, the major product isolated from the silica gel column corresponded to 1-prop-2-ynyl-1,3-dihydroindol-2-one (**26**) (87%) which was obtained as a white crystalline solid: mp 97–98 °C; IR (neat) 3251, 2944, 2118, and 1699 and cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 2.02 (s, 1H), 3.46 (s, 2H), 4.47 (s, 2H), 7.01 (m, 2H), and 7.22 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 28.5, 34.7, 72.1, 77.6, 108.7, 122.1, 124.2, 124.6, 127.4, 143.4, and 173.1; HRMS calcd for $C_{11}H_9NO$ 171.0684, found 171.0676.

When rhodium(II) perfluorobutyrate was used as the catalyst in the above reaction, 3-ethoxy-5-phenyl-5,6-dihydrofuro[3,4-*c*]pyrrol-4-one (**27**) was obtained as the major product (98%) and was isolated as a crystalline solid: mp 117-118 °C; IR (neat) 3140, 1680, and 746 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.43 (t, 3H, J = 6.9 Hz), 4.64 (s, 2H), 4.71 (q, 2H, J = 6.9 Hz), 6.69 (s, 1H), 7.10 (t, 1H, J = 7.3 Hz), 7.34 (t, 2H, J = 7.3 Hz), and 7.67 (d, 2H, J = 7.3 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.8, 45.4, 69.6, 96.0, 119.6, 122.5, 124.0, 124.8, 128.9, 140.1, 155.6, and 161.7. Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.40; N, 5.76. Found: C, 68.85; H, 5.44; N, 5.67.

Preparation and Rhodium(II)-Catalyzed Reaction of 2-Diazo-*N*-(2-hydroxyethyl)-*N*-phenylmalonamic Acid Ethyl Ester (28). A solution of 1.0 g (7.29 mmol) of 2-anilinoethanol in 25 mL of THF at 0 °C was treated with 1.29 g (7.29 mmol) of ethyl-2-diazomalonyl chloride. This mixture was warmed to rt and was stirred at 25 °C for 2 h. The reaction mixture was taken up in ether, and washed with a saturated aqueous $NaHCO_3$ solution and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 1.33 g (66%) of 2-diazo-*N*-(2-hydroxyethyl)-*N*-phenylmalonamic acid ethyl ester (**28**) as a yellow oil: IR (neat) 3445, 2114, 1716, and 1680 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.03 (t, 3H, J = 6.9 Hz), 3.30 (bs, 1H), 3.64 (t, 2H, J = 5.1 Hz), 3.91 (m, 4H), 7.18 (d, 3H, J = 7.0 Hz), and 7.29 (t, 2H, J = 7.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.9, 53.4, 59.6, 61.1, 66.2, 126.4, 126.9, 129.2, 142.2, 161.4, and 161.7.

A solution of 100 mg (0.36 mmol) of **28** in 5 mL of CH_2Cl_2 was treated with 20 mg (0.045 mmol) of $Rh_2(OAc)_4$ and the mixture was stirred at rt for 48 h. The mixture was concentrated under reduced pressure and the residue was subjected to flash silica gel chromatography to give 89 mg (90%) of 3-oxo-4-phenylmorpholine-2-carboxylic acid ethyl ester (**29**): mp 66–67 °C; IR (neat) 1737 and 1662 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.32 (t, 3H, J = 7.2 Hz), 3.81 (m, 2H), 4.06 (m, 1H), 4.29 (q, 2H, J = 7.2 Hz), 4.40 (m, 1H), 4.87 (s, 1H), 7.29 (m, 3H), and 7.39 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.1, 49.5, 62.0, 62.4, 77.0, 125.2, 127.2, 129.2, 141.1, 162.8, and 167.5. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.08; N, 5.62. Found: C, 62.47; H, 6.08; N, 5.52.

