Electronic Effects of Rh(II)-Mediated Carbenoid Intramolecular C−H Insertion: A Linear Free Energy Correlation Study

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The relative rates of the Rh(II)-mediated carbenoid insertion into the benzylic C−H bonds of a series of para-substituted phenyl substrates have been measured by an indirect intramolecular competition method. Three catalysts, rhodium(II) acetate, rhodium(II) trifluoroacetate, and rhodium(II) acetamide, were investigated. The effect of solvent was also studied on the reactions with rhodium(II) acetate as catalyst. The relative rates were analyzed by the Hammett equation. The relative rates are found to correlate better with σ than with σ^+ for all three catalysts when CH_2Cl_2 is the solvent. For the insertion reactions catalyzed by $Rh_2(OAc)_4$, $Rh_2(O_2CCF_3)_4$, and $Rh_2(acam)_4$ in CH_2Cl_2, the Hammett correlations of the relative rates with σ give reaction constants of −1.26 (r = 0.98), −0.66 (r = 0.97), and −1.39 (r = 0.98), respectively. The Hammett analysis also indicates no significant solvent effect. The mechanistic significance of these Hammett correlations is discussed.

Introduction

The electronic effects of Rh(II)-mediated carbenoid intramolecular C−H insertion reactions have been of considerable interest in recent years.[1] Pioneering work by Taber and several other groups has revealed that the reactivity of the target C−H bond is enhanced by an electron-donating group while an electron-withdrawing group retards the C−H insertion, thus indicating the electron demanding character of the carbene−Rh complex.[2] Electronic effects have also been observed to affect diasteroselectivity of the C−H insertions.[3] In addition to the electronic factors, steric and conformational factors are also found to sensitively influence the C−H insertion selectivity, and, in certain cases, the latter may override the electronic preference.[2c,4] It is generally true that if a substituent is close to the reaction center, the possibility exists that it may affect the reaction by a purely steric process so that electronic effects are masked. Consequently, it would be desirable to evaluate the electronic effects under the condition in which the possible steric and conformational effects could be minimized. One such effort was reported by Wang and Adams,[2d] in which case a conformationally restricted cyclohexane system was employed. Our objective is to study this problem in a freely rotating acyclic system, which would have more generality. An attractive way to achieve this goal is to measure the relative reactivities of competing carbenoid insertions into a series of substituted benzylic C−H bonds.

If we could obtain such relative reactivities, Hammett correlation analysis may be applied to the data. This powerful method for analyzing electronic effects has been applied to almost every type of organic reaction, but it has not been used so far in C−H insertions by carbenoids. It would be difficult to study electronic effects with Hammett analysis in intermolecular carbenoid C−H insertions, since poor chemoselectivity will preclude accurate kinetic measurements. However, the high selectivity generally observed in intramolecular C−H insertion by Rh-mediated carbenoids makes it possible to apply Hammett methods in this type of reaction. This analysis will provide quantitative information on the sensitivity of C−H insertions to electronic effects, and a quantitative basis for comparison with other type of reactions, especially intermolecular insertion reactions by carbenoids or free carbenes. Hammett correlation study may also provide insights into the insertion mechanism, which still remains highly speculative. We describe in this paper our results from such an approach.

Results

To measure the relative reactivities of substituted benzylic C−H bonds toward carbene−Rh complex, an indirect approach was employed (Scheme 1).[5] Compound

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(1) For reviews, see: (a) Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797. (b) Mckervey, M. A.; Ye, T. *Chem. Rev. (Washington, D.C.)* **1994**, *94*, 1091. (c) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385. (d) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765. (e) Doyle, M. P. In *Homogeneous Transition Metal Catalysts in Organic Synthesis*; Moser, W. R., Slocum, D. W., Eds.; ACS Advanced Chemistry Series 230; American Chemical Society: Washington, DC, 1992. (f) Taber, D. F. *Comprehensive Organic Synthesis*; Pattenden, G., Ed.; Pergamon Press: Oxford, 1991; vol. 3, p 1045. (g) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919.

(2) (a) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686. (b) Stork, G.; Nakatani, K. *Tetrahedron Lett.* **1988**, *29*, 2283. (c) Doyle, M. P.; Westrum, L. J.; Wolthuis, W. N. E.; See, M. M.; Boone, W. P.; Bagheri, V.; Pearson, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 958. (d) Wang, P.; Adams, J. *J. Am. Chem. Soc.* **1994**, *116*, 3296. (e) Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 8991.

(3) Taber, D. F.; Song, Y. *J. Org. Chem.* **1996**, *61*, 6706.

(4) (a) Doyle, M. P.; Bagheri, V.; Pearson, M. M.; Edwards, J. D. *Tetrahedron Lett.* **1989**, *30*, 7001. (b) Doyle M. P.; Taunton, J.; Pho, H. Q. *Tetrahedron Lett.* **1989**, *30*, 5397. (c) Doyle, M. P.; Pieters, R. J.; Taunton, J.; Pho, H. Q.; Padwa, A.; Hertzog, D. L.; Precedo, L. *J. Org. Chem.* **1991**, *56*, 820. (d) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O. *Tetrahedron* **1991**, *47*, 7403. (e) Wee, A. G. H.; Liu, B.; Zhang, L. *J. Org. Chem.* **1992**, *57*, 4404.

(5) A direct intramolecular competition between 4-nitro-substituted benzylic C−H and its nonsubstituted counterpart gave comparable results. The indirect method was used because of its simplicity in product ratio determination and product structure elucidation.

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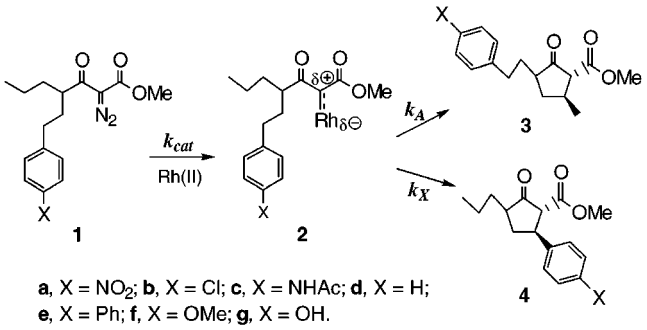
Scheme 1

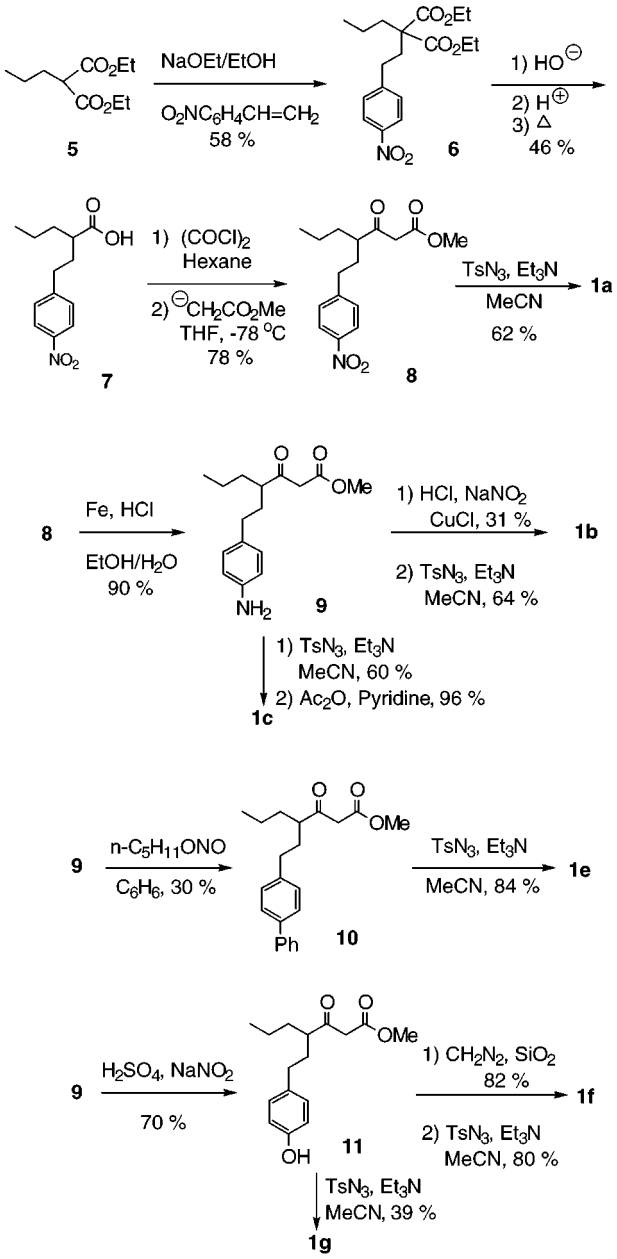


1d was originally used by Taber as a model molecule for determining the relative reactivity of benzylic C−H to secondary aliphatic C−H through intramolecular competition.[2a] We employ this compound as our basic structure and have designed carbonyl diazo compounds **1a**−**g** as the molecules in our study. A model generally accepted for the Rh-mediated intramolecular C−H insertion involves the initial complexation of the negatively polarized carbon of the diazo compound with an empty axial site of the Rh catalyst, followed by extrusion of nitrogen to generate the intermediate carbene−Rh complex **2**.[6] The subsequent rapid insertions determine the final product ratio. In each of our molecules, there are two insertion sites. A benzylic C−H is allowed to compete with a secondary aliphatic C−H, and the relative rate, k_X/k_A, can be expressed in terms of the final product ratio. In the insertion reactions of **1a**−**g**, it is reasonable to assume that steric and conformational perturbations due to the substituent in the para position of the phenyl ring can be neglected because it is far from the reaction center and is relatively small compared to the remainder of the molecule. The major effect of these substituents is to impose electronic influence on the reactivity of the corresponding benzylic C−H toward carbenoid insertion. We can therefore assume that k_A is constant through the series of the insertion reactions. In other words, insertion into this secondary aliphatic C−H serves as an internal standard. The relative reactivity of para-substituted benzylic C−H to nonsubstituted benzylic C−H can be obtained as follows:

$$k_X/k_H = \frac{k_X/k_A}{k_H/k_A} = \frac{[\mathbf{4}/\mathbf{3}]_X}{[\mathbf{4}/\mathbf{3}]_H}$$

The procedure for the syntheses of diazo compounds **1a**,**b**,**c**,**e**,**f**,**g** is described in Scheme 2. Michael addition[7] of the anion of diethyl propylmalonate **5** to 4-nitrostyrene gave **6**, which was subsequently hydrolyzed and decarboxylated to provide acid **7**. The acid **7** was then converted to β-keto ester **8** by a two-step process. Diazo transfer to β-keto ester **8** gave **1a**. To obtain **1b**, the nitro group of the β-keto ester **8** was first reduced to yield **9**, which was then subjected to the Sandmeyer reaction[8] and diazo transfer. On the other hand, diazo transfer was effected directly on **9**, followed by acetylation, to give **1c**. **1e** was obtained by phenylation[9] of **9**, followed by diazo transfer. To obtain **1f**, **9** was hydroxylated[10] to give **11**, which was further methylated with diazomethane,[11] followed by diazo transfer to provide **1f**. Finally, direct diazo transfer to **11** gave **1g**. **1d** was prepared by a different route according to a known procedure.[2a]

Scheme 2



The Rh(II)-mediated C−H insertion was conducted under standard conditions. **1a**−**g** (0.5 mmol) in CH_2Cl_2 or benzene (10 mL) was added to a stirred solution of CH_2Cl_2 or benzene (10 mL) containing 1.0 mol % Rh(II) catalyst at room temperature under nitrogen atmosphere. The green, homogeneous solution was stirred until the completion of the reaction as indicated by TLC. The catalyst was removed by a short column with silica gel and the crude reaction mixture was analyzed by ^{1}H NMR (400 MHz) for the product ratio determination. Further

(6) Recent study by Pirrung has indicated that for Rh(II)-mediated diazo carbonyl transformations, the initial formation of the carbene-Rh complex is the rate-determining step, see: Pirrung, M. C.; Morehead, A. T., Jr. *J. Am. Chem. Soc.* **1996**, *118*, 8162.

