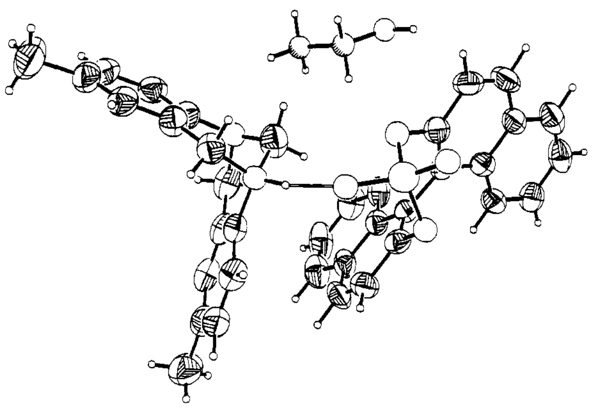

Figure 1. Thermal ellipsoid plot of the (+)-1·(−)-2 salt (3) molecular structure.

toward chiral alcohols. Comparison of ^1H NMR spectra of racemic alcohols 4–8 run alone in $CDCl_3$ with spectra of these alcohols run in the presence (+)-1 led to the observation of anisochrony of at least one set of peaks in the case of five alcohols, all containing at least one phenyl group, at room temperature (Table I). Enantiopure 1 generates intrinsically nonidentical chemical shifts in some of the sensor nuclei of the diastereomeric association complexes formed between the CSA and the alcohol enantiomers. In addition, enantiopure 1 may exhibit stronger nonbonded interaction with one of the enantiomers of each of these alcohols than with the other *in solution*, i.e., the equilibrium constants for formation of the diastereomeric complexes may be unequal.[18] Under appropriate conditions, enantiopure 1 may serve in the determination of the enantiomer purity of such alcohols. Our results are comparable to and complementary with those observed when quinine is used as CSA.[19]

The availability of nice crystals of salt **3** [(+)-**1**·(−)-**2**][20] made it possible for us to undertake an X-ray structural analysis (Figure 1) and to determine independently the absolute configuration of Tröger's base.[21] Since the absolute configuration of acid (−)-2 is known to be *R*,[22] the latter being the configuration shown in the figure, the configuration of (+)-1 in the crystal was established relative to that of (−)-2 as being 5*S*,11*S*. This experimental finding is inconsistent with the configurational assignment 5*R*,11*R*-(+) based on exciton chirality (coupled oscillators) calculation.[4a] The incontrovertible assignment based on crystallography requires that the configuration of Tröger's base that has been cited in the literature since 1967 must be reversed.

The crystal structure determination of salt **3** has also established that the binaphthyl phosphate and protonated TB counterions are hydrogen bonded and that interaction between these ions appears to take place from the top of the TB molecule.

Acknowledgment. This work was supported at CUNY in part by grants from the Professional Staff Congress/CUNY Research Award Program of the City University of New York and from the City College Faculty Senate Research and Publications Committee. The work at Brown University was supported in part by NIH Grants GM-35982 and CA-01330. The X-ray equipment was purchased with an instrument grant from the NSF (CHE-8206423).

Supplementary Material Available: Representative DSC traces of (+)-1, (±)-1, and mixtures of (+)-1 and (−)-1; fusion phase diagram of (+)-1/(−)-1 mixtures; ^1H NMR spectra illustrating application of (+)-1 as a chiral solvating agent; and tables of atomic coordinates and temperature factors, bond lengths and angles, anisotropic thermal parameters, hydrogen coordinates and thermal parameters and torsion angles along with a labeled plot of the crystallographic, asymmetric unit for compound **3** (14 pages). Ordering information is given on any current masthead page.

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[17] Reviews on chiral solvating agents: (a) Pirkle, W. H.; Hoover, D. J. *Top. Stereochem.* **1982**, *13*, 263–331. (b) Weisman, G. R. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1983; Vol. 1, Chapter 8.

[18] (a) Kabachnik, M. I.; Mastryukova, T. A.; Fedin, E. I.; Vaisberg, M. S.; Morozov, L. L.; Petrovskii, P. V.; Shipov, A. E. *Tetrahedron* **1976**, *32*, 1719–1728. (b) Reference 17a, pp 267–68.

[19] Rosini, C.; Uccello-Barretta, G.; Pini, D.; Abete, C.; Salvadori, P. *J. Org. Chem.* **1988**, *53*, 4579–4581.

