A Study of the Stereochemical Course of β-Oxygen Elimination with a Rhodium(I) Complex

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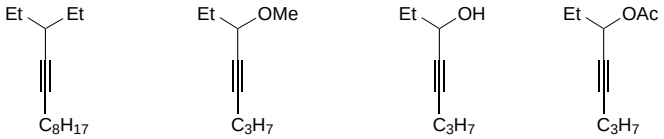
Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

The stereochemical course of β-oxygen elimination of an organorhodium(I) complex was investigated through the Rh-catalyzed addition of phenylboronic acid to a chiral propargyl acetate to produce an allene. The degree of chirality transfer suggests that the β-oxygen elimination takes place in both *syn* and *anti* modes.

Introduction. – Transition metal catalyzed organic transformations constitute an important class of synthetic tools. β-Elimination is often involved in these processes. For example, β-H elimination is a crucial step in the Pd-catalyzed *Mizoroki-Heck* reaction. β-H Elimination is known to proceed in a *syn* mode with a variety of transition metals [1]. On the other hand, little is known about the stereochemical course of β-O elimination, although this is also a common process [2]. *Hacksell* and *Daves* found that β-OH elimination took place *via* a *syn* mode [3] and β-AcO elimination *via* an *anti* mode [4]. *Zhu* and *Lu*, on the other hand, found only *anti* eliminations for β-Cl, β-AcO, and β-OH groups in Pd-catalyzed ene-yne cyclization reactions [5]. This paper provides experimental results that suggest that the β-AcO elimination of an organorhodium(I) complex takes place *via* both *syn* and *anti* modes.

Results and Discussion. – The catalyzed addition of arylboronic acids to alkenes [6] and alkynes [7] has been intensively studied in recent years. For example, in the Rh^I-catalyzed hydroarylation of internal alkynes, an arylrhodium(I) species generated *in situ* by the transmetallation of a Rh^I complex with arylboronic acid undergoes 1,2-addition across the C≡C bond in a *syn* fashion. The resultant vinylrhodium linkage is protonated through the 1,4-shift of Rh to afford an arylated alkene.

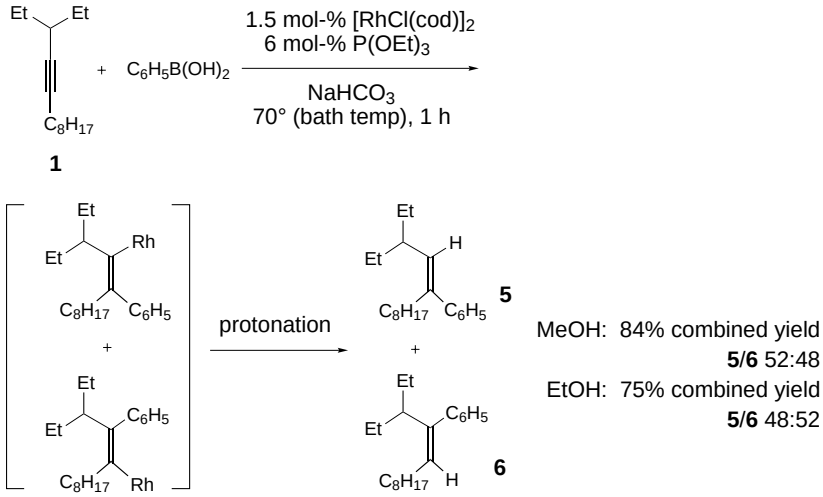
We have been interested in β-O elimination of rhodium complexes [8], and recently reported the Rh-catalyzed addition of arylboronic acid to oxabenzonorbornadienes [9] (*Lautens et al.* have also reported the same reaction in an asymmetric form [10]). The reaction ends with ring-opening of the tetrahydrofuran skeleton by β-O elimination. We next applied the same conditions to internal acetylenic compounds **1**–**4**, the C≡C bonds of which are unsymmetrically flanked by 1° and 2° C-atoms; an alcoholic (MeOH or EtOH) solution of the alkyne (1.0 equiv.) and phenylboronic acid (2.0 equiv.) was heated at 70° (bath temperature) for 1 h in the presence of $NaHCO_3$ (2.0 equiv.) and a Rh complex (0.03 equiv.) prepared *in situ* from $[RhCl(cod)]_2$ and $P(OEt)_3$ (Rh/P 1:2).



