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Hydration of terminal alkynes to aldehydes in aqueous micellar solutions by ruthenium(II) catalysis; first anti-Markovnikov addition of water to propargylic alcohols

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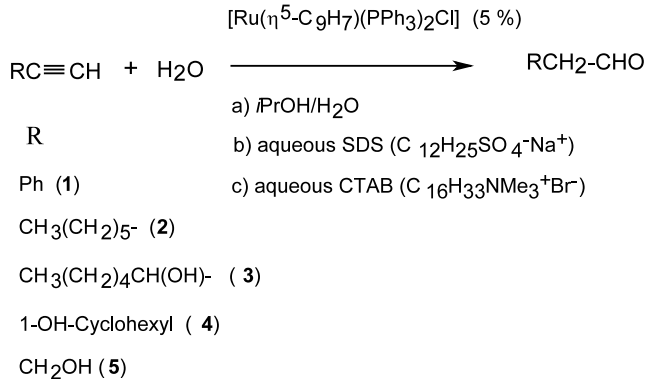
Abstract—The hydration of terminal alkynes and of propargylic alcohols to the corresponding aldehyde derivatives is conveniently carried out at 60°C in an aqueous micellar environment, in the presence of 5 mol% of the indenyl ruthenium(II) complex $[Ru(\eta^5\text{-}C_9H_7)Cl(PPh_3)_2]$. Higher yields and improved regioselectivity of aldehyde versus ketone as well as reaction conditions, in particular temperature and catalyst load, are found with respect to a solvent mixture 2-propanol–water, due to the aggregating conditions of the micellar solution. The reactions of the propargylic alcohols indicate the tolerance of the hydroxy functionality by the ruthenium complex.

Hydration of terminal alkynes catalyzed by metal complexes represents a convenient method for the preparation of carbonyl compounds. The reaction proceeds by addition of water to the metal π-alkyne complex, according to Markovnikov's rule, to form the corresponding ketone compound.[1] In contrast, it has been recently reported that the reaction can be regioselectively oriented to the formation of aldehydes in alcoholic aqueous media (ca. 25% water in 2-propanol) by catalysis of ruthenium(II) complexes, e.g. $[RuCl_2(\eta^6\text{-}C_6H_6)\{PPh_2(C_6F_5)\}]$ (10 mol%), in the presence of a large excess of fluorinated phosphines.[2] The excess of phosphine can be avoided by the use of cyclopentadienyl complexes bearing bidentate or monodentate phosphine ligands, such as $[Ru(\eta^5\text{-}C_5H_5)(dppm)Cl]$ (dppm = diphenylphosphinomethane), while high temperatures (100°C) are still required.[3] The key species for formation of aldehyde versus ketone has been proposed to be a ruthenium vinylidene intermediate, prone to nucleophilic attack by water at the α-carbon atom. Such an effect on the regioselectivity as well as the potential for the use of water as reagent and reaction medium have prompted our interest in this subject.

In light of the possibilities offered by surfactants to perform organic reactions in water,[4] and to affect the regiochemistry,[5] we have explored the hydration of terminal alkynes in aqueous micelles, as well as in aqueous 2-propanol. The cationic hexadecyltrimethylammonium bromide (CTAB), or the anionic sodium dodecylsulfate (SDS), which are both inexpensive commercially available materials, have been used as surfactants.[6] We have used the indenyl complex $[Ru(\eta^5\text{-}C_9H_7)Cl(PPh_3)_2]$ as catalyst, which is known to activate terminal alkynes in the stoichiometric formation of vinylidene and allenylidene complexes,[7] as well as to promote the isomerization of allylic alcohols to ketones.[8] The hydration reaction has been carried using



Scheme 1.

Keywords: aldehydes; micelles; ruthenium; acqueous reactions; catalysis.

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as substrates the lipophilic aromatic phenylacetylene (**1**) and aliphatic 1-octyne (**2**), and the propargylic alcohols 1-octyn-3-ol (**3**), 1-ethynyl-1-cyclohexanol (**4**) and 2-propyn-1-ol (**5**) (Scheme 1).

The results of the reaction carried out in the mixture 2-propanol/water, at 90°C, in the presence of [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] (5 mol%) are shown in Table 1.

