J. Am. Chem. Soc. **1996,** *118,* 8162−8163

Saturation Kinetics in Dirhodium(II) Carboxylate-Catalyzed Decompositions of Diazo Compounds

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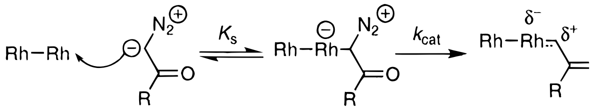
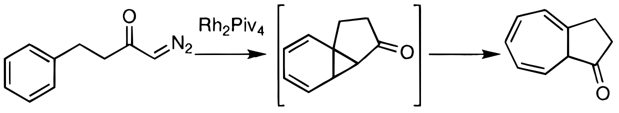
Received May 29, 1996

Rhodium(II) carboxylate salts have gained wide use in synthetic organic chemistry for the decomposition of diazo compounds.[1] Direct mechanistic data that could be useful in rationally modifying these reactions is sparse. Hubert and Noels have determined that the cyclopropanation of styrene by ethyl diazoacetate catalyzed by rhodium acetate is first order in catalyst,[2] and bimolecular rates of C−H insertion into dioxane catalyzed by rhodium acetate have also been determined.[3] Recent studies of regioselectivity,[4] enantioselectivity,[5] and chemoselectivity[6] in rhodium-mediated reactions have shown that an impressive degree of control can be exerted by the ligands.



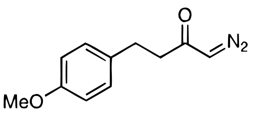
(1)



1 **2** (2)

A model proposed by Yates[7] for these reactions involves complexation of the negatively-polarized carbon of the diazo compound to the axial site of the coordinately-unsaturated rhodium complex followed by loss of nitrogen (eq 1). If the first step were pre-equilibrium and the second rate determining, these processes might obey saturation kinetics. In order to investigate this point, the intramolecular Buchner reaction[8] of diazo ketone **1** catalyzed by rhodium pivalate (0.2 μM) in methylene chloride (eq 2) was studied at a range of substrate concentrations (5−25 mM). The reaction progress could be easily followed at 340 nm, at which wavelength the product **2** has a much greater absorptivity ($\epsilon = 187\ \mathrm{M^{-1}\ cm^{-1}}$) than does the reactant ($\epsilon = 37\ \mathrm{M^{-1}\ cm^{-1}}$). A direct kinetic plot (v *versus* [S], supporting information) shows a hyperbolic form. An Eadie−Hofstee plot[9] (Figure 1) was used to determine the kinetic parameters $K_m = 15$ mM and $k_{cat} = 1100\ \mathrm{s^{-1}}$. Calculation of k_{cat}/K_m, the effective second-order rate constant for the reaction between the diazo compound and the catalyst, gives a value of $7.3 \times 10^4\ \mathrm{M^{-1}\ s^{-1}}$.

The saturation kinetic model was further supported by study of compounds **3** and **4**. They would be expected to show different kinetic constants if the carbon-carbon bond-forming process were rate limiting, in the first instance based on a more electron-rich aromatic ring and in the second case based on the *gem*-dialkyl effect, but in fact both show parameters essentially identical to those of **1**. For **3**, $K_m = 15$ mM and $k_{cat} = 1090\ \mathrm{s^{-1}}$. For **4**, $K_m = 13$ mM and $k_{cat} = 1170\ \mathrm{s^{-1}}$.



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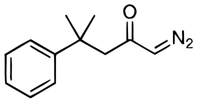

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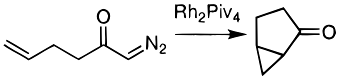
A second reaction where saturation kinetics were observed is shown in eq 3. In this case, the loss of the diazo ketone absorption of **5** (0.2 μM rhodium pivalate, methylene chloride) was followed spectrophotometrically at 370 nm. Kinetic analysis gave $K_m = 14$ mM, $k_{cat} = 1120\ \mathrm{s^{-1}}$, and $k_{cat}/K_m = 8.0 \times 10^4\ \mathrm{M^{-1}\ s^{-1}}$, also very close to the kinetic constants for **1**.



