Chinese Journal of Chemistry, **2004**, *22*, 1413—1416 **Article**

Formation, Isolation and Characterization of a New Ruthenium Complex in Reaction of Acetone Masked Terminal Alkynone with Transfer Hydrogenation Catalyst

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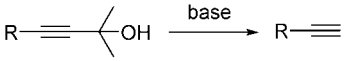
Reaction of [1*S*,2*S*-(Ts-diphen)Ru(II)(*p*-cymene)] (1*S*,2*S*-Ts-diphen = 1*S*,2*S*-*N*-tosyl-1,2-diphenylethylenediamine) and 2-hydroxy-2-methyl-non-3-yn-5-one under transfer hydrogenation condition gave a ruthenium complex bearing a 2,5-dihydrofuran moiety. The complex was characterized and a possible mechanism for the formation of the complex was proposed.

Keywords ruthenium, transfer hydrogenation, alkyne, alkynone, dihydrofuran

Introduction

Chiral propargylic alcohols are useful building blocks for the synthesis of various biologically active and structurally interesting compounds.[1] They were obtained by stoichiometric asymmetric reduction of acetylenic ketones with chirally modified metal hydride,[2] reductive cleavage of chiral acetylenic acetals,[3] enantioselective alkynylation of aldehydes,[4] enzymatic transformations[5] or asymmetric hydroboration of α,β-ynones with chiral oxazaborolidines.[6] Recently, Noyori's group reported the first catalytic asymmetric transfer hydrogenation of conjugated alkynones using chiral Ru(II) catalysts and 2-propanol as the hydrogen donor.[7] This method allows highly selective reduction of structurally diverse acetylenic ketones to propargylic alcohols with high enantioselectivity, leaving the carbon-carbon triple bond intact. However, the unsubstituted ethynyl ketones are not suitable substrates in such conditions. With the terminal acetylene protected by trimethylsilyl group, the substrate can be reduced easily under neutral conditions.[7a] But the incorporation of trimethylsilyl group is somewhat tedious and such a protective group is sensitive to both acidic and basic conditions.

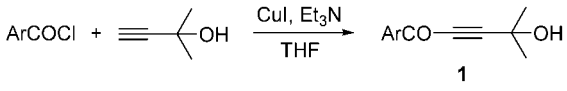
It was reported that substituted 2-methyl-but-3-yn-2-ols might lose one molecule of acetone to give terminal alkynes under basic conditions [Eq. (1)],[8] therefore, they could be regarded as protected terminal alkynes.



(1)

Since 2-methyl-but-3-yn-2-ol is readily available and very cheap, recently we have developed a method to synthesize 4-hydroxy-4-methyl-1-aryl-pent-2-yn-1-one (**1**) by employing 2-methyl-but-3-yn-2-ol and aroyl chloride under the catalysis of CuI (Scheme 1).[9]

Scheme 1 Preparation of α,β-unsaturated alkynone



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In this paper, we report the reaction of acetone masked terminal alkynones under transfer hydrogenation condition and the formation, isolation and characterization of an unexpected ruthenium complex bearing a 2,5-dihydrofuran moiety.

Reasults and discussion

When **1** was treated with Noyori's transfer hydrogenation catalyst **7**, it was found that the expected reduction did not happen and **1** was recovered almost quantitatively (Scheme 2).

It is known that an inherent problem of the transfer hydrogenation is the reversibility of the reaction. The overall efficiency is strongly affected by the structures of the ketone substrates and the properties of the hydrogen donors as well as the reaction conditions.[7b] The transfer hydrogenation with isopropanol as hydrogen donor is an equilibrium as shown in Eq. (2).

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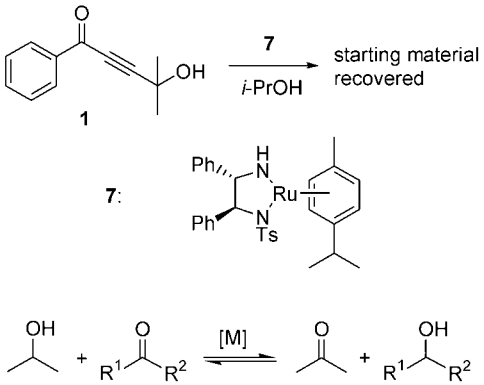
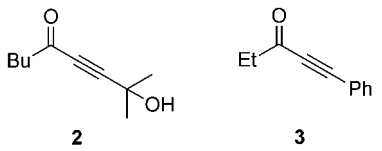
Scheme 2 Transfer hydrogenation of *α*,*β*-unsaturated alkynone with an adjacent hydroxy group



(2)

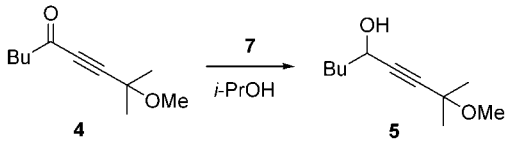
The equilibrium position is determined by the redox potentials of the hydrogen donors and acceptors present in the reaction system. The *α*,*β*-ynone substrates[7] reported by Noyori and others were only limited to the alkyl acetylenic ketones, and no aryl acetylenic ketones were reported. In order to prove our hypothesis, the structurally similar substrate 2-hydroxy-2-methyl-non-3-yn-5-one (**2**) was synthesized.



