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Ruthenium Complex-Catalyzed *anti*-Markovnikov Hydration of Terminal Alkynes

Toshiaki Suzuki,[†] Makoto Tokunaga,[‡] and Yasuo Wakatsuki*[,†]

RIKEN (The Institute of Physical and Chemical Research) and PRESTO (Japan Science and Technology Corporation), Wako-shi, Saitama 351-0198, Japan

waky@postman.riken.go.jp

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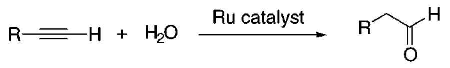
ABSTRACT

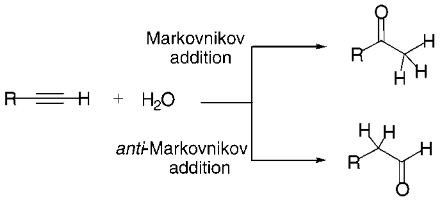


R = *n*-alkyl, *t*-Bu, Ph, NC(CH$_2$)$_3$, *etc.*

Highly regioselective, efficient, and substituent-tolerant *anti*-Markovnikov hydration of terminal alkynes occurs to give *n*-aldehyde by use of a catalytic amount of easily available cyclopentadienylruthenium complexes bearing appropriate bidentate or monodentate phosphine ligands. Typically, RuCpCl(dppm) (1 mol %) catalyzes the addition of water to 1-hexyne at 100 °C to give hexanal in 95% yield: 2-hexanone is not detected at all.

The use of water as an inexpensive and benign reagent in organic synthesis is an important topic, and the hydration of alkynes is a typical example of such use because the resultant carbonyl compounds are often useful as chemical intermediates for further elaboration. The reactions are slow in aqueous acid but are catalyzed by mercuric salt,[1] $NaAuCl_4$,[2] Ru(III),[3] $RhCl_3$,[4] $[PtCl_2(CH_2{=}CH_2)]_2$,[5] $PtCl_4$,[6] and other metals.[7] The addition of water across terminal alkynes promoted by these catalysts exclusively follows Markovnikov's rule to give methyl ketones. Prior to our work, the only reliable method for generating aldehydes from terminal alkynes involved hydroboration using stoichiometric amounts of hindered boranes.[8] In 1998, we reported the first *anti*-Markovnikov addition of water to terminal alkynes catalyzed by a Ru(II) complex, $[RuCl_2(C_6H_6)]_2$ or $RuCl_2(C_6H_6)$(phosphine) with additional specific phosphine ligands, $PPh_2(C_6F_5)$, or $P(3\text{-}C_6H_4SO_3Na)_3$, to give aldehydes as the major product.[9] Although the principle of the reaction was innovative, the activity of the catalyst as well as the selectivity remained unsatisfactory: ca. 10 mol % of the catalyst was required and a small amount of corresponding ketone was always found in the reaction mixture.

We report here a rather widely applicable catalytic system that effects the *anti*-Markovnikov addition of water to terminal alkynes with a dramatic improvement in both activity and selectivity. With the series of readily available ruthenium catalysts reported here, the formation of *n*-aldehyde via hydration of terminal alkynes may no longer be an unusual reaction.



In an initial attempt to improve our original reaction, $RuCpCl(PPh_3)_2$ was examined as a catalyst for the hydration

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[*] To whom correspondence should be addressed.

[†] RIKEN.

[‡] PRESTO, JST.

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of 1-octyne at 100 °C in 2-propanol. Since the activity of this complex turned out to be quite low, it had to be used in 30 mol % to generate octanal in 35% yield. Hence, the reaction was only slightly catalytic. Importantly, however, the selectivity of the reaction was excellent, since 2-octanone was not detected at all. The major byproduct was *n*-heptane, which was obtained in 18% yield, while the lost carbon was trapped as the CO ligand on ruthenium, with RuCpCl(CO)-(PPh_3) isolated in 65% yield from the reaction mixture. Taken together, these observations are fully consistent with the presence of an intermediate complex with a Ru−C(O)−(n-C_7H_{15}) linkage.