(7) Dale, W. J.; Strobel, C. W. *J. Am. Chem. Soc.* **1954**, *76*, 6172.

(8) Marvel, C. S.; McElvain, S. M. *Organic Syntheses*; Wiley: New York, 1941; Coll. Vol. I, p 170.

(9) Cadogan, J. I. G. *J. Chem. Soc.* **1962**, 4257.

(10) Icke, R. N.; Redemann, C. E.; Wisegarver, B. B.; Alles, G. A. *Organic Syntheses*; Wiley: New York, 1955; Coll. Vol. III, p 564.

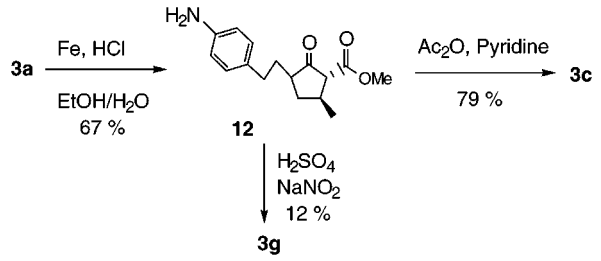
(11) Ohno, K.; Nishiyama, H.; Nagase, H. *Tetrahedron Lett.* **1979**, 4405.

Table 1. Products Ratio of the Competitive C−H Insertions and the Relative Rates of Benzylic C−H toward Rh(II)-Mediated Carbenoids[a]

		$Rh_2(OAc)_4$ CH_2Cl_2		$Rh_2(O_2CCF_3)_4$ CH_2Cl_2		$Rh_2(acam)_4$ CH_2Cl_2		$Rh_2(OAc)_4$ benzene	
1	X	**3**:**4**[b]	k_X/k_H	**3**:**4**[c]	k_X/k_H	**3**:**4**[d]	k_X/k_H	**3**:**4**[e]	k_X/k_H
a	NO_2	96:4	0.093	91:9	0.28	94:6	0.057	94:6	0.12
b	Cl	74:26	0.78	77:23	0.85	62:38	0.54	74:26	0.68
c	NHAc	67:33	1.10	68:32	1.34	44:56	1.13	47:53	2.19
d	H	69:31[f]	1.00	74:26	1.00	47:53	1.00	66:34	1.00
e	Ph	66:34	1.15	73:27	1.05	47:53	1.00	62:38	1.19
f	OMe	46:54	2.61	67:33	1.40	33:67	1.80	40:60	2.91
g	OH	47:53	2.51	63:37	1.67	28:72	2.28	43:57	2.57

[a] All reactions were run at room temperature. The relative yields were determined by ^{1}H NMR (400 MHz) of the crude reaction mixture. [b] Average standard deviation is 2.2%. Isolated yields ranged from 68 to 96%. [c] Average standard deviation is 2.9%. Isolated yields ranged from 46 to 86%. [d] Average standard deviation is 2.4%. Isolated yields ranged from 61 to 77%. [e] Average standard deviation is 1.6%. Isolated yields ranged from 59 to 74%. [f] A ratio of 2.3:1 was previously reported, see ref 2a.

Scheme 3



column chromatography and preparative TLC provided pure products for identification and characterization. For **1c** and **1g**, since the insertion products are inseparable by column chromatography, pure samples of **3c** and **3g** were prepared from **3a** and then were compared with the mixture of **3c**, **4c** and **3g**, **4g** (Scheme 3).

Three different Rh(II) catalysts, rhodium(II) acetate, rhodium(II) trifluoroacetate, and rhodium(II) acetamide, were investigated in the current study. These catalysts were chosen because of the different electron-withdrawing ability of the ligands (O_2CCF_3 > OAc > acam), which has been known to be an important factor to influence the selectivities of C−H insertions.[2c,e,4c,12] For one catalyst, $Rh_2(OAc)_4$, the effect of solvent has also been studied, since we are aware of recent reports on the dramatic influence of solvent polarity on the chemoselectivity of Rh(II)-mediated carbenoid reactions.[12c,13] The product ratios and the relative rate constants, k_X/k_H, are collected in Table 1.

It is obvious from the relative rate constants that the electronic property of the substituents markedly affects the insertion reaction. Electron-releasing groups enhance the reactivity of benzylic C−H while electron-withdrawing groups decrease its reactivity. This is consistent with the well-known electron-demanding character of the carbene−Rh complex.

Table 2. Correlation of log k_X/k_H with Substituent Constants σ and σ^+ [a]

constants used	$Rh_2(OAc)_4$ CH_2Cl_2	$Rh_2(O_2CCF_3)_4$ CH_2Cl_2	$Rh_2(acam)_4$ CH_2Cl_2	$Rh_2(OAc)_4$ benzene
σ	$\rho = -1.26$	$\rho = -0.66$	$\rho = -1.39$	$\rho = -1.22$
	($r = 0.98$)[b]	($r = 0.97$)	($r = 0.98$)	($r = 0.96$)
σ^+	$\rho^+ = -0.75$	$\rho^+ = -0.41$	$\rho^+ = -0.83$	$\rho^+ = -0.78$
	($r = 0.92$)[b]	($r = 0.94$)	($r = 0.92$)	($r = 0.96$)

[a] Substituent constants were taken from ref 15. [b] ρ = reaction constant with σ; ρ^+ = reaction constant with σ^+; r = correlation coefficient.

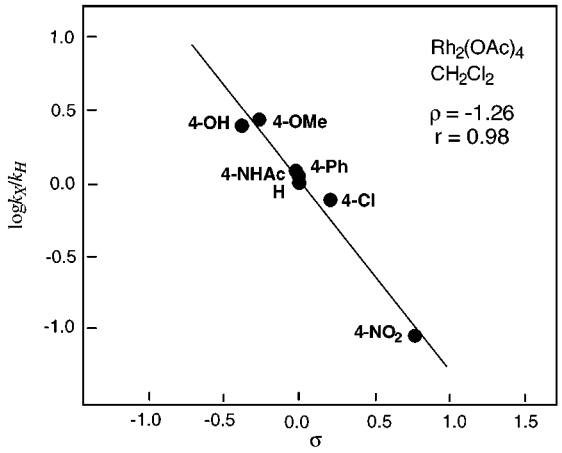


Figure 1. Plot of log k_X/k_H against σ for the C−H insertions of $Rh_2(OAc)_4$-catalyzed reaction with CH_2Cl_2 as solvent.

For $Rh_2(O_2CCF_3)_4$, the ratios of **3** to **4**, or the relative reactivities of aliphatic secondary C−H vs benzylic secondary C−H, are unexpected. The carbene−Rh complex generated by this catalyst is known to be very reactive, and, thus gives low selectivity. It was reported that C−H insertions mediated by this catalyst proceeded with statistical product distribution, which led to the speculation that free carbene might be released from the carbenoid.[2e,14] It is therefore surprising to find that in our study the C−H insertions with $Rh_2(O_2CCF_3)_4$ as catalyst do not tend to be indiscriminative. On the contrary, insertions into secondary aliphatic C−H increase slightly when the catalyst is changed from $Rh_2(OAc)_4$ to $Rh_2(O_2CCF_3)_4$, except when X = NO_2. It is interesting to compare this observation with the high control and selectivity reported in a number of carbenoid reactions catalyzed by rhodium(II) perfluorobutyrate (aromatic substitution > tertiary C−H insertion > cyclopropanation ∼ aromatic cycloaddition > secondary C−H insertion).[12b] The moderately high site selectivities observed in the reactions catalyzed by $Rh_2(O_2CCF_3)_4$ suggest that the involvement of free carbene in the reactions that we have investigated is not likely. On the other hand, C−H insertions catalyzed by $Rh_2(acam)_4$, a catalyst known to make less electron-deficient carbenoid, show decreased selectivity of insertion into aliphatic secondary C−H relative to the insertion reactions catalyzed by $Rh_2(OAc)_4$ (Table 1).

The relative rates in Table 1 are then fitted to Hammett equation with both σ and σ^+.[15] The results are shown in Table 2 and in Hammett plots (Figures 1−4,

(12) (a) Padwa, A.; Austin, D. J.; Hornbuckle, S. F.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N. *J. Am. Chem. Soc.* **1992**, *114*, 1874. (b) Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669. (c) Wee, A. G. H.; Yu, Q. *J. Org. Chem.* **1997**, *62*, 3324. (d) Padwa, A.; Austin, D. J.; Hornbuckle, S. F. *J. Org. Chem.* **1996**, *61*, 63. (e) Doyle, M. P.; Dyatkin, A. B. *J. Org. Chem.* **1995**, *60*, 3035.

(13) Davies, H. M. L.; Saikali, E.; Young, W. B. *J. Org. Chem.* **1991**, *56*, 5696.

(14) Demonceau, A.; Noels, A. F.; Costa, J.-L.; Hubert, A. J. *J. Mol. Catal.* **1990**, *58*, 21.

(15) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev. (Washington, D.C.)* **1991**, *91*, 165.

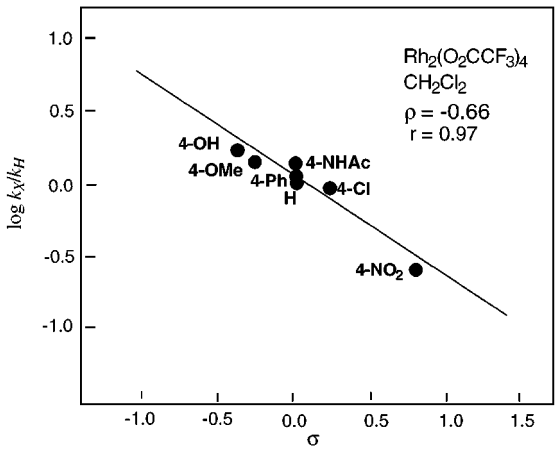


Figure 2. Plot of log k_X/k_H against σ for the C−H insertions of $Rh_2(O_2CCF_3)_4$-catalyzed reaction with CH_2Cl_2 as solvent.

