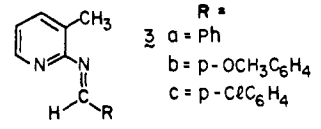
Activation of Aldehyde C–H Bonds to Oxidative Addition via Formation of 3-Methyl-2-aminopyridyl Aldimines and Related Compounds: Rhodium Based Catalytic Hydroacylation

Sir:

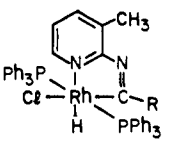
Hydroformylation, in which a synthetic equivalent of formaldehyde is added across an olefin by means of a transition metal catalyst to produce an aldehyde, is one of the most useful applications of transition metal organometallics to organic synthesis.[1] No corresponding process exists for hydroacylation, the addition of a generalized aldehyde to a simple olefin.[2] Recently we have shown that the acylrhodium hydride derived from 8-quinolinecarboxaldehyde (**1**) and $(PPh_3)_3RhCl$ will hydroacylate terminal olefins, giving linear 8-quinolinyl alkyl ketones.[3] We now report how a generalized aldehyde can be activated toward hydroacylation.

We wished to convert an aldehyde to a derivative in which, as in **1**, a 1,5- relationship would exist between a potentially coordinating group and the aldehyde C–H bond. In principle, 2-aminopyridyl aldimines should suffice; the reaction of 2-aminopyridine with aldehydes gives, however, only 1,1-diamines (aminals).[4] The desired aldimines can be obtained by heating the aminals above 100 °C; however, they are unstable compounds, being converted to the aminal and excess aldehyde with trace amounts of water. With the more hindered 3-methyl-2-aminopyridine (**2**),[5] the aldimines **3a–c** could be prepared in high yield from **2** and the corresponding aldehyde in THF at reflux in the presence of 3-Å molecular sieves.[6,7] This procedure fails for aldehydes with α hydrogens.

Three possible sites are available for metalation in **3**. The pyridyl nitrogen directs attack toward the imine C–H bond, while the imine nitrogen can facilitate metalation on the methyl group or at an ortho site of the aldehyde-derived aryl group. When the aldimines **3a–c** were heated in THF at 55 °C for



3 R = a: Ph; b: p-$OCH_3C_6H_4$; c: p-$C\ell C_6H_4$



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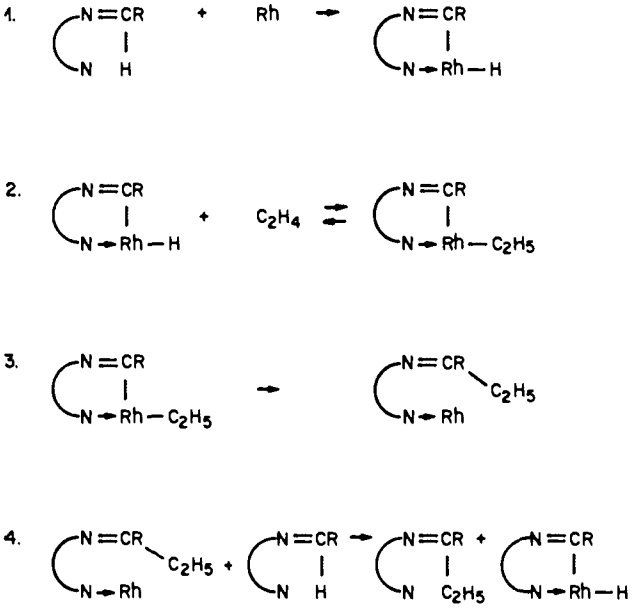
5–30 min with $(PPh_3)_3RhCl$, followed by addition of hexane, a single air-stable, yellow compound was isolated in >90% yield in each instance. Spectral and chemical (see below) data are consistent with these compounds being the desired iminoacylrhodium(III) hydrides **4a–c. 4a:** IR (KBr) 2025, 1590; NMR (CD_2Cl_2, 90 MHz, δ) −11.15 (1 H, overlapping d of t, J_{Rh-H} = 13, J_{P-H} = 12 Hz), 2.50 (3 H, s). Analogous spectral properties were found for **4b** and **4c**.[6] The imine C–H singlets at ca. δ 9 in **3a–c** are absent in **4a–c**.[8] Unexpectedly, 2-aminopyridyl aminals under the above conditions also give iminoacylrhodium(III) hydrides. Presumably, $(PPh_3)_3RhCl$ traps the small amount of aldimine in equilibrium with the aminal. From these adducts complexes derived from alkyl adehydes (including *n*-decanal and cyclohexanecarboxaldehyde) are available.