In the reaction of (PNP)$RuCl_2(PPh_3)$ (PNP = *n*-PrN(CH_2-$CH_2PPh_2)_2$) with excess phenylacetylene and water, Bianchini et al. found that quantitative (based on Ru) amounts of (PNP)$RuCl_2$(CO) and toluene are formed.[10] According to their detailed investigation, the reaction involves the tautomerization of Ru(1-alkyne) to Ru(vinylidene), attack by water of the vinylidene to form Ru{C(O)CH_2Ph}, and its further transformation to the decarbonylated intermediate (CO)Ru(CH_2Ph). Similarly, the Cp-ligated cationic (vinylidene)ruthenium complex, $[RuCp(C{=}CHPh)(PPh_3)(L)]^+$, has been reported to react with water to afford the phenylacetyl complex, $[RuCp(COCH_2Ph)(PPh_3)(L)]$ (L = CO), or the benzyl carbonyl complex, $[RuCp(CH_2Ph)(CO)(L)]$ (L = PPh_3).[11] Therefore, it is very likely that the hydration of 1-octyne to octanal, which is promoted by $RuCpCl(PPh_3)_2$, takes place via a vinylidene intermediate. Since RuCpCl-(CO)(PPh_3) is too stable to show catalytic activity, the key to better catalytic efficiency is obviously suppression of decarbonylation from the metal−acyl intermediate so that hydrogen uptake by the acyl group can lead to the liberation of aldehyde and re-formation of active Ru species.

Indeed, bidentate phosphines have been found to have an excellent effect. The reaction of 1-hexyne with water, carried out in the presence of 1 mol % of RuCpCl(dppm) in 2-propanol at 100 °C for 12 h, resulted in the complete conversion of 1-hexyne and gave hexanal quantitatively, while neither 2-hexanone nor pentane was observed (Table 1, entry 1). 2-Propanol has been found to be a far better solvent than other alcohols or organic solvents.

Table 1. Ruthenium Complex-Catalyzed *anti*-Markovnikov Hydration of 1-Hexyne[a]

entry	catalyst[b]	mol %	time, h	yield, %[c]
1	RuCpCl(dppm)	1.0	12	>99 (95)
2	RuCpCl(dppe)	4.0	12	>99
3	RuCpCl(dppp)	5.0	36	73
4	RuCpCl(dppb)	5.0	36	97
5	RuCpCl(dppbts)	5.0	12	84
6	RuCpCl(dmpm)	5.0	36	38
7	RuCpCl(depe)	5.0	36	47
8	$RuCpCl(PMePh_2)_2$	5.0	12	>99
9	$RuCpCl(PMe_2Ph)_2$	1.5	12	97
10	$RuCpCl(PMe_3)_2$	3.0	12	97

[a] 1-Hexyne, 1.0 mmol; Ru catalyst, 1−5 mol %; H_2O, 0.75 mL; 2-propanol, 2.5 mL in a sealed tube under argon at 100 °C (bath temperature). [b] dppm, bis(diphenylphosphino)methane; dppe, 1,2-bis(diphenylphosphino)ethane; dppp, 1,3-bis(diphenylphosphino)propane; dppb, 1,4-bis(diphenylphosphino)butane; dppbts, 1,2-bis(di-4-sulfonatophenylphosphino)benzene tetrasodium; dmpm, bis(dimethylphosphino)methane; depe, 1,2-bis(diethylphosphino)ethane. [c] GC yield, isolated yield in parentheses.

The addition of NH_4PF_6, HPF_6, or NaOH did not accelerate the reaction. As indicated in Table 1, the dppm ligand gives the best results among the bidentate phosphines. Although RuCpCl(dppe), RuCpCl(dppp), and RuCpCl(dppb) also gave aldehyde selectively without forming ketones, more than 4−5 mol % of ruthenium catalyst and/or prolonged heating were required to give yields of 70−90% (entries 2−4). The water-soluble bidentate phosphine, o-$C_6H_4\{P(p\text{-}C_6H_4SO_3Na)_2\}_2$ (dppbts), is also a good ligand (entry 5), but Ru complexes with the bidentate trialkyl phosphine, dmpm and depe, show lower activity (entries 6 and 7). The activities of ruthenium catalysts with a monodentate phosphine ligand, $PMePh_2$, PMe_2Ph, and PMe_3, were somewhat unexpected (entries 8−10). These, and in particular $RuCpCl(PMe_2Ph)_2$, also showed high activities for the hydration of 1-hexyne to exclusively give hexanal, perhaps due to the higher basicity and stronger coordination ability of these phosphines compared to PPh_3.

Using RuCpCl(dppm) as a catalyst, the scope of the *anti*-Markovnikov hydration of various 1-alkynes was examined (Table 2). With the exception of entries 4 and 9, reactions using 2−10 mol % of catalyst in 2-propanol at 100 °C gave the desired aldehydes in good to excellent yields after 12 h.