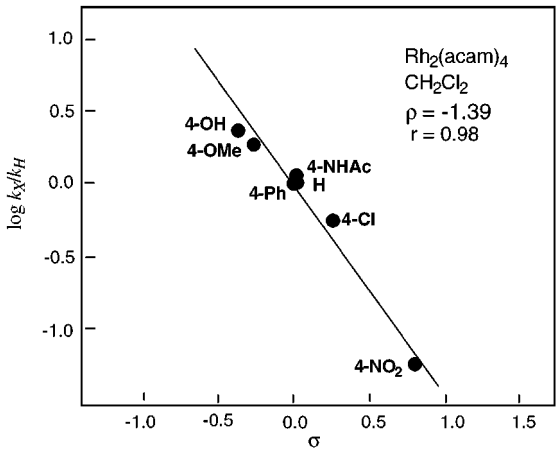


Figure 3. Plot of log k_X/k_H against σ for the C−H insertions of $Rh_2(acam)_4$-catalyzed reaction with CH_2Cl_2 as solvent.

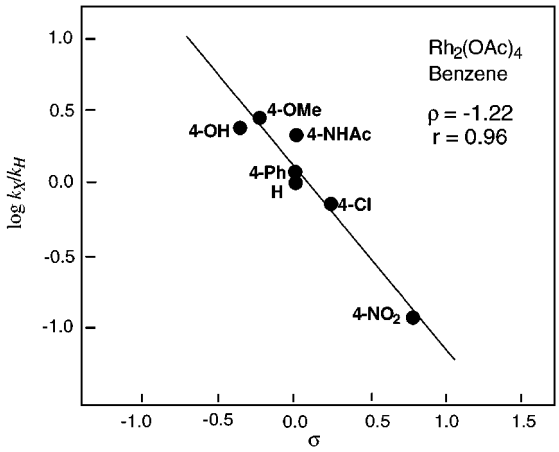


Figure 4. Plot of log k_X/k_H against σ for the C−H insertions of $Rh_2OAc)_4$-catalyzed reaction with benzene as solvent.

with σ only). In all cases, good linear correlations are obtained, and except in the case of $Rh_2(OAc)_4$ with benzene as solvent, better linear correlations are observed with σ than with σ^+. The negative values are consistent with the expected electrophilic character of the carbene−Rh complex. The small magnitude of the values indicates the charge separation in the transition state is not large. For the C−H insertions catalyzed by $Rh_2(O_2CCF_3)_4$, although they show high selectivity for secondary aliphatic C−H bond, Hammett analysis of the relative rates of benzylic C−H insertions indeed results in numerically smallest value of reaction constant, thus showing that $Rh_2(O_2CCF_3)_4$ is least sensitive to substituent effects. On the other hand, $Rh_2(acam)_4$ is most sensitive to substituent effects, as shown by the reaction constant. Hammett analysis also indicates there is no significant solvent effect in the insertion process, as shown by the tiny change of reaction constant when the solvent is changed from CH_2Cl_2 to benzene.

Discussion

The relatively small and negative values of the reaction constants from the Hammett analysis are in agreement with a transition state of a concerted insertion process with a small positive charge developed at the benzylic carbon atom. The concerted nature of the C−H insertion was early strongly evidenced by the report that the reaction proceeded with retention of configuration at the carbon where the insertion occurred.[16] The Hammett analyses further suggest that the involvement of significant charge separation or discrete ionic intermediates in the mechanism is not likely.[2d,17]

Doyle proposed a three-center complex as a transition state in the insertion process.[2c,18,19] According to this model, increased electron-withdrawing ability of the ligand attached to the Rh will make the carbene−Rh complex more reactive, and, thus an earlier transition sate. Decreased electron withdrawal will lead to a less reactive carbene−Rh complex and a later transition state. The results of the current Hammett analysis are in accordance with this picture. The electrophilic attack of the carbene−Rh complex onto the C−H bond should lead to the development of a partial positive charge at the benzylic carbon in the transition state. In the C−H insertions catalyzed by $Rh_2(O_2CCF_3)_4$, the reaction will occur through an earlier transition state according to Doyle's model. This means that the partial positive charge at the benzylic carbon is much less developed, thus the substituent effects are mainly electron inductive. In this case, a smaller reaction constant should be expected. A less electron-withdrawing ligand, as in the case of $Rh_2(acam)_4$, will lead to a later transition state. In this case, the positive charge, although partial, will be relatively more developed, and a larger reaction constant is thus expected. The observed ρ value of −0.66 (with σ) for $Rh_2(O_2CCF_3)_4$ is numerically much smaller than the ρ value for $Rh_2(OAc)_4$ ($\rho = -1.26$ with σ), while $Rh_2(acam)_4$ gave the numerically largest ρ value ($\rho = -1.39$ with σ).

The generally increased selectivity of benzylic secondary C−H vs aliphatic secondary C−H in the carbenoid insertions when the catalyst is changed from $Rh_2(O_2CCF_3)_4$ to $Rh_2(OAc)_4$ to $Rh_2(acam)_4$, as shown by the comparison of the **3** to **4** ratios in each row of the Table 1, might be

(16) Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, *107*, 196.
(17) Wee, A. G. H.; Liu, B. *Tetrahedron Lett.* **1996**, *37*, 145.
(18) Doyle, M. P.; Kalinin, A. V.; Ene, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 8837.
(19) On the other hand, Taber proposed a different mechanism. In this mechanism, a two-electron, three-center complex was taken as an intermediate rather than a transition state. The insertion proceeds from this intermediate through the transition state in which the C.-Rh bond is aligned with the target C.-H bond (a four-center transition state). See: ref 3 and Taber, D. F.; You, K. K.; Rheingold, A. L. *J. Am. Chem. Soc.* **1996**, *118*, 547.

attributed to the change in the degree of partial positive charge development at the carbon where the insertion occurs. In the reactions catalyzed by $Rh_2(acam)_4$, the insertions proceed through a later transition state in which partial positive charge is more developed. In such a transition state, the adjacent aromatic ring plays a relatively significant role in the stabilization of the partial positive charge at the benzylic carbon through resonance effects, thus leading to the increased selectivity for benzylic C−H insertion. By contrast, the partial positive charge is much less developed in the C−H insertions catalyzed by $Rh_2(O_2CCF_3)_4$ due to an earlier transition state. In this case, resonance effects are hardly involved in the stabilization of the transition state, and purely electronic inductive effects should play a major role in affecting site selectivity. This explains the decreased selectivity of benzylic C−H vs aliphatic C−H in the insertion reactions catalyzed by $Rh_2(O_2CCF_3)_4$. In connection to this rationalization, we have noticed the previous observation that C−H insertions are activated by an adjacent alkoxy group.[20] Since the inductive effects of alkoxy groups are electron-withdrawing, it is likely that the C−H activation is due to stabilization of the partial positive charge in the transition state by the adjacent oxygen through resonance effects.[21] Similarly, an adjacent amide group, whose inductive effect is known to be electron-withdrawing but whose resonance effect is electron-donating, has been reported to activate C−H insertion.[4c,e] On the other hand, the reported deactivation of C−H by an adjacent ester group[2b] should be due to the fact that for ester groups, both inductive and resonance effects are electron-withdrawing.

The similarity between carbene−Rh complex and difluorocarbene has been recently pointed out in terms of the similar factors which influence the selectivity of rhodium carbenoids and free halocarbenes.[2e] It is interesting to compare the ρ values obtained in the present study with that previously reported for the intermolecular insertion of dichlorocarbene into substituted benzylic C−H bond, in which case a reaction constant of −1.19 is obtained with σ.[22] This is comparable to the ρ value obtained in the insertions catalyzed by $Rh_2(OAc)_4$. Intermolecular insertion of dichlorocarbene into Si−H gives a smaller reaction constant ($\rho = -0.63$ with σ).[23] This is understandable because the Si−H bond is much more basic than C−H bond, thus more reactive toward electron-demanding carbenes. This result might be compared with the case of $Rh_2(O_2CCF_3)_4$ in our study, in which a more reactive carbene−Rh complex led to a numerically smaller reaction constant. Recent study by Landais on the intermolecular Si−H insertion by carbene−Rh complex provided a reaction constant of −0.31 with σ.[24] Other points worthy of note are that in these intra- or intermolecular insertion reactions, the insertions all proceed with retention of configuration at the carbon or silicon reaction site,[16,22,24,25] and kinetic isotope effect data available indicate small effects in all cases (within the range of 1.2 to 2.5).[2d,14,22,24] These experimental evidences seem to imply mechanistic similarity between the Rh(II)-mediated intramolecular C−H insertions and the intermolecular C−H or Si−H insertions by carbenoids or free halocarbenes.

In summary, the electronic effects of the Rh(II)-mediated intramolecular C−H insertion have been studied under the condition where possible steric and conformational interference are minimized. The study has demonstrated for the first the time the linear correlation between substrate substituent effects and Hammett polar constants in Rh(II)-mediated C−H insertions. The data provide further evidence for the concerted nature of the insertion process.

Experimental Section

General. Melting point was determined in capillary and was uncorrected. All reactions with air- and moisture-sensitive components were performed under a nitrogen atmosphere in a flame-dried reaction flask, and the components were added via syringe. All solvents were distilled prior to use. The boiling point of petroleum ether is between 30 and 60 °C. MeCN was distilled from P_2O_5. EtOH and CH_2Cl_2 were freshly distilled from CaH_2 before use. THF and hexane were distilled from sodium. For chromatography, 100−200 mesh silica gel (Qingdao, China) was employed. For preparative TLC, 10−40 μm, silica gel GF_{254} (Qingdao, China) was used. TLC for detection was Merck Kieselgel 60 F_{254} silica gel. ^1H and ^{13}C NMR spectra were recorded at 400 and 100.6 MHz, respectively, in $CDCl_3$ with a Brucker ARX400 spectrometer, and chemical shifts are reported in ppm. IR spectra were recorded with a Nicolet 5MX-S infrared spectrometer. Mass spectra were obtained on a VG ZAB-HS mass spectrometer. Diisopropylamine was distilled from NaOH. Methyl acetate was dried over anhydrous K_2CO_3 and then distilled. Rhodium(II) acetate and rhodium(II) trifluoroacetate were purchased from Aldrich. Rhodium(II) acetamide was prepared according to a literature procedure.[26] 4-Nitrostyrene was prepared in two steps from phenylethyl bromide.[27] *p*-Toluenesulfonyl azide was prepared from *p*-toluenesulfonyl chloride and sodium azide according to a literature procedure.[28] Butyllithium was prepared from lithium and butyl chloride in hexane and was titrated before use.