The use of these activated aldehydes in hydroacylation is shown by the reaction of **3a** and $(PPh_3)_3RhCl$ (5 mol %) in THF under an initial ethylene pressure of 150 psi in a stainless steel pressure vessel at 160 °C for 6 h. Upon hydrolysis of the reaction mixture over moist silica gel and bulb to bulb distillation, propiophenone was obtained in 45% yield (900% based on $(PPh_3)_3RhCl$).[9] Under the same conditions, ethylene was hydroacylated with the 2-aminopyridyl aminal of cyclohexanecarboxaldehyde, giving ethyl cyclohexyl ketone in 40% yield. The terminal olefin 1-octene gave, with **3a** and $(PPh_3)_3RhCl$ (5 mol %) at 160 °C in THF, *n*-octyl phenyl ketone in 10% yield. The ^1H NMR spectrum showed none of the branched chain isomer, under conditions where 10% of it would have been visible.

A likely mechanism for hydroacylation, which guided us in the design of this reaction, is given below. This mechanism is supported by the occurrence of a stochiometric hydroacylation reaction between iminoacylrhodium(III) hydrides and monosubstituted olefins under the conditions given above. In particular, reaction of **4a** with ethylene (initial pressure 150 psi) for 2 h at 170 °C gives (after treatment of the reaction mixture with CO to precipitate the rhodium as $(PPh_3)_2Rh(CO)Cl$ and hydrolysis of the ketimine with wet silica gel) propiophenone in 80% isolated yield.



Hydroacylation thus provides a new connective ketone synthesis from readily available precursors. It illustrates the potential of the cyclometalation reaction,[10] and conceptually related strategies, in organic synthesis.

Acknowledgment is made to M. L. Schilling for obtaining NMR spectra and A. P. Ginsberg for making available certain facilities.

References and Notes

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(2) Symmetrical ketones can be made the major product in hydroformylation reactions.[1] Some other approaches to hydroacylation include: M. P. Cooke, Jr., and R. M. Parlman, *J. Am. Chem. Soc.*, **97**, 6863 (1975); J. Schwartz and J. B. Cannon, *ibid.*, **96**, 4721 (1974); H. Stetter and H. Kuhlmann, *Tetrahedron Lett.*, 4505 (1974); I. Fleming and A. Pearce, *J. Chem. Soc., Chem. Commun.*, 633 (1975).
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(4) A. Kirpnal and E. Reiter, *Chem. Ber.*, **60**, 664 (1927); R. Tiollais, G. Bouget, and H. Bouget, *C. R. Hebd. Seances Acad. Sci.*, **254**, 2597 (1962).
(5) Aldrich Chemical Co., Milwaukee, Wis.
(6) All new compounds gave satisfactory combustion analysis (C, H, N).
(7) As is usual for aldimines, only one isomer was detected. This is assumed to be the anti isomer: C. G. McCarty, "The Chemistry of the Carbon-Nitrogen Double Bond", S. Patai, Ed., Wiley, London, New York, 1970, p 363.
(8) The stereochemistry shown is suggested by analogy to recently prepared compounds[3] and the fairly low Rh–Cl stretching frequency (255 cm^{-1}).
(9) No reaction takes place in the absence of $(PPh_3)_3RhCl$.
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