A solution of 50 mg (0.18 mmol) of **28** in 4 mL of CH_2Cl_2 was treated with 5 mg (0.011 mmol) of $Rh_2(NHCOC_3F_7)_4$ and the reaction was stirred at rt for 3 h. The reaction mixture was then cooled to 0 °C and 44 μL (0.54 mmol) of pyridine was added followed by 63 μL (0.54 mmol) of benzoyl chloride. The reaction was warmed to rt and stirred for 4 h. The mixture was taken up

(45) Roberts, R.; Hussein, F. *J. Am. Chem. Soc.* **1960**, *82*, 1950.
(46) Barluenga, J.; Campos, P.; Canal, G. *Synthesis* **1989**, *1*, 33.

in CH_2Cl_2 and washed with saturated aqueous NH_4Cl followed by brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 82 mg (90%) of 2-(benzoyloxy)-1-[2-(benzoyloxy)ethyl]-1*H*-indole-3-carboxylic acid ethyl ester (**31**): mp 140-141 °C; IR (neat) 1760, 1719, and 1695 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.10 (t, 3H, J = 7.2 Hz), 4.21 (q, 2H, J = 7.2 Hz), 4.46 (t, 2H, J = 5.4 Hz), 4.63 (t, 2H, J = 5.4 Hz), 7.40 (m, 8H), 7.65 (t, 1H, J = 7.2 Hz), 7.89 (d, 2H, J = 7.8 Hz), 8.13 (d, 2H, J = 7.8 Hz), and 8.21 (m, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 41.3, 59.6, 62.5, 95.2, 109.5, 121.8, 122.5, 122.8, 125.0, 127.8, 128.3, 128.7, 129.4, 129.7, 130.7, 132.0, 133.2, 134.3, 146.6, 163.5, and 166.2. Anal. Calcd for $C_{27}H_{23}NO_6$: C, 70.88; H, 5.08; N, 3.06. Found: C, 70.62; H, 5.10; N, 2.99.

Preparation and Rhodium(II)-Catalyzed Reaction of 2-Diazo-*N*-(2-oxo-2-phenylethyl)-*N*-phenylmalonamic Acid Ethyl Ester (32). Following the procedure of Dieter,[47] to a solution containing 2.0 g (21.5 mmol) of aniline in 40 mL of benzene at rt was added 3.6 g (35.9 mmol) of Et_3N. The solution was treated with 4.19 g (21.5 mmol) of α-bromoacetophenone and was then heated at reflux for 10 h. The mixture was cooled to rt, taken up in CH_2Cl_2, and washed with a saturated aqueous NH_4Cl solution, H_2O, and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 3.10 g (70%) of 1-phenyl-2-(phenylamino)ethanone[48] as a white solid: mp 91–92 °C; IR (neat) 3410, 1680, and 741 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 4.60 (s, 2H), 4.92 (brs, 1H), 6.72 (m, 3H), 7.21 (t, 2H, J = 7.5 Hz), 7.50 (t, 2H, J = 7.2 Hz), 7.61 (t, 1H, J = 7.5 Hz), and 8.01 (d, 2H, J = 7.2 Hz).

A solution of 100 mg (0.47 mmol) of the above amine in 5 mL of THF at 0 °C was treated with 84 mg (0.47 mmol) of ethyl 2-diazomalonyl chloride. The reaction mixture was stirred at rt for 2 h and was then taken up in ether and washed with a saturated aqueous $NaHCO_3$ solution and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 107 mg (65%) of 2-diazo-*N*-(2-oxo-2-phenylethyl)-*N*-phenylmalonamic acid ethyl ester (**32**) as a pale yellow solid: mp 89–90 °C; IR (neat) 2121, 1725, 1701, and 1641 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.12 (t, 3H, J = 7.2 Hz), 4.02 (q, 2H, J = 7.2 Hz), 5.19 (s, 2H), 7.23 (m, 1H), 7.34 (m, 4H), 7.44 (t, 2H, J = 7.5 Hz), 7.56 (t, 1H, J = 7.2 Hz), and 7.92 (d, 2H, J = 7.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 57.1, 61.2, 65.6, 126.3, 127.0, 127.8, 128.6, 129.2, 133.5, 134.7, 142.8, 160.7, 161.6, and 192.8.