[20] Salt **3**, mp 161–62 °C, $[\alpha]^{25}{}_{589}$ −336.6° (*c* 1.065, CH_3OH), analyzed as follows: calculated for $C_{39}H_{37}N_2O_5P$ $[(C_{17}H_{18}N_2)\cdot(C_{20}H_{13}O_4P)\cdot(C_2H_5OH]$, 72.65% C, 5.79% H, 4.35% N, 4.80% P; found, 72.31% C, 5.95% H, 4.29% N, 4.76% P.

[21] Salt **3** [(+)-**1**·(−)-**2**] crystallized in the noncentrosymmetric, orthorhombic, space group $P2_12_12_1$. The unit cell parameters were determined to be $a = 10.432$ (3) Å, $b = 16.164$ (3) Å, and $c = 19.879$ (4) Å based upon least-squares fitting of 25 reflections in the range $24° < 2\theta < 26°$. The unit cell contains four asymmetric units of molecular formula $[(C_{17}H_{18}N_2)\cdot(C_{20}H_{13}O_4P)\cdot(C_2H_5OH)]$ in a volume of 3351.9 (1.2) Å^3 which produces a calculated density of 1.28 g/cm^3. A total of 2857 reflections were recorded in the range $3.5° < 2\theta < 47°$ with a Nicolet $R3_m/E$ crystallographic system using the θ–2θ scan routine and graphite monochromated Mo Kα radiation ($\lambda = 0.71069$ Å). After Lorentz and polarization corrections and an absorption correction based upon a crystal measurement (0.3 mm × 0.3 mm × 0.6 mm), the structure was solved by the SHELXTL 5.1 programs. All non-hydrogens were refined anisotropically except the terminal carbon of the somewhat disordered ethanol molecule. The approximate location of all hydrogen atoms was determined by Fourier difference synthesis. In the final stages of refinement the hydrogen atoms were placed in calculated positions and allowed to ride with the atom to which they are attached. The final agreement factors are $R = 0.056$ and $R_w = 0.058$ for 2407 unique, observed reflections $[F_o > 3\sigma(F_o)]$ and 421 independent variables.

[22] Jacques, J.; Fouquey, C.; Viterbo, R. *Tetrahedron Lett.* **1971**, 4617–4620.

Ruthenium-Catalyzed Allylation of Primary Alcohols by Allylic Acetates: A Novel Synthesis of α,β-Unsaturated Ketones

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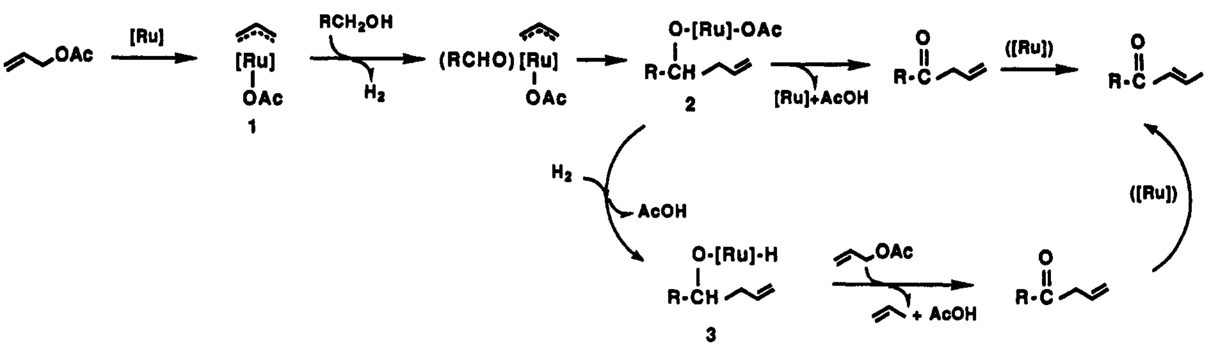
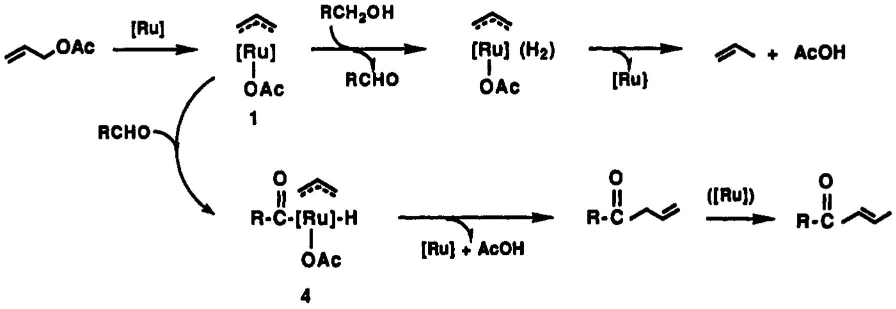
Summary: Certain ruthenium complexes show high catalytic activity in the synthesis of α,β-unsaturated ketones from primary alcohols and allylic acetates. Here, π-allylruthenium intermediates apparently operate as nucleophiles rather than as electrophiles.

