Ruthenium Alkoxycarbene Complexes from an Acetal Function by C−O Bond Cleavage and Alcohol Elimination

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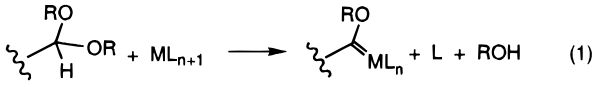
Received April 26, 1996[⊗]

*Summary: Heating solutions of acetal complexes {CpRu(CH₃CN)₂[η¹-P-2-(Ph₂P)[CH(OR)₂]C₆H₄]}OTf (**3**; R = Me, Et) at 60−95 °C results in loss of one CH₃CN ligand and the alcohol ROH, with concomitant formation of carbene complexes CpRu(CH₃CN)[η²-C,P-2-(Ph₂P)[C(OR)]-C₆H₄]}OTf (**4**) in high yield. Kinetic and reactivity studies suggest that the rate-determining step of the conversion of **3** to **4** is oxidative addition of an acetal C−O bond to the ruthenium center, which occurs under neutral, mild conditions.*

Metal−carbene complexes are exceedingly versatile stoichiometric reagents in organic synthesis[1] and highly active catalysts for alkene metathesis.[2] A common preparation of late transition metal carbene complexes relies on a combination of strongly basic, nucleophilic, and electrophilic reagents with a metal carbonyl[1,3] or on the action of metal complexes on reactive groups such as cyclopropenes[2,4] or diazo compounds,[5] both of which are of limited accessibility. Because acetals are stable compounds,[6] easily made from widely available carbonyl compounds, we examined a new reaction for aldehyde acetals, summarized in eq 1. This metal-induced net



(1)

β-elimination of an alcohol is a new route to an alkoxycarbene complex.[7] The closest precedents might be net α-elimination of H_2 from ethers (double C−H activation)[8a−d] or net elimination of Me_2NH from an aminal on an osmium cluster,[8e] in mechanistically uncharacterized processes. Here, we report that eq 1 has been realized in what has the characteristics of a C−O bond activation process, leading to ruthenium carbene complexes **4**. In preliminary studies, the carbene complex **4a** shows intriguing ability to isomerize allylic alcohols to saturated aldehydes.

On the basis of the known stability of CpRu alkoxycarbene complexes to boiling alcohols,[9] the conversion of **3** to **4** (Scheme 1) was chosen for initial study. Benzaldehyde acetals with a 2-diphenylphosphino substituent (**1**) were synthesized by adapting known methods.[10] The ruthenium component **2** was prepared in 82% yield by a modification of the published method for the PF_6^- salt.[11] Addition of **1** to **2** in $CDCl_3$ resulted in the immediate formation of **3**,[12,13] which could be isolated in ≥90% yield but was usually used directly in subsequent reactions. Heating a solution of **3** in $CDCl_3$ at 60 °C for 3 h (**3a**) or 1 d (**3b**) led to carbene complex **4**,[14] CH_3CN, and ROH, all in ≥90% yield as determined by NMR integration; **4** was isolated as air-stable red solid in ≥78% yield after chromatography over SiO_2 using CH_2Cl_2−CH_3CN mixtures and recrystallization from CH_2Cl_2−Et_2O. The formation of a carbene ligand in **4** was indicated by a downfield doublet in ^{13}C NMR spectra:[15] for **4a** and **4b**, δ 300.25 (d, J = 7.6 Hz) and 297.34 ppm (d, J = 7.6 Hz), respectively. Other spectral changes accompanying the transformation of **3a** to **4a**

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1996.

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(11) (a) Gill, T. P.; Mann, K. R. *Organometallics* **1982**, *1*, 485−488. (b) In the photolysis of [CpRu(benzene)]$^+$TfO$^-$ in CH_3CN used to make **2**,[11a,12] it was found that careful monitoring of the reaction was required to minimize formation of $Ru(CH_3CN)_6^{2+}(TfO^-)_2$.[11c] (c) Rapaport, I.; Helm, L.; Merbach, A. E.; Bernhard, P.; Ludi, A. *Inorg. Chem.* **1988**, *27*, 873−879.

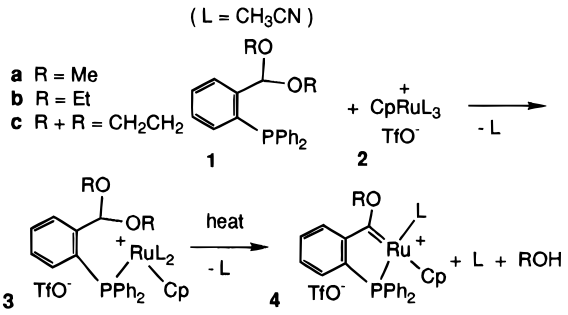
(12) Experimental procedures and spectral data not mentioned in the text or footnotes, derivations of rate laws, and kinetic traces appear as Supporting Information. All compounds were characterized by ^1H, ^{13}C, $^{31}P\{^1H\}$ NMR, IR and (with the exception of **3**) elemental analysis.