Diethyl 2-Propyl-2-[2-(4-nitrophenyl)ethyl]malonate (6). To absolute EtOH (9 mL) was added sodium (0.59 g, 25.6 mmol). When the solution was complete, diethyl propylmalonate (**5**) (25.1 g, 124 mmol) was added dropwise, and the solution was allowed to reflux for 40 min. A solution of 4-nitrostyrene (18.5 g, 124 mmol) in absolute EtOH (110 mL) containing hydroquinone (1 g, 9 mmol) was added dropwise during a period of 1 h. The resulting dark red solution was gently refluxed for 20 h. Ethanol was removed by distillation, and the mixture was cooled to 0°CC with an ice-bath. A cool solution of 5% aqueous HCl (300 mL) was added, and the mixture was extracted with Et_2O (3 × 100 mL). The combined ethereal solution was washed with H_2O twice and dried over anhydrous $MgSO_4$. Removal of solvent gave a dark oil which was subjected to column chromatography. Gradient eluting with 40:1, 20:1, 15:1, 10:1, and 4:1 of petroleum ether/EtOAc gave a light yellow solid of **6** (25.5 g, 58%). Recrystallization from petroleum ether gave a pure sample for analysis: mp 49−50 °C; $R_f = 0.57$ (petroleum ether/EtOAc = 4:1); ^1H NMR δ 0.95 (t, $J = 7.2$ Hz, 3H), 1.25−1.29 (m, 2H), 1.27 (t, $J = 7.1$

(20) (a) Adams, J.; Frenette, R. *Tetrahedron Lett.* **1987**, *28*, 4773. (b) Adams, J.; Poupart, M.-A.; Grenier, L.; Schaller, C.; Quimet, N.; Frenette, R. *Tetrahedron Lett.* **1989**, *30*, 1749.

(21) A different reaction pathway for carbenoid insertion on to the C−H bond adjacent to alkoxy group has been speculated in a recent report, see: Clark, J. S.; Dossetter, A. G.; Russell, C. A.; Whittingham, W. G. *J. Org. Chem.* **1997**, *62*, 4910.

(22) Seyferth, D.; Cheng, Y. M. *J. Am. Chem. Soc.* **1973**, *95*, 6763.

(23) Seyferth, D.; Damrauer, R.; Mui, J. Y.-P.; Jula, T. F. *J. Am. Chem. Soc.* **1968**, *90*, 2944.

(24) Landais, Y.; Parra-Rapado, L.; Planchenault, D.; Weber, V. *Tetrahedron Lett.* **1997**, *38*, 229.

(25) Sommer, L. H.; Ulland, L. A.; Parker, G. A. *J. Am. Chem. Soc.* **1972**, *94*, 3469.

(26) Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906.

(27) (a) H. Sobotka, *Ber.* **1929**, *62*, 2191. (b) Strassburg, R. W.; Gregg, R. A.; Walling, C. *J. Am. Chem. Soc.* **1947**, *69*, 2141.

(28) Leffler, J. E.; Tsuno, Y. *J. Org. Chem.* **1963**, *28*, 902.

Hz, 6H), 1.92−1.97 (m, 2H), 2.16−2.21 (m, 2H), 2.61−2.66 (m, 2H), 4.21 (q, J = 7.1 Hz, 4 H), 7.34 (d, J = 8.7 Hz, 2H), 8.14 (d, J = 8.7 Hz, 2H); ^{13}C NMR 14.04, 14.31, 17.41, 30.68, 33.94, 34.97, 57.34, 61.19, 123.62, 129.11, 146.42, 149.36, 171.30; IR 2955, 1720, 1600, 1520, 1350, 1260, 1210, 1150 cm^{-1}; MS (*m*/*z*, relative intensity) 306 [(M − OEt)$^+$, 4], 278 (2), 232 (2), 202 (41), 173 (100), 156 (10), 127 (26). Anal. Calcd for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N,3.99. Found: C, 61.33; H, 7.32; N, 4.03.

4-(4-Nitrophenyl)-2-propylbutanoic Acid (7). Diester **6** (20.0 g, 57.0 mmol) was dissolved in 95% EtOH (500 mL) and 20 mL of aqueous KOH (3.52 g, 62 mmol, 1.1 equiv) was added. The homogeneous solution was refluxed for 4 h. EtOH was removed by distillation, and then H_2O (150 mL) was added. The mixture was washed with Et_2O (2 × 30 mL), and the aqueous solution was acidified with concentrated HCl at 0 °C. The mixture was extracted with Et_2O (3 × 100 mL), and the combined ethereal solution was washed with H_2O (3 × 100 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent gave an oily product, which was heated at 165 °C for 6 h until CO_2 evolution was stopped. The monoester obtained (7.6 g) was again subjected to hydrolysis, and usual workup gave final title compound **7** as a yellow oil (6.57 g, 46% from **6**): ^{1}H NMR δ 0.92 (t, J = 7.2 Hz, 3H), 1.31−1.42 (m, 2H), 1.48−1.56 (m, 1H), 1.67−1.78 (m, 1H), 1.79−1.88 (m, 1H), 1.98−2.07 (m, 1H), 2.39−2.48 (m, 1H), 2.73−2.85 (m, 2H), 7.36 (d, J = 8.8 Hz, 2H), 8.25 (d, J = 8.8 Hz, 2H); ^{13}C NMR δ 13.89, 20.36, 33.04, 33.48, 34.26, 44.64, 123.64, 129.24, 146.38, 149.37, 182.49. IR 3080, 2970, 1705, 1600, 1520, 1350 cm^{-1}; MS (*m*/*z*, relative intensity) 251 (M$^+$, 7), 233 (2), 207 (4), 150 (46), 102 (62), 73 (100); HRMS calcd for $C_{13}H_{17}NO_4$ 251.1158, found 251.1158.

Direct hydrolysis of **6** to diacid with excess KOH and then decarboxylation gave much lower yield.

Methyl 3-Oxo-6-(4-nitrophenyl)-4-propylhexanoate (8). To acid **7** (8.5 g, 33.8 mmol) was added dry hexane (70 mL) and oxalyl chloride (21.5 g, 169 mmol). The solution was then heated under gentle reflux for 1 h. Solvent and excess oxalyl chloride were removed by distillation, and the residue was kept in vacuo for 24 h. The acyl chloride thus obtained was used for the next step without further purification.

Diisopropylamine in dry THF (160 mL) was cooled to −70 °C under N_2. Butyllithium (0.8 M, 84 mL, 67.7 mmol) was added dropwise, and the solution was stirred at −78 °C for 15 min. Methyl acetate (5.4 mL, 67.7 mmol) was added dropwise in 20 min, and the solution was stirred at −78 °C for another 25 min. The acyl chloride in dry THF (20 mL) was then introduced in one portion, and the solution was allowed to warm to room temperature. Aqueous HCl (5%), was added and the THF was removed in vacuo. The resulting mixture was extracted with Et_2O (4 × 50 mL), and the combined ethereal solution was washed with H_2O (2 × 50 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude oil (10 g), which was subjected to column chromatography with 5:1 petroleum ether/EtOAc to yield a light yellow oil of **8** (8.1 g, 78%): R_f = 0.33 (petroleum ether/EtOAc = 8:1); ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, enol form, 30%), 0.91 (t, J = 7.2 Hz, keto form, 70%), 1.26−1.35 (m, 2H), 1.43−1.50 (m, 1H), 1.59−1.78 (m, 2H), 1.92−2.08 (m, 1H), 2.60−2.73 (m, 3H), 3.50 (s, keto form), 3.75 (s, keto form), 3.76 (s, enol form), 5.01 (s, enol form), 7.33 (d, J = 8.4 Hz, enol form), 7.34 (d, J = 8.4 Hz, keto form), 8.14 (d, J = 8.8 Hz, 2H), 12.10 (s, enol form); ^{13}C NMR, keto form: δ 14.09, 20.25, 31.81, 33.28, 33.44, 51.20, 51.60, 52.38, 123.73, 129.20, 146.45, 149.94, 167.53, 205.60; enol form: δ 13.96, 20.44, 33.53, 33.83, 35.01, 45.07, 51.20, 90.05, 123.64, 129.20, 146.35, 149.54, 172.93, 180.09; IR 2970, 1745, 1710, 1520, 1345, 1240 cm^{-1}; MS (*m*/*z*, relative intensity) 307 (M$^+$, 4), 265 (10), 234 (37), 206 (28), 158(84), 129(100); HRMS calcd for $C_{16}H_{21}NO_5$ 307.1420, found 307.1436.

Methyl 3-Oxo-6-(4-aminophenyl)-4-propylhexanoate (9). The nitro compound **8** from previous step (6.5 g, 0.22 mmol) was dissolved in 80% EtOH/H_2O (125 mL), followed by the addition of 20 drops of concentrated aqueous HCl and iron powder (12.3 g, 0.22 mmol). The mixture was heated under reflux for 1 h while stirring with a mechanical stirrer. After completion of the reduction, the black powder in the reaction mixture was removed by filtration, and EtOH was removed in vacuo. The remaining mixture was extracted with Et_2O (3 × 50 mL), and the combined ethereal solution was washed with H_2O and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude oil which was subjected to column chromatography, eluting with 2:1 petroleum ether/EtOAc to yield a yellow oil of the title compound **9** (5.26 g, 90%): R_f = 0.62 (petroleum ether/EtOAc = 1:1); ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, 3H), 1.24−1.30 (m, 2H), 1.40−1.49 (m, 1H), 1.55−1.72 (m, 2H), 1.78−1.98 (m, 1H), 2.39−2.62 (m, 3H), 3.43 (s, keto form, 90%), 3.42−3.60 (m, 1H), 3.72 (s, 3H), 4.99 (s, enol form, 10%), 6.62 (d, J = 8.4 Hz, 2H), 6.94 (d, J = 8.4 Hz, 2H); ^{13}C NMR, keto form: δ 14.14, 20.37, 32.48, 33.01, 33.38, 48.14, 51.68, 52.28, 115.31, 129.13, 131.40, 144.47, 167.67, 206. 24; enol form: δ 14.04, 20.46, 32.62, 34.74, 35.02, 44.98, 51.09, 89.64, 115.26, 129.13, 132.01, 144.23, 173.07, 181.22; MS (*m*/*z*, relative intensity) 277 (M$^+$, 6), 119 (100), 120 (21), 106 (84), 77 (8); HRMS calcd for $C_{16}H_{23}NO_3$ 277.1676, found 277.1678.