Among the carbon–carbon bond forming reactions promoted by transition-metal complexes, allylic alkylations, especially those catalyzed by palladium complexes, have been extensively studied and have been successfully applied in organic synthesis.[1] In contrast, comparatively

Scheme I

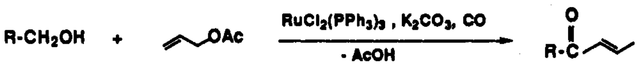


Scheme II



little is known about alkylation reactions involving π-allylruthenium intermediates, despite the current interest in the synthesis of π-allylruthenium complexes.[2]

In the course of studies of catalysis by ruthenium complexes,[3] we found that π-allylruthenium intermediates act as nucleophiles rather than as electrophiles in reactions with aldehydes to give homoallylic alcohols.[4] This reactivity is quite different from that of π-allylpalladium complexes which generally act as electrophiles.[5] Because many biologically important natural products possess an enone functionality, and because the synthesis of such compounds has been the target of much effort over the last decade,[6] we attempted to apply ruthenium catalysis to the synthesis of enones. Therefore, in this paper, we describe a novel synthesis of α,β-unsaturated ketones from primary alcohols and allylic acetates via π-allylruthenium intermediates (eq 1).



(1)

As the examples in Table I show, primary alcohols reacted with allylic acetates to give the corresponding α,β-unsaturated ketones, generally in good yield.[7] Because both but-3-en-2-yl acetate and (*E*)-but-2-en-1-yl acetate gave the same products (runs 4 and 5), the allylation reaction must proceed via a common π-allylruthenium intermediate. Addition occurred regioselectively at the more substituted carbon atom of the π-allyl ligand. This same phenomenon was also observed in earlier work.[4]

In the allylation of 1-hexanol with allyl acetate, the α,β-unsaturated ketone was obtained in 75% yield (run 8). 2-Hexanol was only dehydrogenated, to afford 2-hexanone, in quantitative yield. Furthermore, *tert*-amyl alcohol was unreactive. Therefore, the reaction appeared to be chemoselective for primary alcohols.

As for the catalyst, both zero valent and divalent ruthenium complexes, such as $RuCl_2(PPh_3)_3$, $Ru(CO)_3(PPh_3)_2$, and $Ru(OAc)_2(CO)_2(PPh_3)_2$, showed high activity (runs 1–3). Other ruthenium–triphenylphosphine catalysts, such as $RuH_2(PPh_3)_4$, $RuCl_3{\cdot}nH_2O$–$3PPh_3$, Ru$_3$-

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(1) For a review, see: (a) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385. (b) Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: New York, 1980. (c) Trost, B. M.; Verhoeven, T. R. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: New York, 1982; Vol. 8, p 799. (d) Heck, R. F. *Palladium Reagents in Organic Syntheses*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Academic Press: London, 1985; Chapter 5, p 117.

(2) (a) Bennet, M. A.; Bruce, M. I.; Matheson, T. W. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: New York, 1982; Vol. 4, p 691. (b) Wuu, Y.-M.; Wrigton, M. S. *Organometallics* **1988**, *7*, 1839. (c) Nagashima, H.; Mukai, K.; Shiota, Y.; Ara, K.-I.; Itoh, K.; Suzuki, H.; Oshima, N.; Moro-oka, Y. *Organometallics* **1985**, *4*, 1314.

(3) (a) Watanabe, Y.; Tsuji, Y.; Ige, H.; Ohsugi, Y.; Ohta, T. *J. Org. Chem.* **1984**, *49*, 3359. (b) Tsuji, Y.; Kotachi, S.; Huh, K.-T.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 580. (c) Kondo, T.; Akazome, M.; Tsuji, Y.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 1286.