(13) Partial data[12] for **3a**: $^{31}P\{^1H\}$ NMR (161.9 MHz, $CDCl_3$) δ 46.30. Data for **3b**: ^1H NMR (400 MHz, $CDCl_3$) δ 5.63 (s, 1H), 4.33 (s, 5H, Cp), 3.27 [quintet, J = 7.6 ($^2J_{HH} = {}^3J_{HH}$), 2H], 2.84 [quintet, J = 7.4 ($^2J_{HH} = {}^3J_{HH}$), 2H], 2.13 (s, 6H, CH_3CN), 0.93 (t, J = 7.6, 6H); $^{31}P\{^1H\}$ NMR (161.9 MHz, $CDCl_3$) δ 46.44.

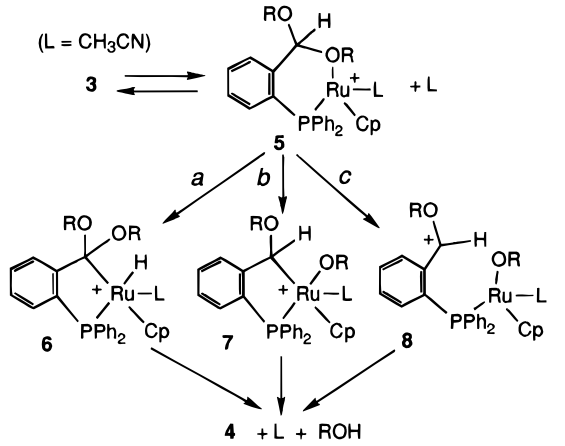
(14) Additional data[12] for **4a**: $^{31}P\{^1H\}$ NMR (161.9 MHz, $CDCl_3$) δ 76.38. Partial data for **4b**: ^1H NMR (400 MHz, $CDCl_3$) δ 5.32 (qd, J = 7.0, 10.6, 1H), 5.01 (qd, J = 7.0, 10.6, 1H), 4.88 (s, 5H), 1.86 (s, 3H), 1.71 (t, J = 7.0, 3H); $^{31}P\{^1H\}$ NMR (161.9 MHz, $CDCl_3$) δ 76.97; correct analyses for C, H, N, and S.

S0276-7333(96)00317-2 CCC: $12.00

Scheme 1



Scheme 2



included downfield shifts of the signals for the Cp protons (from δ 4.36 to 4.89) and -OCH_3 protons (from 3.00 to 4.84 ppm). The presence of a CH_3CN ligand was shown by a three-proton singlet at δ 1.84 ppm in the ^1H NMR spectrum, by weak IR absorption at 2284 cm^{-1},[16] and by correct combustion analysis for C, H, N, and S. Homolog **4b** exhibited similar spectral features, with diastereotopic methylene protons on the ethoxy group.[14]

Three mechanisms for the formation of **4** were considered (Scheme 2). All begin with coordination of an oxygen to the metal, giving **5**, although direct conversion of **3** to **6**, **7**, or **8** is also imaginable. Mechanism *a* would give **6** by oxidative addition of the methine C−H bond to the ruthenium center[17] and **4** by subsequent elimination of ROH.[18] Alternatively, in mechanism *b*, oxidative addition of the C−O bond[19] would produce **7**, which would lose ROH to form the metal−carbene bond. In the final mechanism *c*, the metal in **5** would act as Lewis acid, facilitating formation of a carbocation (**8**), which would transfer a proton[20] to the ruthenium-bound alkoxide to give **4** and ROH.