5 **6** (3)

An initial investigation of the influence of catalyst on the kinetics for **1** showed a parabolic direct plot when rhodium trichloroacetate was substituted for rhodium pivalate, suggesting substrate inhibition. Substrate concentrations >50 mM were therefore examined for rhodium pivalate-catalyzed reactions of **1** and **3**; the direct plots (Figure 2) are also parabolic. Compound **3** shows greater substrate inhibition than does **1**, suggesting competitive binding of the more electron-rich aromatic ring to the catalyst. Treatment of the data from these studies by the method of Dixon and Webb[10] gives substrate K_i values for **1** of 265 mM and for **3** of 96 mM.[11] More detailed investigation of the rhodium trichloroacetate-catalyzed decomposition of **1** showed $K_m = 1.0$ mM, $k_{cat} = 625\ \mathrm{s^{-1}}$, and $k_{cat}/K_m = 6.25 \times 10^5\ \mathrm{M^{-1}\ s^{-1}}$ from the linear portion of an Eadie−Hofstee plot (data not shown). The substrate K_i for this reaction is 10 mM.

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(11) Interestingly, **4** does not show substrate inhibition, evidently because of steric effects.

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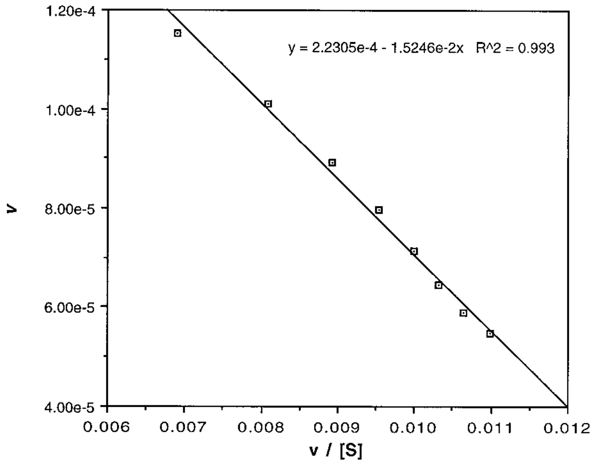


Figure 1. Eadie–Hofstee plot of the rate of decomposition of diazo ketone **1** by rhodium pivalate at low substrate concentration [5–25 mM].

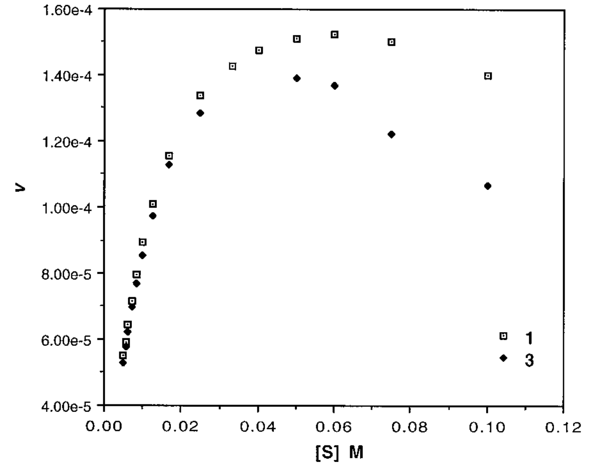


Figure 2. Direct plots of the velocity of the decomposition of diazo ketones **1** and **3** by rhodium pivalate at high substrate concentration [5–100 mM].