To a refluxing solution containing 95 mg (0.85 mmol) of *N*-methylmaleimide and 5 mg (0.011 mmol) of $Rh_2(OAc)_4$ in 10 mL of benzene was added 0.30 g (0.85 mmol) of diazo compound **32** in 2 mL of benzene over a 5-min period. The reaction was heated at reflux for 4 h. The mixture was cooled to rt and the precipitated white solid was collected by filtration. The remaining filtrate was triturated with hexane and the resulting white solid was also collected. Recrystallization of the combined solid from a 1:1 CH_2Cl_2–hexane mixture gave 275 mg (64%) of 4-methyl-3,5,10-trioxo-7,9-diphenyl-11-oxa-4,9-diazatricyclo[5.3.1.$0^{2,6}$]undecane-1-carboxylic acid ethyl ester (**33**) as a crystalline solid: mp 279–280 °C; IR (KBr) 1739, 1707, 1683, and 1099 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.43 (t, 3H, J = 6.9 Hz), 2.74 (s, 3H), 3.80 (d, 1H, J = 7.2 Hz), 4.16 (m, 3H), 4.48 (m, 2H), 7.25 (d, 2H, J = 9.3 Hz), and 7.36 (m, 8H); ^{13}C-NMR (20:1 mixture of $CDCl_3$/CF_3COOD, 75 MHz) δ 13.3, 25.3, 53.0, 54.9, 60.6, 64.4, 84.5, 85.1, 123.7, 125.9, 128.8 129.1, 129.5, 129.9, 134.0, 138.7, 164.7, 165.1, 173.2, and 175.3. Anal. Calcd $C_{24}H_{22}N_2O_6$: C, 66.35; H, 5.11; N, 6.44. Found: C, 66.18; H, 5.06; N, 6.43.

A mixture of 101 mg (0.287 mmol) of **32** in 5 mL of benzene and 5 mg (0.011 mmol) of $Rh_2(OAc)_4$ was heated at reflux for 3 h. The reaction mixture was cooled to rt and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 71 mg (77%) of 3-oxo-4,6-diphenyl-3,4-dihydro-2*H*-[1,4]oxazine-2-carboxylic acid ethyl ester (**35**) as a light yellow oil: IR (neat) 1742, 1696, and 750 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.28 (t, 3H, J = 6.6 Hz), 4.30 (q, 2H, J = 6.6 Hz), 5.31 (s, 1H), 6.40 (s, 1H), 7.39 (m, 8H), and 7.26 (d, 2H, J = 7.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.0, 62.3, 77.1, 107.9, 124.6, 125.3, 127.6, 128.4, 128.6, 129.2, 131.5, 138.7, 140.8, 158.4, and 166.1; HRMS calcd for $C_{19}H_{17}NO_4$ 323.1157, found 323.1151.

A solution of 77 mg (0.22 mmol) of **32** in 4 mL of CH_2Cl_2 was treated with 5 mg (0.011 mmol) of $Rh_2(NHCOC_3F_7)_4$ and the reaction was stirred at rt for 3 h. The reaction mixture was then cooled to 0 °C and 53 μL (0.65 mmol) of pyridine was added, followed by 76 μL (0.65 mmol) of benzoyl chloride. The reaction was warmed to rt and stirred for 4 h. The mixture was taken up in CH_2Cl_2 and washed with saturated aqueous NH_4Cl, and brine. The organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 84 mg (90%) of 2-(benzoyloxy)-1-(2-oxo-2-phenylethyl)-1*H*-indole-3-carboxylic acid ethyl ester (**37**) as a white crystalline solid: mp 182–183 °C; IR (neat) 1760, 1696, and 1234 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 1.12 (t, 3H, J = 6.9 Hz), 4.23 (q, 2H, J = 6.9 Hz), 5.45 (s, 2H), 7.13 (d, 1H, J = 7.8 Hz), 7.27 (m, 2H), 7.50 (t, 4H, J = 7.5 Hz), 7.64 (m, 2H), 7.99 (d, 2H, J = 7.5 Hz), and 8.21 (t, 3H, J = 7.8 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 14.2, 48.2, 59.2, 95.3, 104.1, 109.2, 121.9, 122.5, 122.9, 125.0, 127.8, 128.0, 128.7, 129.0, 130.8, 132.4, 134.2, 134.4, 146.8, 163.3, 163.5, and 191.0. Anal. Calcd for $C_{26}H_{21}NO_5$: C, 73.06; H, 4.96; N, 3.28. Found: C, 72.94; H, 4.99; N, 3.21.

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Supplementary Material Available: Copies of ^1H-NMR and ^{13}C-NMR spectra of new compounds lacking analyses (11 pages). This material is contained in 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.

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