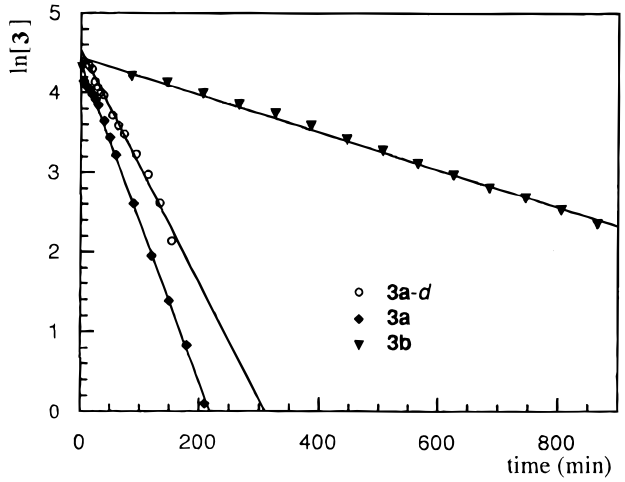


Figure 1. Rate plot for reaction of **3** generated from **1** and **2** in $CDCl_3$, 60 °C. The concentration of **3** is represented by signal integration (^1H NMR) in arbitrary units. For each data point, a single transient was acquired with a pulse width of 90°, acquisition time <3 s, with $d_1 > 5T_1$. Reactions were followed for at least 3 half-lives. For **3a**, $k = 1.9933 (\pm 0.0763) \times 10^{-2}$ min^{-1} ($R^2 = 0.998$); for **3a**-d_1, $k = 1.4654 (\pm 0.1148) \times 10^{-2}$ min^{-1} ($R^2 = 0.992$); for **3b**, $k = 2.3583 (\pm 0.1311) \times 10^{-3}$ min^{-1} ($R^2 = 0.995$). All deviations are expressed at the 99% confidence level.

A series of kinetic and other experiments were performed to shed light on the mechanism of the new transformation. Solutions of **3a** in $CDCl_3$[21] were monitored by ^1H NMR spectroscopy. At 60 °C, resonances for species other than **3a**, **4a**, CH_3CN, or CH_3OH were not detected. Because **2** undergoes CH_3CN exchange by a dissociative pathway,[22] and because equilibrium between added CD_3CN (10 equiv) and bound CH_3CN in **3a** was reached within 80 s at room temperature, we propose that CH_3CN loss from **3a** is more facile than conversion to **4a**, which requires several hours at 60 °C for completion. If the first step toward **4** is a rapid equilibrium between **3** and **5**, lying on the side of **3**,[23] before the rate-determining step, the rate law for disappearance of **3** should be first-order in **3**.[12] For all complexes examined this was shown to be the case over at least 3 half-lives (Figure 1).[12] If mechanism *a* were

(15) Leading references: Gamasa, M. P.; Gimeno, J.; Martín-Vaca, B. M.; Borge, J.; García-Granda, S.; Perez-Carreño, E. *Organometallics* **1994**, *13*, 4045−4057. Pilette, D.; Ouzzine, K.; Le Bozec, H.; Dixneuf, P. H.; Rickard, C. E. F.; Roper, W. R. *Organometallics* **1992**, *11*, 809−817.

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(17) C-H activations of alkanes and arenes: Jones, W. D.; Feher, F. J. *Acc. Chem. Res.* **1989**, *22*, 91−100. Crabtree, R. H.; Hamilton, D. G. *Adv. Organomet. Chem.* **1988**, *28*, 299−338. Ryabov, A. D. *Chem. Rev.* **1990**, *90*, 403−424.

(18) Treatment of α-alkoxyalkyl complexes with acid or other electrophiles can lead to carbene complexes with loss of the alkoxy group: Jolly, P. W.; Pettit, R. *J. Am. Chem. Soc.* **1966**, *88*, 5044−5055. Review: Brookhart, M.; Studabaker, W. B. *Chem. Rev.* **1987**, *87*, 411−432.

(19) This is apparently unknown for acetals: Yamamoto, A. *Adv. Organomet. Chem.* **1992**, *34*, 111−147.

(20) Deprotonation of dialkoxycarbonium ions by hindered amines: Olofson, R. A.; Walinsky, S. W.; Marino, J. P.; Jernow, J. L. *J. Am. Chem. Soc.* **1968**, *90*, 6554−6555. See also ref 7.

(21) Purification of $CDCl_3$ was effected by initial distillation from K_2CO_3 and subsequent redistillation from P_4O_{10} onto K_2CO_3 for storage in the dark in a glovebox. Addition of HOTf (ca. 0.1 equiv) or Me_3SiOTf (ca. 0.1 equiv) to reactions of **3a** led to faster but considerably messier reactions, and the non-coordinating base 2,4,6-tris(*tert*-butyl)pyridine (1 equiv) had little effect on the rate. The negligible influence of added base shows that traces of acidic impurities are not responsible for the reactions described.

(22) Luginbühl, W.; Zbinden, P.; Pittet, P. A.; Armbruster, T.; Bürgi, H.-B.; Merbach, A. E.; Ludi, A. *Inorg. Chem.* **1991**, *30*, 2350−2355.