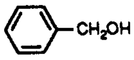
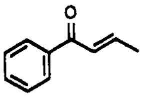
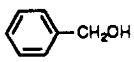
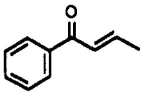
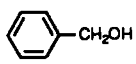
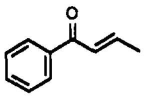
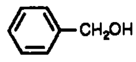
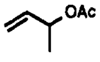
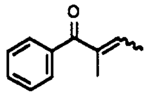
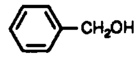
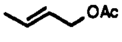
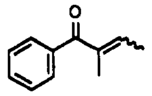
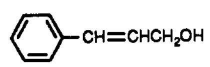
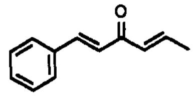
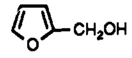
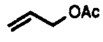
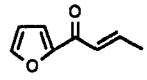
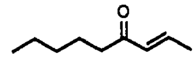
(4) Tsuji, Y.; Mukai, T.; Kondo, T.; Watanabe, Y. *J. Organomet. Chem.* **1989**, *369*, C51.

(5) In the palladium-catalyzed allylation of aldehydes, it is necessary to add other reagents to effect "Umpolung" of the electrophilic π-allylpalladium intermediate. See: (a) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 601. (b) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 1195. (c) Masuyama, Y.; Hayashi, R.; Otake, K.; Kurusu, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 44. (d) Masuyama, Y.; Takahara, J. P.; Kurusu, Y. *J. Am. Chem. Soc.* **1988**, *110*, 4473.

(6) Thebtaranonth, C.; Thebtaranonth, Y. *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Chichester, 1989; Chapter 7, p 199.

(7) **General Procedure**. A mixture of alcohol (4.0 mmol), allylic acetate (20 mmol), K_2CO_3 (10 mmol), Ru catalyst (0.10 mmol), and THF (8.0 mL) was placed in a 50-mL stainless steel autoclave (Yuasa Giken SUS 316) equipped with a glass liner and a magnetic stirring bar. The unit was sealed and purged of air by pressurization with carbon monoxide to 10 kg cm^{-2}, and then depressurization to atmospheric pressure. This pressurization–depressurization cycle was repeated twice. The reactor was then again pressurized to 10 kg cm^{-2} with carbon monoxide at room temperature, and was heated to 150 °C over 10 min, with stirring. The stirred mixture was held at this temperature for 12 h. The reaction was then quenched by rapid cooling, and the gaseous products were allowed to escape. The yellow solution that resulted was analyzed by GLC and FT-IR. The products were isolated by medium-pressure column chromatography on silica gel or aluminum oxide (hexane/ethyl acetate) and Kugelrohr distillation.

Table I. Ruthenium-Catalyzed Synthesis of α,β-Unsaturated Ketones from Primary Alcohols and Allylic Acetates[a]

run	alcohol	allylic acetate	catalyst	product	yield (%)[b]
1			$RuCl_2(PPh_3)_3$		60 (80)
2			$Ru(CO)_3(PPh_3)_2$		(76)
3			$Ru(OAc)_2(CO)_2(PPh_3)_2$		(77)
4[c]			$RuCl_2(PPh_3)_3$		81 (*E*:*Z* = 15:85)
5[c]			$RuCl_2(PPh_3)_3$		53 (*E*:*Z* = 13:87)
6			$RuCl_2(PPh_3)_3$		27
7			$RuCl_2(PPh_3)_3$		40
8[d]			$RuCl_2(PPh_3)_3$		58 (75)

[a] A mixture of alcohol (4.0 mmol), allylic acetate (20 mmol), K_2CO_3 (10 mmol), catalyst (0.10 mmol), and THF (8.0 mL) was heated at 150 °C for 12 h under pressure (initially 10 kg cm^{-2} of carbon monoxide at room temperature). [b] Isolated yield based on alcohol. Numbers in parentheses are yields determined by GLC analysis. [c] Reaction temperature = 180 °C. [d] Reaction temperature = 160 °C.