1 **2** **3** **4**

Unsymmetrical alkyne **1** lacking an O-functionality afforded a regioisomeric mixture of trisubstituted alkenes **5** and **6** in an almost 1:1 ratio (*Scheme 1*). As reported [7], a phenylrhodium(I) species, generated by transmetallation, undergoes 1,2-addition across the C≡C bond in a *syn* fashion. Protonation follows either indirectly through a 1,4-shift of Rh or directly by the solvent alcohol. To our surprise, the steric bulk of a 2° alkyl group had no effect on the regioselectivity of the 1,2-addition process.

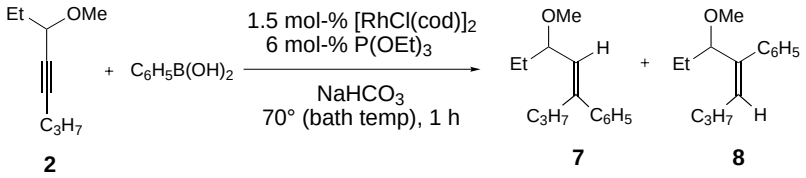
Scheme 1



In the case of propargylic methyl ether **2**, the formation of **7** was favored over that of **8** with ratios of 64:36 in MeOH and 62:38 in EtOH (*Scheme 2*). The dominant product **7** resulted from the addition of Rh to the *sp* C-atom proximal to the MeO group. It is likely that coordination of the O-atom to Rh is responsible for the observed selectivity. The regiochemical bias became more evident (79:21 and 85:15) in the reactions of propargylic alcohol **3** (*Scheme 3*).

With propargylic acetate **4** as the acetylenic substrate, a mixture of trisubstituted allene **12** and allyl acetate **14** was obtained in ratios of 78:22 (in EtOH) and 82:18 (in MeOH) (*Scheme 4*). The relative amounts of **12** and **14** are similar to the regioisomeric ratios **9/10** observed with propargylic alcohol **3**. A plausible mechanistic explanation for the formation of the mixture of **12/14** is illustrated in *Scheme 4*. The addition of phenylrhodium(I) across the C≡C bond in a *syn* fashion affords regioisomeric intermediates **11** and **13**, with the former predominating (*ca.* 8:2) due to coordination of the AcO group to Rh. The greater leaving-group ability of the AcO group compared with MeO or OH groups [4][5] grants an additional reaction manifold to intermediate

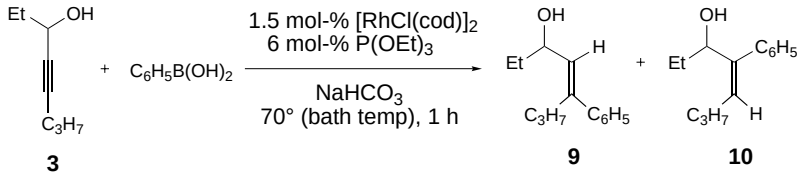
Scheme 2



2 **7** **8**

MeOH: 47% combined yield
7/8 64:36
EtOH: 49% combined yield
7/8 62:38

Scheme 3



3 **9** **10**

MeOH: 84% combined yield
9/10 79:21
EtOH: 60% combined yield
9/10 85:15

11, *i.e.*, β-AcO elimination to afford allene **12**. In intermediate **13**, the AcO group is distal to Rh, making β-elimination impossible. Thus, **14** is produced by protonation. It is reasonable to assume that trisubstituted allene **12** is formed predominantly *via* this addition-β-AcO elimination pathway on the basis of the similarity between the product ratios **12/14** and the regioisomeric ratios **9/10**, although it is impossible to completely rule out the involvement of an oxidative addition pathway in the formation of **12** [11].