Table 2. RuCpCl(dppm)-Catalyzed *anti*-Markovnikov Hydration of Terminal Alkynes[a]

entry	alkyne	product	RuCpCl(dppm) mol %	yield, %[b]
1	$n\text{-}C_6H_{13}{-}{\equiv}$	$n\text{-}C_7H_{15}CHO$	2.0	93
2	$n\text{-}C_{10}H_{21}{-}{\equiv}$	$n\text{-}C_{11}H_{23}CHO$	3.0	94
3	${\equiv}{-}(CH_2)_6{-}{\equiv}$	$OHC(CH_2)_8CHO$	10.0	89
4	$t\text{-}Bu{-}{\equiv}$	$t\text{-}BuCH_2CHO$	10.0	81[c]
5	$Ph{-}{\equiv}$	$PhCH_2CHO$	5.0	90
6	$PhCH_2{-}{\equiv}$	$PhCH_2CH_2CHO$	3.0	93
7	$PhCH_2O(CH_2)_2{-}{\equiv}$	$PhCH_2O(CH_2)_3CHO$	3.0	94
8	$PhCO_2(CH_2)_2{-}{\equiv}$	$PhCO_2(CH_2)_3CHO$	8.0	85
9	$NC(CH_2)_3{-}{\equiv}$	$NC(CH_2)_4CHO$	10.0	88[d]

[a] Alkyne or dialkyne, 1.0 mmol; RuCpCl(dppm), 2−10 mol %; H_2O, 0.75 mL; 2-propanol, 2.5 mL in a sealed tube under argon at 100 °C for 12 h. [b] Isolated yield, except entry 4 which shows GC yield. [c] Heated for 24 h. [d] At 130 °C in 2-methoxyethanol.

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Simple and linear 1-alkynes, such as 1-octyne and 1-dodecyne, react as does 1-hexyne, but we noted a slight decrease in the reaction rate as the alkyl chain lengthened, and therefore a longer 1-alkyne requires a higher concentration of catalyst (entries 1 and 2). 1,9-Decadiyne was converted to the corresponding dialdehyde quantitatively, and the monoaldehyde was not observed (entry 3). *tert*-Butylacetylene and phenylacetylene, which were not catalyzed by our previous system of $RuCl_2(C_6H_6)\{PPh_2(C_6F_5)\}/PPh_2(C_6F_5)$ due to steric limitations,[9] now give 3,3-dimethylbutyraldehyde and phenylacetaldehyde, respectively, although prolonged heating and 10 mol % of catalyst are necessary in the case of sterically demanding *tert*-butylacetylene (entries 4 and 5). It should be noted that, in principle, neither 3,3-dimethylbutyraldehyde nor phenylacetaldehyde can be obtained by the hydroformylation of olefins. The hydration of benzylacetylene gives the desired 3-phenylpropionaldehyde cleanly without the formation of styrene, which was the major byproduct in our previous hydration system using $RuCl_2(C_6H_6)\{PPh_2(C_6F_5)\}/PPh_2(C_6F_5)$.[9] The alkyl substituent of the 1-alkyne can possess an ether or ester group, as in entries 7 and 8, respectively, to afford the corresponding substituted *n*-aldehyde in good yields. Even 5-cyanopent-1-yne reacts with water cleanly to give 5-cyanopentanal, i.e., the nitrile group remains intact (entry 9). In this case, however, 10 mol % of catalyst was added and a higher reaction temperature of 130 °C was required to attain a reasonable reaction rate, probably because coordination of the cyano group to the metal interferes with interaction between the C−C triple bond and the metal center. Thus, the results shown in Table 2 demonstrate the wide applicability of the present *anti*-Markovnikov hydration to aldehydes catalyzed by the CpRu system.

In summary, we have realized the highly regioselective, efficient, and substituent-tolerant *anti*-Markovnikov hydration of terminal alkynes to *n*-aldehyde through the use of catalytic amounts of cyclopentadienylruthenium complexes bearing appropriate bidentate or monodentate phosphine ligands. This addition of water to a C−C triple bond is a remarkably clean reaction: in general, the reaction mixture simply consists of solvent, unreacted reactants (1-alkyne and water), and the product *n*-aldehyde, regardless of the conversion, with only trace, if any, of byproducts. The details of the mechanism of this fairly easy reaction are now under investigation.

Supporting Information Available: Experimental details and characterization of products. This material is available free of charge via the Internet at http://pubs.acs.org.

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