The reactions did not proceed appreciably below 90°C. The aliphatic substrates as well as phenylacetylene and propargylic alcohols were converted into products in the absence of additives, with larger formation of the aldehyde than of the ketone species, except for 2-propyn-1-ol, which showed small conversion and no selectivity. To the best of our knowledge, this is the first report of catalytic hydration of propargylic alcohols to the aldehyde derivatives.

We have recently shown that the complex [Ru(η^5-C_9H_7)Cl(COD)] (COD = 1,5-cyclooctadiene) catalyzes the hydration of alkynes (**1**, **2** and **4**) to form ketones in high yields.[9]

Since the bis-phosphine and the COD complexes are characterized by different electron density at the metal, these results show the role played by the π-alkyne/vinylidene equilibrium (see Scheme 2 for a graphical representation of these species) in the regioselectivity. In fact an electrophilic ruthenium center is expected to favor a π-alkyne intermediate and direct the addition of water in a Markovnikov fashion,[10] as in the case of the COD complex with π-acidic properties ($E^0 = 0.61$ V),[11] while the electron rich bis-phosphine complex ($E^0 = 0.07$ V)[11] is expected to favor the vinylidene form.[12]

Homogeneous aqueous solutions of alkyne (0.04 M), surfactant (0.1 M) and [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] (5 mol%) were heated at 60°C for the appropriate time.[13] Reaction conditions and yields are reported in Table 2.

Table 1. Product analysis[a] of the hydration reaction in 2-propanol/water (1.25/0.37, cm^3) in the presence of [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] (5 mol%)[b] at 90°C (48 h)

Alkyne[c]	% Conversion	Aldehyde (%)	Ketone (%)	By-products
1	>99	71 (69)	17	12
2	89	63 (61)	15	11
3	>99	63	21	16
4	94	68	13	12
5	74	24	19	31

[a] Gas chromatographic yields (yields of isolated products).
[b] 0.025 mmol, 0.015 M.
[c] 0.5 mmol.

With respect to the reactions in aqueous 2-propanol, yields, selectivity (aldehyde/ketone and carbonyl compounds/by-products), and reaction conditions (temperature) are favored in the presence of surfactants. The results indicate that the reaction occurs within the micelle, which aggregates both catalyst and substrate. One remarkable feature of this aggregation is that the catalyst operates in the concentration range $1–2\times10^{-3}$ M, while in aqueous 2-propanol the concentration of the ruthenium complex is 0.015 M. In the case of 2-propyn-1-ol (**5**), the solubility of the alkyne in water yields scarce interaction with the catalyst in the micelle and hence lower conversions. Nevertheless, the reaction of **5** proceeds in the micellar aggregate, and not in the water phase, yielding a selectivity as high as that of the more lipophilic alkynes.

In the case of phenylacetylene, the formation of acetophenone and of phenylacetaldehyde in SDS or CTAB (0.1 M) solutions was followed at different reaction times (Fig. 1). The plot confirms higher selectivity for the aldehyde in the anionic SDS than in the cationic CTAB surfactant, suggesting that the organometallic intermediates are cationic species, formed in larger

Table 2. Product analysis[a] of the hydration reaction in aqueous micellar solutions in the presence of [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] (5 mol%) at 60°C[b]

Alkyne	Surfactant (M)	T (h)	Conversion	Aldehyde	Ketone
1	SDS (0.1)	12	80	77	3
1	SDS (0.1)	24	99	91 (89)	9
1	SDS (0.5)[c]	24	>99	93 (91)	7
1	CTAB (0.1)	24	79	70	9
1	CTAB (0.1)	48	>99	90	10
2	SDS (0.1)	24	99	93	6
2	CTAB (0.1)	24	>99	88	12
2	SDS (0.5)[c]	24	>99	97 (95)	3
3	SDS (0.1)	12	85	84	1
3	SDS (0.1)	24	95	93	1.4
3	CTAB (0.1)	30	98	93	4
4	SDS (0.1)	36	92	88	4
4	CTAB (0.1)	48	98	87	5
5	SDS (0.1)	36	27	25	1.5
5	CTAB (0.1)	48	27	25	1

[a] Gas chromatographic yields (isolated products).
[b] 0.5 mmol of surfactant (0.1 M), 0.20 mmol of alkyne (0.04 M), 0.01 mmol (8 mg) of ruthenium complex (2×10^{-3} M) in 5 cm^3 of water solution.
[c] 12.5 mmol of surfactant (0.5 M), 5 mmol of alkyne (0.2 M), 0.25 mmol (200 mg) of ruthenium complex (2×10^{-3} M) in 25 cm^3 of water solution.