Methyl 2-Diazo-3-oxo-6-(4-nitrophenyl)-4-propylhexanoate (1a). To a solution containing **8** (680 mg, 2.21 mmol) and triethylamine (0.62 mL, 4.42 mmol) in MeCN (30 mL) was added dropwise a solution of *p*-toluenesulfonyl azide (872 mg, 4.42 mmol) in MeCN (10 mL). The solution was stirred at room temperature under N_2 atmosphere for 6 h. Solvent was removed in vacuo, and the residue was dissolved in Et_2O. The ethereal solution was washed with 5% aqueous NaOH and H_2O and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude product, which was subjected to column chromatography, eluting with 15:1 petroleum ether/EtOAc (containing 0.5% Et_3N) to yield **1a** (453 mg, 62%): R_f = 0.33 (petroleum ether/EtOAc = 8:1). ^{1}H NMR δ 0.89 (t, J = 7.2 Hz, 3H), 1.26−1.36 (m, 2H), 1.38−1.46 (m, 1H), 1.65−1.80 (m, 1H), 2.64−2.75 (m, 2H), 3.65−3.73 (m, 1H), 3.84 (s, 3H), 7.32 (d, J = 8.6 Hz, 2H), 8.12 (d, J = 8.6 Hz, 2H); ^{13}C NMR δ 14.16, 20.32, 32.78, 33.60, 34.36, 46.48, 52.23, 76.37, 123.61, 129.18, 146.35, 149.99, 161.44, 195.80; IR 2980, 2880, 2145, 1720, 1655, 1520, 1355, 1315, 1205 cm^{-1}; MS (*m*/*z*, relative intensity) 305 [(M − N_2)$^+$, 2], 262 (4), 230 (3), 200 (31), 184 (3), 172 (13), 155 (51), 107 (12), 91 (100); HRMS calcd for (M − N_2)$^+$, $C_{16}H_{19}NO_5$ 305.1263, found 305.1273.

Methyl 2-Diazo-3-oxo-6-(4-chlorophenyl)-4-propylhexanoate (1b). A two-step procedure was followed. Sandmeyer reaction was performed according to a literature procedure.[8] To **9** (1.39 g, 5 mmol) were added H_2O (15 mL) and concentrated HCl (0.25 mL, 15 mmol). The mixture was warmed for 10 min until it turned to be homogeneous solution. TLC check of the mixture indicated that all free amine had turned to its salt. The solution was then cooled to 0 °C with ice bath, and a solution of $NaNO_2$ (518 mg, 7.5 mmol) in H_2O (30 mL) was added dropwise with stirring. The resulting solution was stirred between 0 and 5°C for 1 h, and then urea (150 mg, 2.5 mmol) was added to remove the excess $NaNO_2$. The mixture was added dropwise to CuCl [freshly prepared from $CuSO_4$·$5H_2O$ (3.75 g, 15 mmol)] at 0 °C with stirring. The mixture was allowed to warm to room temperature. After stirring at room temperature for 1 h, the mixture was heated between 50 and 60 °C for 45 min. After cooling, the mixture was extracted with Et_2O (3 × 100 mL). The combined ethereal solution was washed with 5% aqueous NaOH, H_2O, concentrated H_2SO_4, and finally H_2O and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude oil which was subjected to column chromatography, eluting with 15:1 petroleum ether/EtOAc to yield methyl 3-oxo-6-(4-chlorophenyl)-4-propylhexanoate as a light yellow oil (462 mg, 31%): R_f = 0.51 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 0.86 (t, J = 7.2 Hz, enol form, 25%), 0.88 (t, J = 7.4 Hz, keto form, 75%), 1.24−1.32 (m, 2H), 1.35−1.43 (m, 1H), 1.50−1.70 (m, 2H), 1.80−2.10 (m, 1H), 2.41−2.60 (m, 3H), 3.43 (d, J = 15.5 Hz, keto form), 3.47 (d, J = 15.5 Hz, keto form), 3.71 (s, keto form), 3.73 (s, keto form), 4.98 (s, enol form), 7.07 (d, J = 8.4 Hz, enol form), 7.08 (d, J = 8.4 Hz, keto form), 7.21 (d, J = 8.4 Hz, enol form), 7.25 (d, J = 8.4 Hz, keto form), 12.07 (s, enol form). ^{13}C NMR, keto form: δ 14.07, 20.26, 32.36, 32.59, 33.36, 48.07, 51.53, 52.27, 128.36, 128.48, 129.67, 139.93, 167.5, 205.80; enol

form: δ 13.97, 20.41, 32.66, 34.23, 34.97, 44.95, 51.09, 89.79, 128.30, 128.45, 129.69, 140.37, 172.95, 180.59. IR 2960, 1750, 1715, 1635, 1445, 1240 cm^{-1}; MS (*m*/*z*, relative intensity) 296 (M^+, 3), 265 (8), 223 (6), 158 (100), 129 (100), 97 (35), 84 (27); HRMS calcd for $C_{17}H_{26}ClO_3$ 296.1179, found 296.1183.

Following the procedure for the synthesis of **1a**, diazo transfer was performed on methyl 3-oxo-6-(4-chlorophenyl)-4-propylhexanoate (362 mg, 1.22 mmol). The crude product was chromatographed with petroleum ether/EtOAc. The resulting oil was further subjected to preparative TLC, developed with 100:1 petroleum ether/EtOAc for three times to give a pure **1b** as a yellow oil (250 mg, 64%): R_f = 0.46 (petroleum ether/EtOAc = 10:1); ^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.25−1.36 (m, 2H), 1.38−1.49 (m, 1H), 1.65−1.76 (m, 2H), 1.98−2.09 (m, 1H), 2.51−2.60 (m, 2H), 3.60−3.70 (m, 1H), 3.82 (s, 3H), 7.08 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 14.18, 20.36, 33.06, 33.39, 34.39, 46.55, 52.17, 76.39, 128.28, 128.36, 129.72, 140.46, 161.50, 196.10; IR 2980, 2145, 1725, 1660, 1315, 1205 cm^{-1}; MS (*m*/*z*, relative intensity) 322 (M^+, 0.2), 251 (8), 219 (7), 184 (100), 155 (12), 125 (96), 100 (36); HRMS calcd for $C_{16}H_{19}ClN_2O_3$ 322.1084, found 322.1087.

Methyl 2-Diazo-3-oxo-6-(4-acetaminophenyl)-4-propylhexanoate (1c). A two-step procedure was followed. Diazo transfer procedure as for the synthesis of **1a** was followed for **9** (415 mg, 1.5 mmol). The crude product was subjected to column chromatography, eluting with 8:1 petroleum ether/EtOAc (containing 0.5% Et_3N) to give methyl 2-diazo-3-oxo-6-(4-aminophenyl)-4-propylhexanoate as a yellow oil (274 mg, 60%): R_f = 0.33 (petroleum ether/EtOAc = 8:1); ^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.27−1.33 (m, 2H), 1.35−1.50 (m, 1H), 1.60−1.72 (m, 2H), 1.93−2.06 (m, 1H), 2.44−2.51 (m, 2H), 3.53 (broad, 2H), 3.61−3.68 (m, 1H), 3.80 (s, 3H), 6.58 (d, *J* = 8.3 Hz, 2H), 6.93 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR δ 14.20, 20.38, 32.82, 34.02, 34.34, 46.67, 52.10, 76.33, 115.12, 129.09, 131.92, 144.36, 161.54, 196.31; IR 3395, 2990, 2140, 1720, 1645, 1310, 1200 cm^{-1}; MS (*m*/*z*, relative intensity) 303 (M^+, 4), 275 (12), 243 (14), 119 (68), 106 (100); HRMS calcd for $C_{16}H_{21}N_3O_8$ 303.1561, found 303.1572.

A solution of methyl 2-diazo-3-oxo-6-(4-aminophenyl)-4-propylhexanoate (250 mg, 0.83 mmol), acetic anhydride (0.87 mL, 8.3 mmol), and pyridine (0.67 mL, 8.3 mmol) was stirred for 1 h at room temperature under N_2 atmosphere. After completion of the reaction, ice−water (10 mL) was added and the mixture was extracted with Et_2O (3 × 20 mL). The combined ethereal solution was washed with 5% aqueous HCl (3 × 10 mL) and saturated aqueous NaCl (3 × 10 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent gave an oily residue which was subjected to column chromatography, eluting with 2:1 petroleum ether/EtOAc to give the title compound **1c** as a yellow oil (263 mg, 96%): R_f = 0.37 (petroleum ether/EtOAc = 1:2); ^{1}H NMR δ 0.85 (t, *J* = 7.2 Hz, 3H), 1.21−1.30 (m, 2H), 1.37−1.44 (m, 1H), 1.60−1.71 (m, 2H), 1.91−2.00 (m, 1H), 2.10 (s, 3H), 3.62−3.80 (m, 1H), 3.79 (s, 3H), 7.04 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.96 (s, broad, 1H); ^{13}C NMR δ 14.19, 20.38, 24.40, 33.11, 33.63, 34.38, 46.65, 52.18, 76.42, 126.08, 128.74, 136.62, 137.93, 161.51, 168.64, 196.35; IR 3320, 2970, 2145, 1720, 1660, 1600, 1540, 1440, 1375, 1315 cm^{-1}; MS (*m*/*z*, relative intensity) 345 (M^+, 6), 317 (5), 274 (20), 243 (17), 184 (11), 162 (22), 106 (100), 86 (32); HRMS calcd for $C_{18}H_{23}N_3O_4$ 345.1689, found 345.1697.

Methyl 2-Diazo-3-oxo-6-phenyl-4-propylhexanoate (1d). A literature procedure was followed for preparing **1d**.[2a] ^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.22−1.38 (m, 2H), 1.40−1.51 (m, 1H), 1.62−1.80 (m, 2H), 1.98−2.12 (m, 1H), 2.52−2.62 (m, 2H), 3.60−3.72 (m, 1H), 3.81 (s, 3H), 7.12−7.18 (m, 3H), 7.22−7.30 (m, 2H).

Methyl 2-Diazo-3-oxo-6-(4-phenylphenyl)-4-propylhexanoate (1e). A two-step procedure was followed. Phenylation was performed following a literature procedure.[9] A solution of **9** (1.38 g, 5 mmol) and *n*-pentyl nitrite (878 mg, 7.5 mmol) in benzene (25 mL) was stirred for 20 min until gas evolution was stopped. The solution was then refluxed for 1.5 h. Solvent was removed in vacuo, and the residue was subjected to column chromatography, eluting with 15:1 petroleum ether/EtOAc to yield methyl 3-oxo-6-(4-phenylphenyl)-4-propylhexanoate **10** as a light yellow oil (500 mg, 30%): R_f = 0.5 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 0.87 (t, *J* = 7.2 Hz, enol form 30%), 0.89 (t, *J* = 1.2 Hz, keto form 70%), 1.24−1.35 (m, 2H), 1.42−1.50 (m, 1H), 1.63−1.70 (m, 1H), 1.70−1.78 (m, 1H), 1.95−2.10 (m, 1H), 2.50−2.65 (m, 3H), 3.44 (d, *J* = 15.6 Hz, keto form), 3.48 (d, *J* = 15.6 Hz, keto form), 3.72 (s, keto form), 3.73 (s, enol form), 5.02 (s, enol form), 7.18−7.24 (m, 2H), 7.28−7.31 (m, 1H), 7.37−7.45 (m, 2H), 7.48−7.52 (m, 2H), 7.56−7.58 (m, 2H), 12.05 (s, enol form). ^{13}C NMR keto form: δ 14.13, 20.32, 32.57, 32.97, 33.41, 48.13, 51.71, 52.29, 126.59, 127.04, 127.16, 128.72, 128.80, 138.97, 140.91, 141.01, 167.58, 206.01; enol form: δ 14.03, 20.45, 33.17, 34.39, 35.04, 45.11, 51.10, 89.78, 127.01, 127.08, 128.33, 128.44, 128.77, 138.73, 141.01, 141.11, 173.02, 180.88. IR 2960, 1760, 1720, 1445, 1240 cm^{-1}; MS (*m*/*z*. relative intensity) 338 (M^+, 3), 265 (4), 180 (100), 167 (18), 158 (36), 129 (38), 97 (11), 91 (20); HRMS calcd for $C_{22}H_{26}O_3$ 338.1882, found 338.1886.