(23) Heating a solution of **3c** prepared *in situ* from **1c** and **2** (60 °C, 24 h) leads to a mixture containing **3c** (25%) and a new, chromatographically unstable product (32%) with at least one stereogenic center, as revealed by the number of signals for the CH_2CH_2 bridge (four one-proton multiplets between δ 3.2 and 4.0). On the basis of the unexceptional chemical shift of an associated one-proton singlet (5.28 ppm), **6c** is ruled out, leaving tentative formulation as **7c** or **8c**. Decomposition ensues on further heating. Additional data for the intermediate: $^{31}P\{^1H\}$ NMR δ 39.41 ppm. Dissolution of **2** and (2-(methoxymethyl)phenyl)diphenylphosphine, an ether analog of **1a**, in $CDCl_3$ gives the corresponding η^1-*P*-monophosphine complex and CH_3CN, a mixture which shows no sign of forming a η^2-(*O*,*P*)-chelate and a second mole of CH_3CN on heating at 60 °C for several days.

responsible for the formation of **4**, a substantial primary isotope effect might be observed if conversion of **5** to **6** was rate-determining. However, the isotopomer of **3a** featuring a deuterium at the acetal methine site (**3a**-*d*) was used to determine $k_H/k_D = 1.36(16)$. This observed isotope effect is at the lower end of the range of reported values for primary isotope effects in C−H activation processes;[24] alternatively, the isotope effect is at the upper end of values reported for secondary isotope effects in acid-catalyzed acetal hydrolysis, considered to be a model for mechanism *c*, **5** → **8**.[25] A value for the secondary isotope effect in C−O bond activation (mechanism *b*) could not be found for comparison.

To probe the role of charge dispersal during the reaction course, **3a** was heated in CD_3NO_2, a polar yet nondonating solvent.[26] The resulting profound reduction in reaction rate required elevating the temperature by 35 °C to achieve a rate similar to that seen in $CDCl_3$. Although this result must be interpreted with caution, it seems inconsistent with the localization of charge presumed to accompany conversion of **5** to **8**. Furthermore, the ratio of observed rate constants $k_{3a}/k_{3b} = 8.5$-(8) shows a pronounced steric effect on conversion to **4**, which seems too large to be accommodated by a rate-determining C−H bond activation.[27] Taken together, the available evidence seems most consistent with approach of the ruthenium center to the C−O bond as the key step (mechanism *b*, **5** → **7**), which would represent a new reaction for acetals.

To our knowledge, **4** is the first CpRu−carbene complex with a potentially labile CH_3CN ligand.[9,15] Preliminary studies of the reactivity of **4a** show that the acetonitrile ligand is displaced by PMe_3 ($CDCl_3$, room temperature, 3 h; 91% yield).[28] Surprisingly, however, cationic complex **4a** was inert to either O-demethylation[29] or ligand substitution by NaI in CD_3NO_2 (60 °C, 3 d). Exchange of the carbene OCH_3 substituent for OCD_3 by heating with CD_3OD (ca. 1 equiv in $CDCl_3$ or as solvent, 60 °C, 12 h) did not occur, but **4a** catalyzes the isomerization of prop-2-en-1-ol to propanal at room temperature, a reaction which we are investigating further.

This work establishes the first transformation of an acetal to an alkoxycarbene complex. Future and ongoing explorations involve the extension of this chemistry to other aldehyde derivatives and the applications of the resulting chiral carbene complexes.

Acknowledgment. We thank Engelhard Corp. for a generous gift of $RuCl_3$. Dr. Ron Nieman and Camil Joubran assisted with NMR kinetics experiments.

Supporting Information Available: Text giving spectral data, preparations of 12 compounds, and derivations of kinetic equations and rate plots (23 pages). Ordering information is given on any current masthead page.

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(24) Low isotope effects in C-H bond activation processes have been attributed to nonlinear hydrogen transfer or an early transition state; see ref 17.

(25) Shiner, V. J., Jr. In *Isotope Effects in Chemical Reactions*; Collins, C. J., Bowman, N. S., Eds.; Litton Educational Publishing: New York, 1970; pp 135−136. See also: *Reaction Rates of Isotopic Molecules*; Melander, L., Saunders, W. H., Jr., Eds.; Wiley: New York, 1980; pp 172−174.

(26) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: Weinheim, Germany, 1988.

(27) For example, kinetic selectivities of Cp*M(PMe_3) (M = Rh, Ir) for primary C-H bonds of propane and hexane are the same within a factor of 2: Jones, W. D. In *Activation and Functionalization of Alkanes*; Hill, C. L., Ed.; Wiley: New York, 1989.

(28) Partial data for **4** (L = PMe_3, R = Me): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (s, 5H), 4.59 (s, 3H), 0.82 (d, J = 10.0 (J_{PH}), 9H); ^{13}C NMR ($CDCl_3$) δ 290.43 (dd, J = 7.9, 15.8, Ru=*C*); ^{31}P{^{1}H} NMR (161.9 MHz, $CDCl_3$) δ 77.35 (d, J = 35.0), 8.24 (d, J = 35.0, *P*Me_3).

(29) Davison, A.; Reger, D. L. *J. Am. Chem. Soc.* **1972**, *94*, 9237−9238.