However, when we treat **2** under the standard transfer hydrogenation conditions, we found that there was still no transfer hydrogenation reaction product. In order to test the activity of the catalyst, we run the reaction under the same condition with 1-phenyl-pent-1-yn-3-one (**3**), the reaction was finished within 0.5 h and the product was isolated in good yield (92%) with reproducible *ee* (98%)[7a] (in good accordance with Noyori's report).

Meanwhile, a control experiment was conducted with mixed **2** and **3** at 1∶1 ratio under the same condition. It was surprising to find that neither **2** nor **3** was reduced. This implies that substrate **2** is not inert to the catalyst under the above condition. If this were not true, **3** would have been reduced. Apparently, the hydroxy group adjacent to the triple bond must have played a detrimental role under the reaction condition. When the hydroxy group of **2** was protected with methyl group, the resulting acetylenic ketone **4** could be successfully reduced to propargylic alcohol (Scheme 3).

Scheme 3 Transfer hydrogenation of *α*,*β*-unsaturated alkynone with protected hydroxy group



From the above experiments, it can be concluded that contrary to our initial expectation that the hydroxy group in the *α*,*β*-ynones would have little influence on the transfer hydrogenation, it really exhibits substantially negative effect on this process: it can inhibit the transfer hydrogenation catalyzed by Ru-complex **7**, in other words, it may react with the catalyst stoichiometrically to yield some other stable metal species that can not catalyze the transfer hydrogenation reaction.

In order to prove this supposition, a stoichiometric experiment was conducted with equal mole of substrate **2** and Ru-catalyst **7** in isopropanol. The reaction can be monitored by TLC and it showed that the acetylenic ketone **2** was consumed up soon, and a new species was formed. Fortunately, single crystals of this new Ru compound **11** were obtained and the subsequent X-ray structural analysis result was shown in Figure 1.[10]

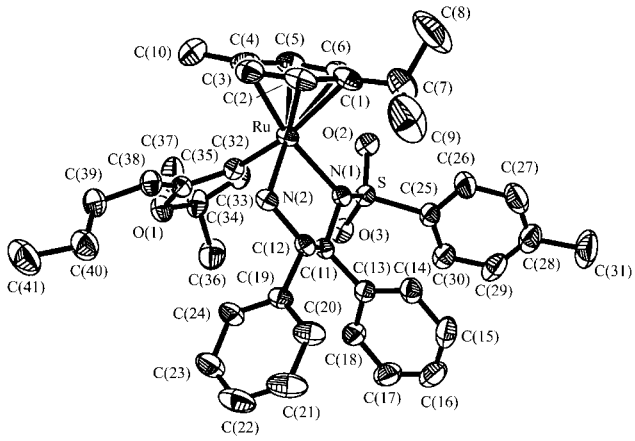


Figure 1 X-ray structure of Ru compound **11**.

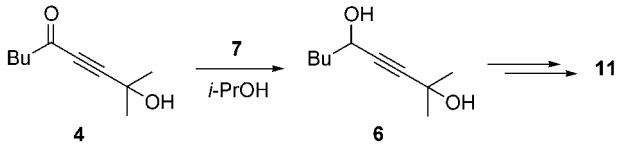
Hydrogen atoms are omitted for clarity. Selected bond lengths (nm) and angles (°): Ru—C(32) 0.2083(4); Ru—N(2) 0.2121(3); Ru—N(1) 0.2171(3); Ru—C(4) 0.2177(5); Ru—C(3) 0.2177(5); Ru—C(5) 0.2178(4); Ru—C(6) 0.2179(4); Ru—C(2) 0.2210(4); Ru—C(1) 0.2294(4); C(32)-Ru-C(5) 94.37(18); N(2)-Ru-C(5) 164.30(17); N(1)-Ru-C(5) 117.14(15); C(4)-Ru-C(5) 38.0(2); C(3)-Ru-C(5) 67.7(2); C(32)-Ru-C(6) 125.59(16); C(32)-Ru-C(2) 145.7(2); C(32)-Ru-C(1) 162.03(17); N(1)-Ru-C(1) 98.23(16); N(2)-Ru-C(1) 112.55(16).

The Ru complex is not very sensitive to air or moisture. But in the crystal lattice, there is a hexane molecule that is very easy to escape in the absence of the solvent. Therefore, the crystal data were collected in the presence of the mother liquor.

The mechanism about the formation of the ruthenium complex is not clear up to now. It is possible that the *α*,*β*-ynone was reduced to diol (**6**) under transfer hydrogenation condition and the diol further reacted with the Ru catalyst to yield the stable Ru complex (Scheme 4).