Following the procedure for the synthesis of **1a**, diazo transfer was performed on **10** (417 mg, 1.23 mmol). Crude oily product was subjected to column chromatography, eluting with 15:1 petroleum ether/EtOAc to give the title compound **1e** as a light yellow oil (375 mg, 84%): R_f = 0.40 (petroleum ether/EtOAc = 10:1); ^{1}H NMR δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.29−1.42 (m, 2H), 1.40−1.57 (m, 1H), 1.70−1.89 (m, 2H), 2.07−2.20 (m, 1H), 2.61−2.76 (m, 2H), 3.70−3.80 (m, 1H), 3.83 (s, 3H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.32−7.40 (m, 1H), 7.41−7.49 (m, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.59−7.67 (m, 2H); ^{13}C NMR δ 14.21, 20.38, 33.35, 33.56, 34.39, 46.71, 52.10, 76.37, 126.95, 126.99, 127.00, 128.69, 128.81, 138.78, 141.04, 141.16, 161.51, 196.14; IR 2970, 2140, 1720, 1650, 1440, 1310, 1200, 1125 cm^{-1}; MS (*m*/*z*, relative intensity) 364 (M^+, 2), 336 (11), 293 (42), 261 (36), 233 (10), 184 (82), 167 (100), 113 (27); HRMS calcd for $C_{22}H_{24}N_2O_3$ 364.1787, found 364.1791.

Preparation of Methyl 3-Oxo-6-(4-hydroxyphenyl)-4-propylhexanoate (11). Hydroxylation was effected to **9** according to a literature procedure.[10] To a mixture of amine **9** (1.11 g, 4 mmol) in H_2O (20 mL) was added aqueous H_2SO_4 (0.5 M, 24 mL, 12 mmol), and the mixture was warmed until it turned homogeneous. TLC check of the mixture indicated that all free amine had turned to its salt. After cooling to 0 °C, a solution of $NaNO_2$ (414 mg, 6 mmol) was added dropwise while the temperature was maintained between 0 and 5 °C. The resulting solution was stirred below 5 °C for another 1.5 h after the addition, and then urea (120 mg, 2 mmol) was added to remove excess $NaNO_2$. Aqueous H_2SO_4 (0.5 M, 20 mL) was added dropwise, and the solution was refluxed for 30 min. After cooling to room temperature, the mixture was extracted with Et_2O (3 × 50 mL), and the combined ethereal solution was washed with H_2O (3 × 20 mL) and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude product, which was subjected to column chromatography, eluting with 4:1 petroleum ether/EtOAc to give methyl 3-oxo-6-(4-hydroxylphenyl)-4-propylhexanoate (**11**) (772 mg, 70%). R_f = 0.54 (petroleum ether/EtOAc = 2:1); ^{1}H NMR δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.22−1.40 (m, 2H), 1.43−1.50 (m, 1H), 1.50−1.70 (m, 2H), 1.81−1.99 (m, 1H), 2.48−2.62 (m, 3H), 3.44 (d, *J* = 15.4 Hz, keto from 90%), 3.48 (d, *J* = 15.4 Hz, keto form), 3.73 (s, keto form), 3.74 (s, enol form, 10%), 5.00 (s, enol form), 6.76 (d, *J* = 8.4 Hz), 6.99 (d, *J* = 8.4 Hz), 12.05 (s, enol form). ^{13}C NMR keto form: δ 14.09, 20.31, 32.43, 32.48, 33.38, 48.12, 51.71, 52.38, 115.29, 129.36, 133.27, 154.01, 167.88, 206.64. IR 3445, 2970, 1755, 1715, 1520, 1445, 1235 cm^{-1}; MS (*m*/*z*, relative intensity) 278 (M^+, 3), 220 (4), 205 (8), 158 (44), 129 (52), 120 (95), 107 (100), 77 (21); HRMS calcd for $C_{16}H_{22}O_4$ 278.2518, found 278.1517.

Methyl 2-Diazo-3-oxo-6-(4-methoxyphenyl)-4-propylhexanoate (1f). A two-step procedure was followed. **11** was methylated according to a literature procedure.[11] To **11** (250 mg, 0.9 mmol) in ether (30 mL) was added silica gel (15 g). The mixture was cooled to 0 °C, and an ethereal solution of CH_2N_2, generated from nitrosomethylurea, was introduced. After 3 h, silica gel was filtered, and the ether and the excess CH_2N_2 were removed from the filtrate by evaporation. The oily product was subjected to column chromatography, eluting with 6:1 petroleum ether/EtOAc give methyl 3-oxo-6-(4-meth-

oxyphenyl)-4-propylhexanoate (43 mg, 82%): R_f = 0.46 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 0.86 (t, J = 7.2 Hz, enol form 25%), 0.88 (t, J = 7.2 Hz, keto form 75%), 1.24−1.30 (m, 2H), 1.45−1.50 (m, 1H), 1.55−1.72 (m, 2H), 1.82−2.20 (m, 1H), 2.45−2.58 (m, 3H), 3.41 (d, J = 15.5 Hz, 1H, keto form), 3.46 (d, J = 15.5 Hz, 1H, keto form), 3.71 (s, enol form), 3.75 (s, enol form), 3.75 (s, keto form), 5.00 (s, enol form), 6.80 (d, J = 8.4 Hz, enol form), 6.81 (d, J = 8.4 Hz, keto form), 7.06 (d, J = 8.4 Hz, 2H), 12.10 (s, enol form); ^{13}C NMR, keto form: δ 14.13, 20.34, 32.45, 32.91, 33.39, 48.10, 51.64, 52.21, 55.17, 113.83, 129.25, 133.50, 157.92, 167.59, 206.07; enol form: δ 14.02, 20.46, 32.60, 34.68, 35.03, 44.99, 51.06, 55.17, 89.70, 113.72, 129.25, 133.99, 157.77, 173.04, 181.03. IR 2960, 1755, 1620, 1518, 1445, 1245 cm^{-1}; MS (*m*/*z*, relative intensity) 292 (M$^+$, 22), 219 (20), 158 (31), 135 (88), 121 (100), 91 (37), 78 (44); HRMS calcd for $C_{17}H_{24}O_4$, 292.1675, found 292.1673.

Diazo transfer procedure as for the synthesis of **1a** was followed (442 mg, 1.5 mmol). The crude product was subjected to column chromatography, eluting with 15:1 petroleum ether/EtOAc to give **1f** as a yellow oil (385 mg, 80%): R_f = 0.3 (petroleum ether = 10:1); ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, 3H), 1.26−1.34 (m, 2H), 1.36−1.47 (m, 1H), 1.63−1.75 (m, 2H), 1.95−2.07 (m, 1H), 2.50−2.55 (m, 2H), 3.60−3.69 (m, 1H), 3.77 (s, 3H), 3.81 (s, 3H), 6.79 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 14.19, 20.39, 32.81, 33.89, 34.38, 46.69, 52.11, 55.23, 76.45, 113.68, 129.27, 134.12, 157.77, 161.54, 196.24; IR 2970, 2140, 1720, 1645, 1310, 1240, 1200 cm^{-1}; MS (*m*/*z*, relative intensity) 318 (M$^+$, 3), 258 (10), 216 (26), 200 (32), 184 (27), 155 (53), 134 (38), 172 (19), 121 (90), 91 (100); HRMS calcd for $C_{17}H_{22}N_2O_4$, 318.1580, found 318.1584.

Methyl 2-Diazo-3-oxo-6-(4-hydroxyphenyl)-4-propylhexanoate (1g). The same diazo transfer procedure as for the synthesis of **1a** was followed for **11** (220 mg, 0.79 mmol). The crude product was subjected to column chromatography, eluting with 4:1 petroleum ether/EtOAc to give **1g** as a yellow oil (95 mg, 39%): R_f = 0.21 (petroleum ether/EtOAc = 4:1). ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, 3H), 1.24−1.38 (m, 2H), 1.40−1.49 (m, 1H), 1.66−1.78 (m, 2H), 1.99−2.10 (m, 1H), 2.55−2.64 (m, 2H), 3.61−3.70 (m, 1H), 3.82 (s), 7.15−7.22 (m, 4H). ^{13}C NMR δ 14.11, 20.28, 33.01, 33.26, 34.31, 46.49, 52.11, 76.40, 121.73, 129.80, 141.48, 147.35, 161.42, 195.95. IR 2960, 2140, 1720, 1645, 1365, 1150; MS (*m*/*z*, relative intensity) 304 (M$^+$, 3), 276 (4), 233 (28), 201 (30), 120 (75), 107 (100); HRMS calcd for $C_{16}H_{20}N_2O_4$ 304.1423, found 304.1399.

General Procedure for Rh(II)-Catalyzed Dinitrogen Extrusion from the Diazo Compound 1a−g. 1a−g (0.5 mmol) in CH_2Cl_2 or benzene (10 mL) was added to a stirring solution of CH_2Cl_2 or benzene (10 mL) containing 1.0 mol % Rh(II) at room temperature under nitrogen atmosphere. The green, homogeneous solution was stirred for 10 to 14 h until the completion of the reaction, as indicated by TLC. The catalyst was removed by a short column, and the crude reaction mixture was analyzed by ^{1}H NMR (400 MHz) for product ratio determination. Further column chromatography and preparative TLC provided pure products for identification and characterization. Our experiment and others[2c] indicated that product ratio was independent of the scale of reaction, substrate concentration, and the catalyst mol %.