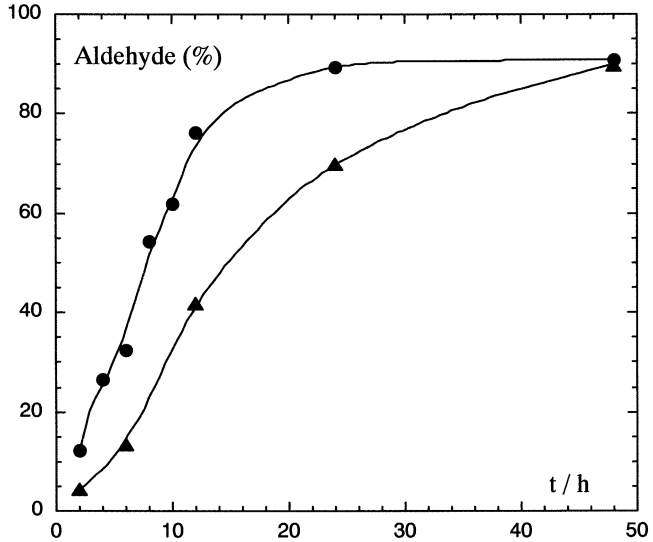
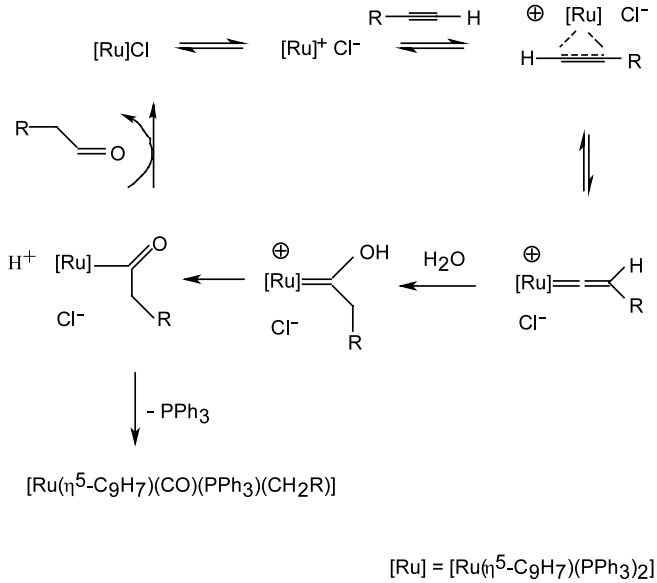


Figure 1. Yield (% from gas chromatographic analysis) of phenylacetaldehyde versus time, from the hydration reaction of phenylacetylene (0.04 M) in aqueous SDS (●) or CTAB (▲) (0.1 M), at 60°C, in the presence of complex [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] (5 mol%, 2×10^{-3} M).

quantities and stabilized in the surfactant with an anionic head group.