$(CO)_{12}$–$6PPh_3$ also showed good catalytic activity. However, when either $Ru_3(CO)_{12}$ or $RuCl_3 \cdot nH_2O$ was employed in the absence of a phosphine ligand, the yields of α,β-unsaturated ketones were dramatically reduced. No matter what catalyst was employed, the same yellow complex[8] was always isolated from the reaction mixture by medium-pressure column chromatography. Also, the presence of carbon monoxide under pressure was essential for catalytic activity. With argon, only dehydrogenation of the alcohol to the aldehyde occurred.[9] It is believed that carbon monoxide aids in the generation and stabilization of an active, low-valent ruthenium carbonylphosphine species.

A tentative catalytic cycle is shown in Scheme I.[10] Thus, oxidative addition of allylic acetate to the ruthenium complex could afford a π-allylruthenium acetate intermediate (1). Dehydrogenation of the alcohol by 1 to the corresponding aldehyde then occurs,[3a] and 1 is inserted to give an alkoxyruthenium acetate intermediate (2). There then exist two possible pathways to the α,β-unsaturated ketone from 2. One pathway involves β-hydride elimination from 2 to give the β,γ-unsaturated ketone, which then isomerizes to the α,β-unsaturated ketone.[11] Another possible route is hydrogenolysis of 2 to a hydrido alkoxyruthenium intermediate (3), which is subsequently dehydrogenated by allyl acetate and K_2CO_3 to the β,γ-unsaturated ketone, together with propene and acetic acid.[12] The possible existence of such a pathway was suggested by the results of the analysis of the gases evolved during the reaction. For example, in the reaction of benzyl alcohol with allyl acetate (run 1), propene (58% yield, based on benzyl alcohol) was detected.[13]

Further studies of the mechanism and attempts to apply the reaction to organic synthesis are in progress.

Acknowledgment. The financial support of Asahi Glass Foundation is gratefully acknowledged.

Supplementary Material Available: Analytical data for all products and a general experimental procedure (3 pages). Ordering information is given on any current masthead page.

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[8] "Yellow complex": IR (KBr) 2020, 1977, 1946 cm^{-1} (ν_{CO}), 1570, 1473 cm^{-1} ($\nu_{acetate}$); ^1H NMR (CD_2Cl_2, 270 MHz) δ 1.71 (s, 3 H, CH_3), 7.38–7.53 (m, 15 H, phenyl H); ^{13}C NMR (CD_2Cl_2, 67.8 MHz) δ 23.5 (q, CH_3), 128.4, 128.5, 128.6, 130.1, 133.3 (d, phenyl C), 133.5 (s, phenyl C), 134.1, 134.2, 134.3 (d, phenyl C), 186.5 (s, $OCOCH_3$), 206.0 (s, C=O).

[9] When benzyl alcohol was treated with allyl acetate and catalyst under an argon atmosphere, only benzaldehyde (67% yield) was obtained.

[10] The reviewers have suggested the possibility of reductive coupling of the π-allyl and the acyl groups in a hydrido acyl π-allylruthenium acetate intermediate. A reaction mechanism based on this suggestion is depicted in Scheme II. The generation of a π-allylruthenium acetate intermediate (1) is similar to that shown in Scheme I. Subsequent hydride abstraction from the alcohol by the metal would yield the aldehyde and a dihydrido or hydrogen π-allylruthenium acetate intermediate, which would then undergo reductive elimination to yield propene and acetic acid, with regeneration of the active ruthenium intermediate. This reaction could be repeated until most of the alcohol was dehydrogenated to the aldehyde. Intermediate 1 could then begin to react with the aldehyde to give a hydrido acyl π-allylruthenium intermediate (4), which could be generated by oxidative addition of the acyl C–H bond of the aldehyde to 1.[3c] Reductive coupling of the π-allyl and the acyl groups of 4 would give the enone products and acetic acid. Given the facts available, this mechanism cannot be excluded completely. Further study is obviously required to completely elucidate the mechanism.

[11] Pollack, R. M.; Bounds, P. L.; Bevins, C. L. *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Chichester, 1989; Chapter 13, p 559.

[12] 1-Phenyl-3-buten-1-ol was in fact converted to (*E*)-1-phenyl-2-buten-1-one by treatment with allyl acetate and K_2CO_3. In the absence of allyl acetate and K_2CO_3, dehydrogenation and isomerization did not occur.

[13] Propyl acetate, the product of hydrogenation of the carbon–carbon double bond of allyl acetate, was not obtained.