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-nitrophenyl)-4-propylhexanoate (1a). Following the general procedure, cyclization was effected on **1a** (167 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 8.13 (d, J = 8.4 Hz), δ 7.36 (d, J = 8.4 Hz) of **3a** and δ 8.19 (d, J = 8.4 Hz), δ 7.48 (d, J = 8.4 Hz) of **4a**. The isolated yields of **3a** and **4a** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 92%; with benzene as solvent, 77%; $Rh_2(O_2CCF_3)_4$, 80%; $Rh_2(acam)_4$, 77%. Pure specimens of **3a** and **4a** were obtained by column chromatography and preparative TLC separation. Methyl 5-methyl-2-oxo-3-[2-(4-nitrophenyl)ethyl]cyclopentanecarboxylate (**3a**): R_f = 0.33 (petroleum ether/EtOAc = 3:1); ^{1}H NMR δ 1.19 (d, J = 6.5 Hz, 3H), 1.13−1.21 (m, 1H), 1.62−1.69 (m, 1H), 2.10−2.19 (m, 1H), 2.27−2.39 (m, 2H), 2.46−2.57 (m, 1H), 2.79 (d, J = 11.7 Hz, 1H), 2.75−2.85 (m, 2H), 3.76 (s, 3H), 7.34 (d, J = 8.4 Hz, 2H), 8.15 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 19.17, 30.95, 33.35, 34.12, 36.21, 49.60, 52.47, 62.78, 123.75, 129.21, 146.48, 149.25, 169.43, 212.26; IR 2960, 1755, 1720, 1340 cm^{-1}; MS (*m*/*z*, relative intensity) 305 (M$^+$, 2), 274 (5), 156 (100), 136 (7), 124 (92), 96 (12); HRMS calcd for $C_{16}H_{19}NO_5$ 305.1263, found 305.1262. Methyl 2-oxo-5-(4-nitrophenyl)-3-propylcyclopentanecarboxylate (**4a**): R_f = 0.51 (petroleum ether/EtOAc = 3:1); ^{1}H NMR δ 0.95 (t, J = 7.2 Hz, 3H), 1.35−1.47 (m, 3H), 1.69 (q, J = 12.2 Hz, 1H), 1.83−1.94 (m, 1H), 2.45−2.55 (m, 1H), 2.58−2.67 (m, 1H), 3.34 (d, J = 12.0 Hz, 1H), 3.74 (s, 3H), 3.87 (dt, J = 6.0, 12.2 Hz, 1H), 7.45 (d, J = 8.4 Hz, 2H), 8.20 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 13.89, 20.50, 31.62, 35.17, 43.64, 50.02, 52.76, 61.83, 124.07, 127.86, 147.09, 148.55, 168.54, 210.14; IR 2990, 1760, 1725, 1520, 1355 cm^{-1}; MS (*m*/*z*, relative intensity) 305 (M$^+$, 17), 274 (12), 263 (75), 246 (100), 231 (72), 203 (41), 176 (51), 160 (22), 115 (23), 97 (21); HRMS calcd for $C_{16}H_{19}NO_5$ 305.1263, found 305.1270.

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-chlorophenyl)-4-propylhexanoate (1b). Following the general procedure, cyclization was effected on **1b** (161 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 3.75 (s), δ 2.76 (d, J = 11.6 Hz) of **3b** and δ 3.72 (s), δ 3.27 (d, J = 12.0 Hz) of **4b**. The isolated yields of **3b** and **4b** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 96%; with benzene as solvent, 63%; $Rh_2(O_2CCF_3)_4$, 72%; $Rh_2(acam)_4$, 61%. Pure specimens of **3b** and **4b** were obtained by preparative TLC separation. Methyl 5-methyl-2-oxo-3-[2-(4-chlorophenyl)ethyl]cyclopentanecarboxylate (**3b**): R_f = 0.46 (petroleum ether/EtOAc = 5:1). ^{1}H NMR δ 1.19 (d, J = 6.5 Hz, 3H), 1.15−1.22 (m, 1H), 1.56−1.60 (m, 1H), 2.07−2.15 (m, 1H), 2.23−2.37 (m, 2H), 2.48−2.56 (m, 1H), 2.60−2.71 (m, 2H), 2.76 (d, J = 11.6 Hz, 1H), 3.75 (s, 3H), 7.10 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 19.01, 31.16, 32.59, 33.94, 36.08, 49.45, 52.23, 62.69, 128.36, 129.56, 131.59, 139.54, 169.34, 212.32; IR 2960, 1755, 1720, 1485, 1200, 1135 cm^{-1}. MS (*m*/*z*, relative intensity) 294 (M$^+$, 3), 263 (5), 169 (4), 156 (100), 138 (12), 124 (73), 101 (11), 69 (33); HRMS calcd for $C_{16}H_{19}ClO_3$ 294.1023, found 294.1020. Methyl 2-oxo-5-(4-chlorophenyl)-3-propylcyclopentanecarboxylate (**4b**) was isolated as mobile fraction: R_f = 0.53 (petroleum ether/EtOAc = 0.53); ^{1}H NMR δ 0.95 (t, J = 7.0 Hz, 3H), 1.31−1.50 (m, 3H), 1.63 (q, J = 12.2 Hz, 1H), 1.81−1.93 (m, 1H), 2.42−2.61 (m, 2H), 3.27 (d, J = 12.0 Hz, 1H), 3.72 (s, 3H), 3.67−3.73 (m, 1H), 7.20 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 13.93, 20.56, 31.72, 35.54, 43.42, 50.19, 52.60, 62.28, 128.25, 128.95, 129.75, 139.57, 169.02, 211.12; IR 2970, 1760, 1720, 1440, 1265, 1125, 1085 cm^{-1}; MS (*m*/*z*, relative intensity) 294 (M$^+$, 13), 263 (10), 235 (100), 220 (25), 201 (35), 165 (30), 131 (16), 101 (13); HRMS calcd for $C_{16}H_{19}ClO_3$ 294.1023, found 294.1027.

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-acetaminophenyl)-4-propylhexanoate (1c). Following the general procedure, cyclization was effected on **1c** (171 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 8.32 (s), δ 7.42 (d, J = 8.2 Hz), δ 7.08 (d, J = 8.2 Hz), δ 3.76 (s), δ 2.76 (d, J = 11.6 Hz) of **3c** and δ 8.44 (s), δ 7.50 (d, J = 8.3 Hz), δ 7.18 (d, J = 8.3 Hz), δ 3.69 (s), δ 3.29 (d, J = 12.0 Hz) of **4c**. The isolated yields of **3c** and **4c** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 83%; with benzene as solvent, 71%; $Rh_2(O_2CCF_3)_4$, 69%; $Rh_2(acam)_4$, 74%. **3c** and **4c** was found to be inseparable with column chromatography and preparative TLC. A pure specimen of methyl 5-methyl-2-oxo-3-[2-(4-acetaminophenyl)ethyl]cyclopentanecarboxylate (**3c**) was synthesized in two steps from **3a** (vide infra). ^{1}H NMR and ^{13}C NMR for **3c** and **4c** were obtained by comparing the spectra of the mixture and that of pure **3c**. Methyl 5-methyl-2-oxo-3-[2-(4-acetaminophenyl)ethyl]cyclopentanecarboxylate (**3c**): ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3H), 1.13−1.22 (m, 1H), 1.55−1.63 (m, 1H), 2.14 (s, 3H), 2.23−2.38 (m, 2H), 2.46−2.73 (m, 3H), 2.76 (d, J = 11.6 Hz, 1H), 3.76 (s, 3H), 7.10 (d, J = 8.2 Hz, 2H), 7.41 (d, J = 8.2 Hz, 2H), 7.74 (s, 1H); ^{13}C NMR δ 19.15, 24.41, 31.39, 32.82, 34.12, 36.20, 49.66, 52.38, 62.90, 120.07, 128.77, 136.08, 137.05, 168.51, 169.60, 212.96; IR 3320, 2960, 1720, 1660, 1600, 1540 cm^{-1}; MS (*m*/*z*, relative intensity) 317 (M$^+$, 11), 286 (10), 161 (100), 124 (76), 119 (90); HRMS

calcd for $C_{18}H_{23}NO_4$ 317.1599, found 317.1613. Methyl 2-oxo-5-(4-acetaminophenyl)-3-propylcyclopentanecarboxylate (**4c**): ^{1}H NMR δ 0.92 (t, J = 7.3 Hz, 3H), 1.75−1.85 (m, 3H), 1.63 (q, J = 12.0 Hz, 1H), 1.79−1.90 (m, 1H), 2.14 (s, 3H), 2.45−2.65 (m, 2H), 3.29 (d, J = 12.0 Hz, 1H), 3.69 (s, 3H), 3.68−3.78 (m, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 8.28 (broad), ^{13}C NMR δ 13.95, 20.56, 24.41, 31.44, 35.61, 43.57, 50.26, 52.55, 62.46, 120.43, 127.26, 136.64, 137.23, 168.98, 169.35, 212.03.

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-phenyl-4-propylhexanoate (1d). Following the general procedure, cyclization was effected on **1d** (130 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 3.73 (s), δ 2.76 (d, J = 11.6 Hz) of **3d** and δ 3.70 (s), δ 3.32 (d, J = 12.0 Hz) of **4d**. The isolated yields of **3d** and **4d** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 85%; with benzene as solvent, 64%; $Rh_2(O_2CCF_3)_4$, 86%; $Rh_2(acam)_4$, 66%. Pure specimens of **3d** and **4d** for identification[2a] were obtained by preparative TLC separation. Methyl 5-methyl-2-oxo-3-(2-phenylethyl)cyclopentanecarboxylate **3d**: ^{1}H NMR δ 1.18 (d, J = 7.5 Hz, 3H), 1.12−1.21 (m, 1H), 1.54−1.65 (m, 1H), 2.11−2.20 (m, 1H), 2.25−2.40 (m, 2H), 2.42−2.58 (m, 1H), 2.57−2.72 (m, 2H), 2.76 (d, J = 11.6 Hz, 1H), 3.75 (s, 3H), 7.15−7.22 (m, 3H), 7.24−7.30 (m, 2H). Methyl 2-oxo-5-phenyl-3-propylcyclopentanecarboxylate (**4d**): ^{1}H NMR δ 0.93 (t, J = 7.3 Hz, 3H), 1.36−1.49 (m, 3H), 1.67 (q, J = 12.1 Hz, 1H), 1.81−1.92 (m, 1H), 2.40−2.51 (m, 1H), 2.52−2.63 (m, 1H), 3.54 (d, J = 12.0 Hz, 1H), 3.73 (s, 3H), 3.68−3.79 (m, 1H), 7.21−7.36 (m, 5H).

