Ruthenium-Catalyzed Enaminoketone Formation from Propargyl Alcohols

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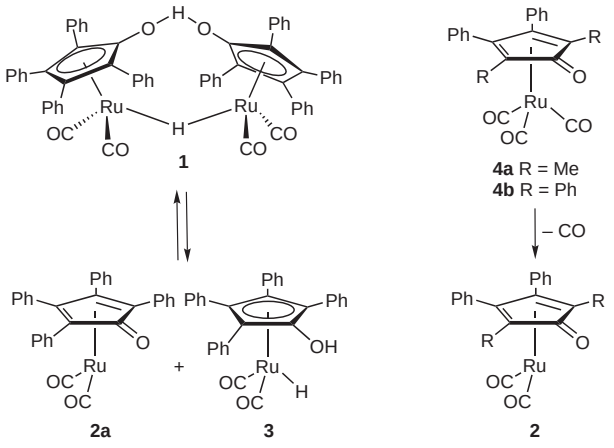
This paper is dedicated to Prof. Henning Hopf.

Abstract: Monomeric ruthenium(0) complexes containing electronically coupled dienone ligands were found to catalyze the formation of enaminoketones from propargyl alcohols.

Key words: aminations, enaminoketones, homogenous catalysis, propargyl alcohols, ruthenium

The Shvo complex [{(η^5-$Ph_4C_4CO)_2H$}$Ru_2((CO)_4)(\mu$-H)] (**1**)[1] catalyzes a broad number of homogeneous hydrogen transfer reactions such as the disproportionation of aldehydes to esters,[2] the reduction of aldehydes and ketones,[3] the Oppenhauer-type oxidation of alcohols and amines,[4,5] the racemization of alcohols and amines[6,7] and the dehydrogenation of alcohols without hydrogen acceptors.[8]

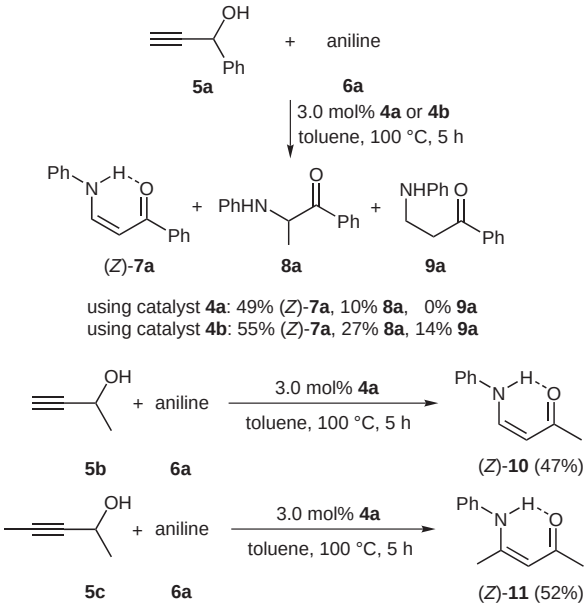
Complex **2**, which is formed from **1** as well as from monomeric complexes of type **4**, represents the reactive species in the oxidation step (Scheme 1).[9]



Scheme 1 Formation of the coordinatively unsaturated species **2**

During studies on the development of new transition-metal-catalyzed aminations of propargyl alcohols, formation of enaminoketones catalyzed by the complexes **4a** or **4b** was detected, whereas no transformation of propargyl alcohols could be observed without the presence of an amine.

1-Phenyl-2-propin-1-ol (**5a**) reacts with aniline **6a** in the presence of 3.0 mol% **4a** to yield (*Z*)-1-phenyl-3-phenylamino-propenone (*Z*-**7a**) and small amounts of the hydroamination product **8a**. Using the sterically more hindered complex **4b** accelerated consumption of the educts is observed but the β-aminoketone **9a** is formed as a second by-product. The aliphatic propargyl alcohol **5b** and the internal propargyl alcohol **5c** show similar reactivity to yield the enaminoketones *Z*-**10** and *Z*-**11**, respectively (Scheme 2).



Scheme 2 Enaminoketone formation from aniline **6a**

The variation of the amine component leads to a broad range in reactivity. Pyrrolidine (**6b**), L-proline methylester (**6c**), allylamine (**6d**) and L-aspartic acid dimethylester (**6e**) show relativly high and benzhydrylamine (**6f**) moderate reactivity. The benzylic amines **6g** and **6h**, (*R*)-1-cyclohexylethylamine (**6i**), tryptamine (**6j**), L-tryptophan methylester (**6k**) and L-alanine methylester (**6l**) react slowly. In general, primary amines form the hydrogen bridged *Z*-enaminoketones, secondary amines give the sterically more favored *E*-enaminoketones. In case of the proline derivative (*E*)-**7c** a rotational barrier regarding the C–N bond is observed. By-products were not detected and unreacted starting material could be recovered in all cases (Scheme 3, Table 1).