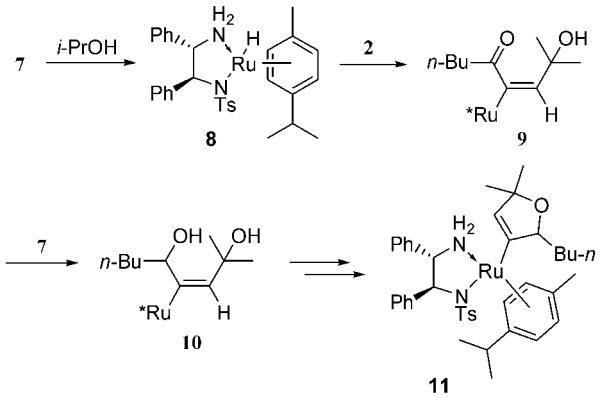
However, when **6** was subjected to the same conditions (with catalyst **7** in isopropanol in the presence of a

Scheme 4 Suggested formation of complex **11**



base), no reaction occurred. This suggests that the triple bond of *α*,*β*-alkynone may be reduced first, then the carbonyl group be reduced under transfer hydrogenation condition catalyzed by another molecule of Ru catalyst, and further dehydration afford the product (Scheme 5).

Scheme 5 A possible mechanism to account for the formation of **11**



Conclusion

In summary, the reaction of acetone masked terminal alkynone under transfer hydrogenation conditions and the isolation of an interesting Ru-complex characterized by ^{1}H NMR, ^{13}C NMR, IR, MS, and X-ray diffraction have been reported. A possible mechanism emphasizing the preferential reduction of triple bond to carbonyl group was suggested.

Experimental

Preparation of the compound 11

275 mg (0.46 mmol) of Ru-catalyst **7** was added to 77 mg (0.46 mmol) of **2** in 5 mL of isopropanol under argon atmosphere. The reaction mixture was stirred at ambient temperature for 0.5 h and TLC showed that the starting alkynone had been consumed up. The solvent was removed by an oil pump and the residue was dissolved in dichloromethane (5 mL). The solution was purified by flash chromatography with CH_2Cl_2 and Et_2O (1∶1). Then the eluent was concentrated to yield an orange yellow solid (192 mg, 50%). Recrystallization from CH_2Cl_2 and hexane afforded needle-like crystals. The crystals were susceptible to lose hexane in the lattice, and were pumped for hours before microanalysis. FT-IR (KBr pellet) *v*: 3276 (m), 3242 (m), 2962 (s), 1632 (m), 1545 (m), 1274 (s), 1260 (s), 1126 (s), 1085 (s), 914 (s), 819 (w), 697 (s), 572 (s) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 7.05—7.00 (m, 5H), 6.84—6.76 (m, 2H), 6.69—6.61 (m, 4H), 6.56—6.48 (m, 4H), 5.66 (d, *J*=5.8 Hz, 1H), 5.18 (d, *J*=5.8 Hz, 1H), 5.00 (d, *J*=5.8 Hz, 1H), 4.93 (d, *J*=5.8 Hz, 1H), 4.03 (brs, 1H), 3.84 (brs, 2H), 3.72 (brs, 1H), 3.58—3.63 (m, 1H), 2.95—3.05 (m, 1H), 2.25 (s, 6H), 2.12 (m, 2H), 1.49—1.41 (m, 12H), 1.35—1.25 (m, 3H), 0.90—0.83 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 167.4, 150.1, 148.6, 145.4, 139.9, 138.2, 137.8, 129.6, 128.4, 127.8, 126.5, 126.0, 110.4, 99.3, 94.3, 89.4, 88.3, 81.0, 80.3, 79.0, 71.7, 69.1, 31.5, 31.1, 28.3, 28.0, 27.3, 24.0, 23.3, 22.6, 21.1, 18.4, 14.1. Anal. calcd for $C_{41}H_{52}N_2O_3RuS$ (free of hexane): C 65.42, H 6.78, N 3.72; found C 65.28, H 6.58, N 3.61.

Loading crystal for X-ray analysis

The capillary tube for holding the crystal was pre-filled with the mother liquor in which the crystal was formed, the wet crystal was carefully loaded into the capillary tube with a piece of tiny copper wire, then the capillary tube was sealed for X-ray analysis.

References and notes

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10 Crystal data for compound **11**: $C_{47}H_{64}N_2O_3RuS$, M_r = 838.13 , orthorhombic, space group $P2_12_12_1$, a = 12. 0458(9) Å, b=14. 7473(10) Å, c=24. 9834(18) Å, V= 4438.1(6) Å^3, T=293(2) K, Z=4, F(000)=1776, Mo Kα radiation (λ=0. 71073 Å), μ=0. 441 mm^{-1}, 26631 reflections measured and 10165 unique (R_{int}=0. 1133) were used in all calculations. The final $wR(F^2)$ was 0. 1202 with $I>$ 2. 00$\sigma(I)$.

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