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-phenylphenyl)-4-propylhexanoate (1e). Following the general procedure, cyclization was effected on **1e** (182 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 3.74 (s), δ 2.78 (d, J = 11.7 Hz) for **3e** and δ 3.73 (s), δ 3.37 (d, J = 12.0 Hz) for **4e**. The isolated yields of **3e** and **4e** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 68%; with benzene as solvent, 59%; $Rh_2(O_2CCF_3)_4$, 81%; $Rh_2(acam)_4$, 64%. Pure specimens of **3e** and **4e** for identification were obtained by further column chromatography and preparative TLC separation. Methyl 5-methyl-2-oxo-3-[2-(4-phenylphenyl)ethyl]cyclopentanecarboxylate (**3e**): R_f = 0.33 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3H), 1.12−1.23 (m, 1H), 1.60−1.68 (m, 1H), 2.15−2.22 (m, 1H), 2.30−2.41 (m, 2H), 2.47−2.57 (m, 1H), 2.65−2.77 (m, 2H), 2.78 (d, J = 11.7 Hz, 1H), 3.75 (s, 3H), 7.25 (d, J = 8.1 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.42 (d, J = 7.2 Hz, 2H), 7.50 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H); ^{13}C NMR δ 19.17, 31.37, 32.98, 34.07, 36.23, 49.71, 52.37, 62.87, 126.94, 127.03, 127.13, 128.68, 128.77, 138.98, 140.29, 140.90, 169.54, 212.68; IR 3050, 2975, 1760, 1722, 1460, 1440, 1205, 1135, 1075 cm^{-1}; MS (m/z, relative intensity) 336 (M^+, 16), 305 (3), 180 (100), 167 (41), 156 (12), 124 (32), 96 (6); HRMS calcd for $C_{22}H_{24}O_3$ 336.1725, found 336.1718. Methyl 2-oxo-5-(4-phenylphenyl)-3-propylcyclopentanecarboxylate (**4e**): R_f = 0.43 (petroleum ether = 4:1); ^{1}H NMR δ 0.94 (t, J = 7.3 Hz, 3H), 1.37−1.47 (m, 3H), 1.70 (q, J = 12.2 Hz, 1H), 1.82−1.90 (m, 1H), 2.47−2.54 (m, 1H), 2.56−2.66 (m, 1H), 3.37 (d, J = 12.0 Hz, 1H), 3.73 (s, 3H), 3.75−3.84 (m, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.31−7.37 (m, 1H), 7.41−7.46 (m, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.55−7.60 (m, 2H); ^{13}C NMR δ 13.98, 20.59, 31.72, 35.66, 43.63, 50.26, 52.61, 62.28, 127.01, 127.25, 127.30, 127.53, 128.78, 140.10, 140.14, 140.61, 169.22, 211.70; IR 3040, 2960, 1755, 1725, 1440, 1270 cm^{-1}; MS (m/z, relative intensity) 336 (M^+, 33), 304 (7), 277 (100), 262 (26), 234 (37), 207 (23), 178 (25), 156 (23), 124 (17), 91 (11); HRMS calcd for $C_{22}H_{24}O_3$ 336.1725, found 336.1728.

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-methoxyphenyl)-4-propylhexanoate (1f). Following the general procedure, cyclization was effected on **1f** (160 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 7.10 (d, J = 8.4 Hz), δ 6.82 (d, J = 8.4 Hz), δ 3.79 (s), δ 3.76 (s), 2.76 (d, J = 11.6 Hz) of **3f** and δ 7.18 (d, J = 8.4 Hz), δ 6.88 (d, J = 8.4 Hz), δ 3.78 (s), δ 3.70 (s), δ 3.27 (d, J = 12.0 Hz) of **4f**. The isolated yields of **3f** and **4f** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 91%; with benzene as solvent, 68%; $Rh_2(O_2CCF_3)_4$, 74%; $Rh_2(acam)_4$, 68%. Pure specimens of **3f** and **4f** were obtained by further separation with column chromatography and preparative TLC. Methyl 5-methyl-2-oxo-3-[2-(4-methoxyphenyl)ethyl]cyclopentanecarboxylate (**3f**): R_f = 0.45 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 1.17 (d, J = 6.5 Hz, 3H), 1.15−1.19 (m, 1H), 1.51−1.60 (m, 1H), 2.05−2.15 (m, 1H), 2.22−2.40 (m, 2H), 2.46−2.73 (m, 3H), 2.76 (d, J = 11.6 Hz, 1H), 3.76 (s, 3H), 3.79 (s, 3H), 6.83 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 19.18, 31.64, 32.46, 34.02, 36.24, 49.68, 52.38, 55.22, 62.89, 113.80, 129.26, 133.22, 157.87, 169.58, 212.79; IR 2960, 1750, 1720, 1515, 1440, 1240 cm^{-1}; MS (m/z, relative intensity) 290 (M^+, 21), 254 (6), 231 (100), 216 (18), 188 (26), 161 (24), 121 (12), 91 (10); HRMS calcd for $C_{17}H_{22}O_4$ 290.1518, found 290.1512. Methyl 2-oxo-5-(4-methoxyphenyl)-3-propylcyclopentanecarboxylate **4f**: R_f = 0.51 (petroleum ether/EtOAc = 4:1); ^{1}H NMR δ 0.93 (t, J = 7.4 Hz, 3H), 1.35−1.40 (m, 3H), 1.63 (q, J = 11.8 Hz, 1H), 1.85−1.88 (m, 1H), 2.44−2.57 (m, 2H), 3.27 (d, J = 12.0 Hz, 1H), 3.65−3.71 (m, 1H), 3.70 (s, 3H), 3.78 (s, 3H), 6.87 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.3 Hz, 2H); ^{13}C NMR δ 13.96, 20.58, 31.71, 35.77, 43.27, 50.27, 52.51, 55.26, 62.58, 114.14, 127.83, 133.05, 158.64, 169.31, 211.93. IR 2980, 1760, 1725, 1520, 1440, 1245, 1180 cm^{-1}; MS (m/z, relative intensity) 290 (M^+, 8), 259 (3), 156 (5), 134 (100), 124 (12), 121 (36), 91 (5); HRMS calcd for $C_{17}H_{22}O_4$ 290.1518, found 290.1512

Rh(II)-Catalyzed Dinitrogen Extrusion of Methyl 2-Diazo-3-oxo-6-(4-hydroxyphenyl)-4-propylhexanoate (1g). Following the general procedure, cyclization was effected on **1g** (139 mg, 0.5 mmol). The product ratios were determined by the integration of the following peaks: δ 7.00 (d, J = 8.5 Hz), δ 3.76 (s), δ 2.79 (d, J = 11.7 Hz) of **3g** and δ 6.81 (d, J = 8.5 Hz), δ 3.71(s), δ 3.29 (d, J = 12.0 Hz) of **4g**. The isolated yields of **3g** and **4g** were as follows: $Rh_2(OAc)_4$, with CH_2Cl_2 as solvent, 84%; with benzene as solvent, 72%; $Rh_2(O_2CCF_3)_4$, 46%; $Rh_2(acam)_4$, 72%. **3g** and **4g** were found to be inseparable with column chromatography and preparative TLC. A pure specimen of methyl 5-methyl-2-oxo-3-[2-(4-hydroxyphenyl)ethyl]cyclopentanecarboxylate (**3g**) was synthesized in two steps from methyl 5-methyl-2-oxo-3-[2-(4-nitrophenyl)ethyl]cyclopentanecarboxylate (**3a**) (vide infra). ^{1}H NMR and ^{13}C NMR for **3g** and **4g** were obtained by comparing the spectra of the mixture and that of pure **3g**. Methyl 5-methyl-2-oxo-3-[2-(4-hydroxyphenyl)ethyl]cyclopentanecarboxylate (**3g**): ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3H), 1.51−1.62 (m, 1H), 2.07−2.17 (m, 1H), 2.24−2.40 (m, 2H), 2.42−2.77 (m, 4H), 2.78 (d, J = 11.6 Hz, 1H), 3.76 (s, 3H), 6.75 (d, J = 8.4 Hz, 2H), 7.01 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 19.18, 31.65, 32.48, 34.16, 36.26, 49.77, 52.47, 62.98, 115.30, 129.53, 133.10, 154.07, 169.82, 213.28; IR 3450, 2960, 1720, 1515, 1440 cm^{-1}; MS (m/z, relative intensity) 276 (M^+, 5), 245 (3), 216 (4), 160 (5), 156 (15), 124 (23), 120 (100), 107 (58); HRMS calcd for $C_{16}H_{20}O_4$ 276.1362, found 276.1374. Methyl 2-oxo-5-(4-hydroxyphenyl)-3-propylcyclopentanecarboxylate (**4g**): ^{1}H NMR δ 0.93 (t, J = 7.3 Hz, 3H), 1.37−1.48 (m, 3H), 1.62 (q, J = 12.1 Hz, 1H), 1.80−1.90 (m, 1H), 2.48−2.70 (m, 2H), 3.27 (d, J = 12.0 Hz, 1H), 3.71 (s, 3H), 3.60−3.73 (m, 1H), 6.79 (d, J = 8.5 Hz, 2H), 7.11 (d, J = 8.5 Hz, 2H); ^{13}C NMR δ 13.96, 20.58, 31.72, 35.80, 43.34, 50.32, 52.63, 62.67, 115.65, 127.97, 132.91, 154.88, 169.58, 212.22.

Methyl 5-Methyl-2-oxo-3-[2-(4-acetaminophenyl)ethyl]cyclopentanecarboxylate (3c). For comparison, a pure title compound was synthesized in two steps from **3a**. The nitro compound **3a** (533 mg, 1.75 mmol) was dissolved in 80% EtOH/H_2O (26 mL), following the addition of concentrated aqueous HCl (5 mL) and iron powder (0.98 g, 17.5 mmol). The mixture was heated under reflux for 1 h while stirring. After completion of the reaction, the black powder was removed by filtration and EtOH was evaporated from filtrate. The remaining residue was extracted with Et_2O (3 × 10 mL), and the combined ethereal solution was washed with H_2O and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude product, which was subjected to column chromatography. Eluting with 2:1 petroleum ether/EtOAc yielded methyl

5-methyl-2-oxo-3-[2-(4-aminophenyl)ethyl]cyclopentanecarboxylate (**12**) (323 mg, 67%): ^{1}H NMR δ 1.17 (d, J = 6.4 Hz, 3H), 1.10−1.20 (m, 1H), 1.47−1.60 (m, 1H), 2.06−2.15 (m, 1H), 2.22−2.38 (m, 2H), 2.42−2.53 (m, 2H), 2.54−2.65 (m, 1H), 2.76 (d, J = 11.6 Hz, 1H), 3.35−3.52 (broad, 1H), 3.75 (s, 3H), 6.62 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.0 Hz, 2H); ^{13}C NMR δ 19.22, 31.73, 32.52, 33.63, 36.29, 49.74, 52.38, 62.96, 115.30, 129.18, 129.29, 131.15, 169.70, 212.96; IR 3470, 3390, 2960, 1755, 1720, 1610, 1260 cm^{-1}; MS (*m*/*z*, relative intensity) 275 (M^+, 11), 244 (2), 119 (100), 106 (73), 77 (6); HRMS calcd for $C_{16}H_{21}NO_3$ 275.1521, found 275.1512.

Amine **12** was then acylated by a standard procedure. The amino compound (96 mg, 0.35 mmol) was dissolved in pyridine (0.3 mL), following by addition of Ac_2O (0.3 mL). The solution was stirred at room temperature for 1 h. Ice−water (10 mL) was added, and the mixture was extracted with Et_2O (3 × 10 mL). The combined ethereal solution was washed with 5% aqueous HCl (3 × 5 mL) and saturated aqueous NaCl and dried over anhydrous $MgSO_4$. Removal of the solvent gave a crude oil, which was subjected to column chromatography. Eluting with 1:1 petroleum ether/EtOAc yielded **3c** (92 mg, 79%): R_f = 0.24 (petroleum ether/EtOAc = 1:2).

Methyl 5-Methyl-2-oxo-3-[2-(4-hydroxyphenyl)ethyl]-cyclopentanecarboxylate (3g). Hydroxylation was effected to amine **12** (185 mg, 0.67 mmol) with the procedure as described for the preparation of **11**. The crude product was subjected to chromatography with 4:1 petroleum ether/EtOAc to give **3g** (21 mg, 12%).

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Supporting Information Available: Hammett plots (with σ^+), and copies of ^{1}H NMR spectra for all new compounds except **6** (27 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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