The substituents of the allene **12** are unsymmetrically arranged, and consequently, the molecule is chiral. If coplanarity of breaking σ bonds is granted for β-O elimination[1]), the reaction with optically active **4** would reveal the stereochemical course of β-O elimination. As shown in *Scheme 5*, optically active **11** gives opposite enantiomers of the allene product **12**, depending on whether the elimination takes place by a *syn* or *anti* mechanism.

Thus, we prepared enantiomerically enriched allyl alcohol (*S*)-**3** by asymmetric hydrogenation [12], acetylated it to (*S*)-**4** (> 95% ee), and carried out the Rh-catalyzed reaction with $PhB(OH)_2$ (*Scheme 6*).

Allylic acetate **14**, produced by simple addition across the C≡C bond, was obtained with complete retention of configuration (> 95% ee). This result suggests that allylic

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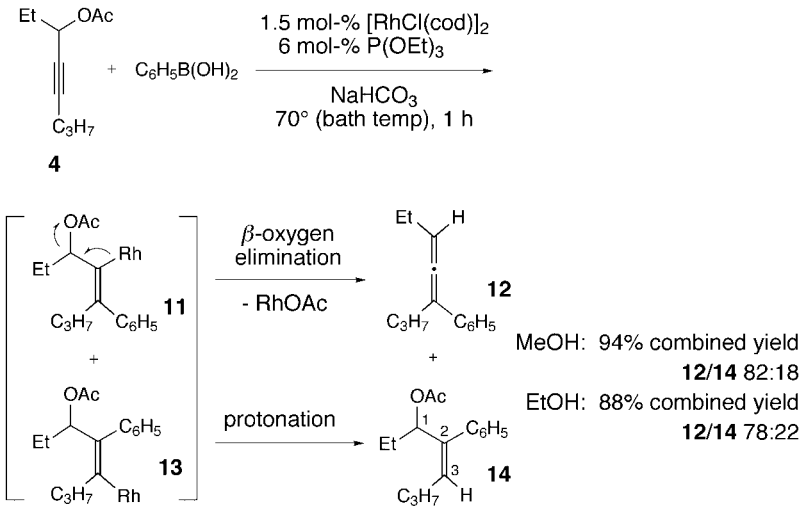
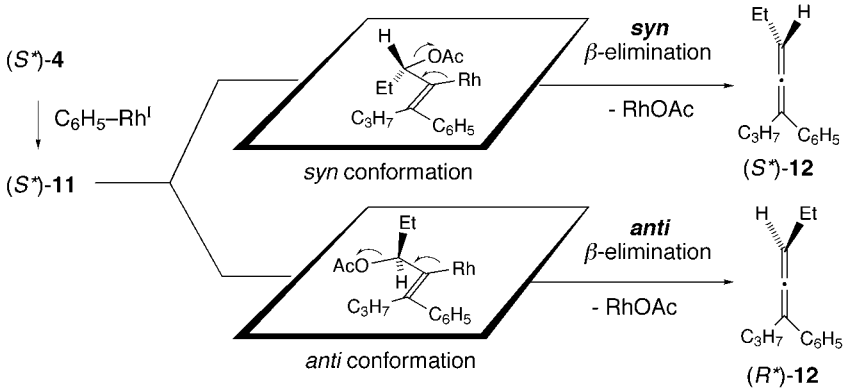
[1]) β-Oxygen elimination produces a C–C π bond with rupture of the C–Rh and C–O σ bonds. Operation of this process has a stereoelectronic requirement that the C–Rh and C–O bonds achieve a nearly coplanar arrangement.