The mechanism of this new transformation is still under investigation. Since the propargyl alcohol can be recovered quantitatively if the reaction is performed without an

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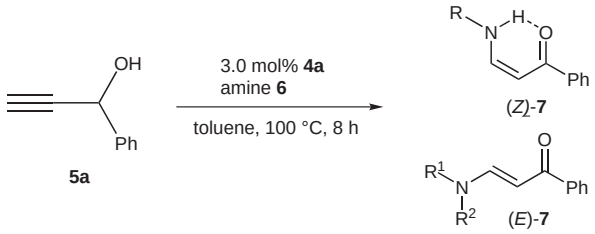

Scheme 3 Enaminoketone formation from **5a** and various amines

Table 1 Ruthenium-Catalyzed Enaminoketone Formation from **5a**

Amine	Product	Yield (%)
Pyrrolidine (**6b**)	*E*-**7b**	48
L-Proline methylester (**6c**)	*E*-**7c**[10]	65
Allylamine (**6d**)	*Z*-**7d**[10]	53
L-Aspartic acid dimethylester (**6e**)	*Z*-**7e**	49
Benzhydrylamine (**6f**)	*Z*-**7f**	39
Benzylamine (**6g**)	*Z*-**7g**	25
(*R*)-α-Methylbenzylamine (**6h**)	*Z*-**7h**	14
(*R*)-1-Cyclohexylethylamine (**6i**)	*Z*-**7i**	20
Tryptamine (**6j**)	*Z*-**7j**	11
L-Tryptophan methylester (**6k**)	*Z*-**7k**	17
L-Alanine methylester (**6l**)	*Z*-**7l**	16

amine and no hydrid acceptor is present in the reaction mixture, an initial isomerization process or the established mechanism of hydrogen transfer reactions mediated by the Shvo complex **1** seem not to take place here. Due to the fact that the internal propargyl alcohol (**5c**) show similar reactivity to the terminal ones **5a** and **5b** an initial activation of the alkyne terminus is unlikely as well. The role of the amine in the catalytic cycle remains crucial; it may be involved in the oxidation step or in the regeneration of the active catalytic species.

In summary, a new catalytic method to generate the synthetically important enaminoketones from easy and in a wide range accessible propargyl alcohols is presented. The simple synthesis and high stability of complexes of type **4** make them attractive, easy to handle and practical catalysts.

General Procedure

Propargyl alcohol (1 mmol) and the amine (1 mmol) were dissolved in toluene (0.5 mL) and the catalyst (0.03 mmol) was added. The mixture was stirred at 100 °C for 5 h or 8 h under argon. Using allylamine (**6d**) the reaction was performed in a closed tube. Aqueous work-up and chromatography on silica furnished the enaminoketones **7**.

Acknowledgment

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(10) **Characterization Data for Typical Enaminoketones.** Compound *E*-**7c**: $C_{15}H_{17}NO_3$, yellow oil (rotamers 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90–2.34 (m, 4 H), 3.50–3.55 (m, 2 H), 3.75 (s, 3 H), 4.16 and 4.29 (t, *J* = 8.1 Hz, 1 H), 5.67 and 5.77 (d, *J* = 12.4 Hz, 1 H), 7.37–7.46 (m, 3 H), 7.87–8.01 (m, 3 H). ^{13}C NMR (75 MHz, DEPT, $CDCl_3$): δ = 23.2 and 25.1 (CH_2), 27.5 and 29.7 (CH_2), 45.1 and 46.0 (CH_2), 52.5 (CH_3), 60.4 and 60.9 (CH), 92.9 and 94.8 (CH), 127.4 and 127.5 (CH), 127.9 and 128.0 (CH), 130.6 and 131.0 (CH), 140.0 and 140.5 (C), 149.3 and 149.8 (CH), 166.3 and 172.1, 188.8 (C). IR: 3056, 3024, 2956, 2878, 1741, 1662, 1633, 1580, 1539, 1449, 1364, 1340, 1304, 1274, 1209, 1166, 1090, 1051, 1026, 1008, 991, 925, 893, 837, 758, 706, 621, 557 cm^{-1}. MS (EI): *m*/*z* (%) = 259 (45) [M^+], 200 (100), 172 (34), 154 (58), 105 (70), 77 (54), 70 (36). HRMS: *m*/*z* calcd: 259.12085; found: 259.12007. Compound *Z*-**7d**: $C_{12}H_{13}NO$, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (tt, *J* = 5.6, 1.6 Hz, 2 H), 5.21 (dq, *J* = 10.2, 1.4 Hz, 1 H), 5.27 (dq, *J* = 17.1, 1.7 Hz, 1 H), 5.75 (d, *J* = 7.5 Hz, 1 H), 5.90 (ddt, *J* = 17.1, 10.3, 5.1 Hz, 1 H), 6.93 (dd, *J* = 12.8, 7.5 Hz, 1 H), 7.38–7.44 (m, 3 H), 7.88 (dd, *J* = 8.2, 1.4 Hz, 2 H), 10.3 (br s, NH). ^{13}C NMR (100 MHz, DEPT, $CDCl_3$): δ = 51.0 (CH_2), 90.7 (CH), 117.1 (CH_2), 127.0 (CH), 128.2 (CH), 130.9 (CH), 134.2 (CH), 139.7 (C), 154.0 (CH), 190.1 (C). IR: 3271, 3059, 3027, 2921, 2855, 1627, 1582, 1541, 1499, 1476, 1442, 1363, 1272, 1227, 1205, 1161, 1048, 1021, 988, 922, 867, 734, 699, 554 cm^{-1}. MS (EI): *m*/*z* (%) = 187(58) [M^+], 186 (39), 105 (100), 82 (89), 77 (55). HRMS: *m*/*z* calcd: 187.09972; found: 187.09941.