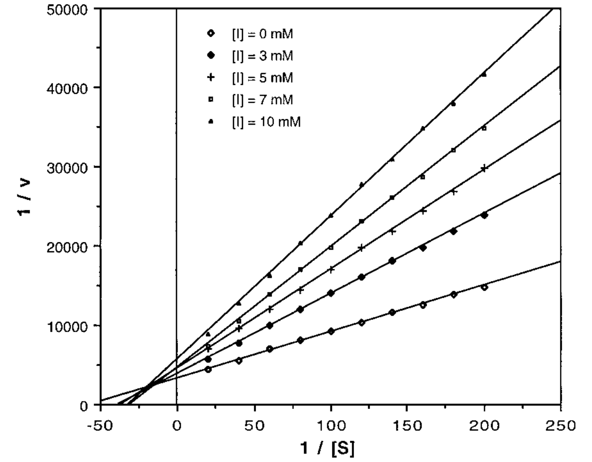
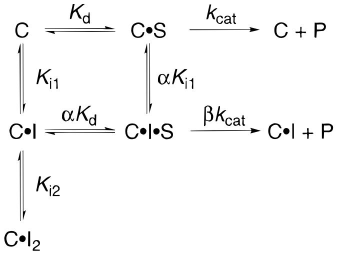


Figure 3. 3. Lineweaver–Burk plot of the inhibition by acetonitrile of the decomposition by rhodium pivalate of diazo ketone **1**.

These data regarding substrate inhibition suggested evaluation of other common rhodium ligands as inhibitors. Powerful ligands (imidazoles, phosphines, sulfides) would prohibit reaction, so the influence of a weaker ligand, acetonitrile, on the decomposition of **1** by rhodium pivalate at inhibitor concentrations of 3–10 mM was investigated (Figure 3). Graphic analysis indicates mixed inhibition, which is readily explained through Scheme 1, wherein C represents catalyst, S substrate, and I inhibitor. Analysis of the data according to this model gives $\alpha = 3$, $\beta = 0$, and $K_{i1} = 5$ mM. This kinetically-determined constant for acetonitrile binding to rhodium pivalate compares to a spectroscopically-determined value of 0.9 mM for the first acetonitrile binding to rhodium butyrate.[12] The magnitude of α suggests that the top line of Scheme 1 carries most of the flux at reasonable substrate concentrations since $\alpha K_{i1} = 15$ mM and $\alpha K_d = 36$ mM. On the basis of an analogy to the substrate inhibition with **3**, a second inhibitor, anisole, was investigated in the decomposition of **4** by rhodium pivalate, which is not subject to substrate inhibition. The anisole K_i is 107 mM, reasonably close to the substrate K_i for **3** of 96 mM.

Scheme 1



Because these dirhodium complexes have two open coordination sites, they might be thought to catalyze reactions at both sites simultaneously. That the second catalytic site becomes less efficient when a ligand is bound at the other site suggests that the conduct of carbenoid chemistry at one site would significantly retard catalysis at the other site. If only one site were to function at a time as described, these complexes could be considered to exhibit "half-of-the-sites" activity, an extreme example of negative cooperativity in the binding step.[13] Our data suggest that the kinetically most efficient pathway involves only one carbenoid ligand per dirhodium catalyst.

While saturation kinetics in other "conventional" organic catalytic processes are precedented,[14] our results do provide a simple new method for the study of reactions mediated by rhodium carboxylate salts. The lack of a dependence of the kinetic constants on diazo ketone structure suggests that the rate-determining step in these processes is generation of the rhodium carbenoid and that kinetic constants characteristic of each diazo compound–catalyst combination, but independent of the type of chemical reaction (C–H insertion, ylide formation, cyclopropanation, etc.), can be obtained.

Acknowledgment. M.C.P. was a Fellow of the John Simon Guggenheim Memorial Foundation. A.T.M. was a C. R. Hauser Fellow and an ACS Division of Organic Chemistry Upjohn Graduate Fellow.

Supporting Information Available: Additional kinetic plots (4 pages). See any current masthead page for ordering and Internet access instructions.

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