A $^{31}P\{^1H\}$ NMR investigation of the reaction in the presence of SDS showed a signal at $\delta=38.5$ ppm, corresponding to [Ru(η^5-C_9H_7)(=C=CHPh)(PPh_3)$_2$]$^+$ ($\delta=38.9$ ppm for [Ru(η^5-C_9H_7)(=C=CHPh)(PPh_3)$_2$][PF_6] in $CDCl_3$), and later a signal at $\delta=51$ ppm, due to [Ru(η^5-C_9H_7)(CO)(CH_2Ph)(PPh_3)]. This carbonyl complex, which has been obtained independently by reaction of [Ru(η^5-C_9H_7)(=C=CHPh)(PPh_3)$_2$][PF_6] with water in methanol,[14] forms by attack of water to the α-vinylidene carbon atom and subsequent phosphine dissociation and decarbonylation. This sequence of reaction steps in ruthenium complexes has already been described.[15] The complex [Ru(η^5-C_9H_7)(CO)(CH_2Ph)(PPh_3)] did not show activity as catalyst in the hydration reaction, therefore the decarbonylation of [Ru(η^5-C_9H_7)($COCH_2Ph$)(PPh_3)$_2$] represents a pathway in competition with the productive release of aldehyde. When the counteranion of complex [Ru(η^5-C_9H_7)(=C=CHPh)(PPh_3)$_2$][PF_6] was exchanged with sodium docecyl sulfate to obtain [Ru(η^5-C_9H_7)(=C=CHPh)(PPh_3)$_2$][$C_{12}H_{25}OSO_3$], the new salt displayed poor activity in the hydration of ethynylcyclohexanol in water (48 h, 9% of conversion and 7% of aldehyde), which confirms the key role played by the micellar aggregate.

A plausible reaction pathway is depicted in Scheme 2. Complex **1** in the micellar aggregate dissociates a chloride ion to give a cationic species, the same step which precedes interaction with the alkyne in the synthesis of vinylidene complexes.[16] The extrusion of chloride is favored in the anionic SDS micelle. On the other hand, the use of a silver salt, $AgBF_4$, in order to abstract the



Scheme 2.

halide and accelerate the reaction in 2-propanol–water has caused larger formation of by-products.

Interaction with the alkyne in the micelle yields a π-adduct, which rearranges in a favored equilibrium toward the vinylidene species, due to the donor properties of the phosphine ligands. The following steps involve addition of water to the cationic vinylidene complex to give an α-hydroxy carbene species, formation of an acyl complex,[15] and release of free aldehyde and catalyst. The fact that conjugated unsaturated aldehydes were not detected in the reactions of the propargylic alcohols **3**–**5** indicates that dehydration of the Ru–vinylidene intermediate to form allenylidene species, as in the stoichiometric activation of these substrates, is disfavored in the aqueous medium of this procedure.

The comparison between two different ruthenium complexes shows that the ligand effects which modulate the equilibrium π-alkyne/vinylidene can also be oriented to the desired regiochemistry in the hydration reaction, versus either ketone or aldehyde, in aqueous 2-propanol. The neutral indenyl complex [Ru(η^5-C_9H_7)Cl(PPh_3)$_2$] can be used effectively for *anti*-Markovnikov addition of water to alkynes by inclusion in aqueous micellar aggregates, with significant improvements of yields, regioselectivity and reaction conditions. Further tuning of the reaction can be obtained by structural changes of the surfactant.

This work represents the first report of catalytic hydration of propargylic alcohols to aldehydes, which implies the tolerance of the ruthenium catalyst to the hydroxyl functional group. Substitution reactions[17] and the dimerization[18] of propargylic alcohols catalyzed by ruthenium complexes have been reported recently, indicating the versatility of this class of compounds as substrates in ruthenium catalysis.

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References

1. (a) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; p. 762; (b) Damiano, J. P.; Postel, M. *J. Organomet. Chem.* **1996**, *522*, 303.
2. Tokunaga, M.; Wakatsuki, Y. *Angew. Chem., Int. Ed.* **1998**, *37*, 2867.
3. Suzuki, T.; Tokunaga, M.; Wakatsuki, Y. *Org. Lett.* **2001**, *3*, 735.
4. (a) Manabe, K.; Mori, Y.; Wakabayashi, T.; Nagayama, S.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 7202; (b) Li, H. R.; Wu, L. Z.; Tung, C. H. *J. Am. Chem. Soc.* **2000**, *122*, 2446; (c) Mori, Y.; Kakumoto, K.; Manabe, K.; Kobayashi, S. *Tetrahedron Lett.* **2000**, *41*, 3107.
5. (a) Jaeger, D. A.; Su, D.; Zafar, A.; Piknova, B.; Hall, S. B. *J. Am. Chem. Soc.* **2000**, *122*, 2749; (b) Schutz, A.; Wolff, T. *J. Photochem. Photobiol. A–Chemistry* **1997**, *109*, 251; (c) Bassetti, M.; Cerichelli, G.; Floris, B. *Gazz. Chim. Ital.* **1986**, *116*, 583.
6. Fendler, J. H.; Fendler, E. J. *Catalysis in Micellar and Macromolecular Systems*; Academic Press: London, 1975.
7. (a) Cadierno, V.; Gamasa, M. P.; Gimeno, J.; Gonzáles-Cueva, M.; Lastra, E.; Borge, J.; García-Granda, S.; Pérez-Carreño, E. *Organometallics* **1996**, *15*, 2137; (b) Cadierno, V.; Gamasa, M. P.; Gimeno, J. *Eur. J. Inorg. Chem.* **2001**, 571.
8. Trost, B. M.; Kulawiec, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 2027.
9. Alvarez, P.; Gimeno, J.; Lastra, E.; Garcia-Granda, S.; Van der Maelen, J. F.; Bassetti, M. *Organometallics* **2001**, *20*, 3762.
10. Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311.
11. Standard potential in dichloromethane (±0.01 V) referred to the pair $[FeCp_2]^+/[FeCp_2]$ (Cp = cyclopentadienyl). Reference electrode:aqueous saturated calomel electrode (SCE) separated from the solution by a porous septum. Working electrode: platinum disk. Electrolite: NBu_4PF_6.
12. Bruce, M. I. *Chem. Rev.* **1998**, *98*, 2797.
13. Solutions of surfactant (0.1 M, 0.5 M) were prepared by dissolving CTAB or SDS in deionized water. The alkyne ([surfactant]/[alkyne] = 2.5 or 5) was added to 5 cm^3 of the solution (25 cm^3 under preparative conditions), in a vessel sealed by a Teflon stopper, and the mixture stirred in a ultrasound bath (30 min). The ruthenium complex was added (5 mol% with respect to the alkyne), the mixture stirred (30 min) and then heated (60°C). The reaction was monitored by gas chromatography, until consumption of the substrate. Petroleum ether (5 cm^3) was then added to the aqueous solution, the organic phase was extracted, dried over anhydrous magnesium sulfate, and analyzed (GC–MS). Under preparative conditions, the organic solvent, after filtration, was removed under vacuum, and the oily residue was purified by chromatography (hexane/silica), or vacuum distilled, to give the product. The organic products described in this work are known. Characterization was obtained by ^1H NMR and by GC–MS.
14. Experimental data for $[Ru(\eta^5\text{-}C_9H_7)(CH_2Ph)(CO)(PPh_3)]$ (597.66) (calcd C, 70.34; H, 4.89. Found C, 70.54; H, 5.02%). ^1H NMR ($CDCl_3$): 2.23 (vt, $J_{HH} = 9$ Hz, 1H, CH_2), 2.84 (dd, $J_{PH} = 9$ Hz, 1H, CH_2), 4.55 (s, 1H, C_9H_7), 5.20 (s, 1H, C_9H_7), 5.30 (s, 1H, C_9H_7), 6.34 (m, 2H, C_9H_7), 6.7–7.4 (m, 22H, Ph, C_9H_7). ^{31}P NMR ($CDCl_3$): 60.8 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 7.9 (d, $J_{CP} = 6.9$ Hz, CH_2), 67.9 (d, $J_{CP} = 7.6$ Hz, C1), 78.3 (s, C3), 106.5 (s, C2), 108.8, 110.2 (s, C3a, C7a), 121.1, 121.7, 124.7, 125.1 (s, C4, C5, C6, C7), 127.0–134.6 (m, Ph), 207.5 (d, $J_{CP} = 19.6$ Hz, CO). ν_{max} (Nujol)/cm^{-1}: 1917 (CO).
15. Bianchini, C.; Casares, J. A.; Peruzzini, M.; Romerosa, A.; Zanobini, F. *J. Am. Chem. Soc.* **1996**, *118*, 4585.
16. Gamasa, M. P.; Gimeno, J.; Martín-Vaca, B. M.; Borge, J.; García-Granda, S.; Pérez-Carreño, E. *Organometallics* **1994**, *13*, 4045.
17. Nishibayashi, Y.; Wakiji, I.; Hidai, M. *J. Am. Chem. Soc.* **2000**, *122*, 11019.
18. Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2001**, *123*, 8862.