Scheme 4

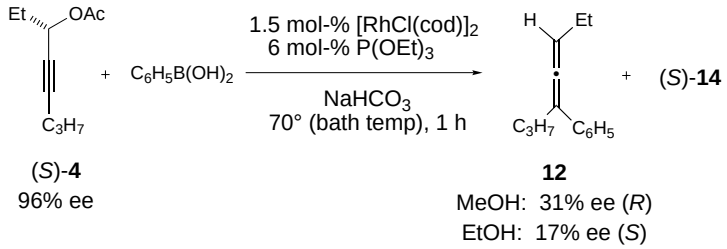


Scheme 5



cations are not formed from the intermediate allylic acetate **13**, and, furthermore, that formation of an allylic cation from **11** under the reaction conditions is unlikely. Therefore, β-AcO elimination from **11** would proceed through a coplanar arrangement of the breaking C–Rh and C–O σ bonds (*E*2-type pathway) rather than through the *E*1-type pathway. Despite this fact, analysis of the enentiomeric purity of the allene **12** (*vide infra*) revealed that the degree of chirality transfer was much lower than observed in the preparation of **14**. In addition, there was a dramatic solvent effect; in MeOH, the (*R*)-allene was the major enantiomer (31% ee), while, in EtOH, the (*S*)-allene predominated (17% ee). Interpreting these selectivities in terms of the mechanistic pathway depicted in *Scheme 5*, *ca.* 66% of **11** undergoes β-O elimination in an *anti* mode, and the remaining 34% in a *syn* mode, when MeOH is solvent. In EtOH, 41% of **11** is eliminated in *anti* mode, and 59% in *syn* mode. The delicate stability balance

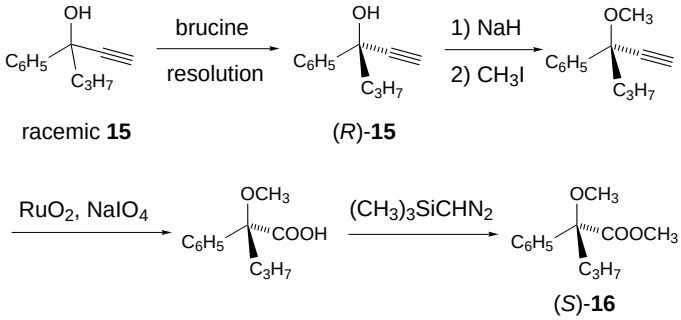
Scheme 6



between the two conformations for the *anti* and *syn* eliminations might be influenced by solvent properties like polarity and steric bulkiness. Regardless, it is noteworthy that both *syn* and *anti* modes are possible for the β-O elimination of alkylrhodium(I) complexes. This is in contrast with the selective behavior of Pd complexes [3–5].

The enantiomeric excess of the allene **12** was analyzed with a shift reagent by a literature procedure [13]. An authentic sample of (*R*)-enantiomer of **12** was prepared by a separate route to determine the absolute configuration of the produced allene **12** by comparison of the optical rotation (*Schemes 7* and *8*). Initially, the enantiomers of racemic tertiary alcohol **15** were separated by fractional crystallization in the presence of (*S*)-brucine [14]. The dextrorotatory enantiomer obtained was found to have (*R*)-configuration by derivatization to (*S*)-**16**, the optical rotation of which is known in the literature [15].

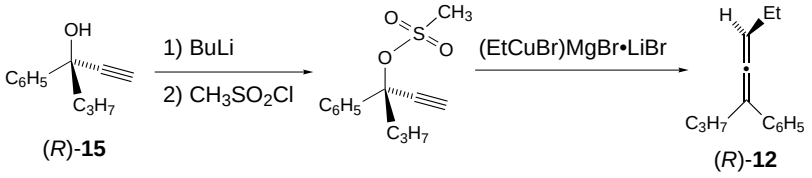
Scheme 7



Next, (*R*)-**15** was sulfenylated for a subsequent reaction with a organocopper reagent (*Scheme 8*), which has been established to proceed through *anti* S_N2' substitution [16]. Thus, authentic (*R*)-allene **12** was synthesized from (*R*)-**15**. In corroboration of the assignment, enantiomerically enriched (*R*)-allene **12** was prepared *via* a different authentic route from (*S*)-**4** with a Pd catalyst [17]. Comparison of the directions of optical rotation established the absolute configuration of the allene **12** obtained from enantiomerically enriched (*S*)-**4**.

Conclusions. – In conclusion, we have examined the stereochemistry of β-O elimination of a Rh^I complex by the addition reaction of $PhB(OH)_2$ to a chiral

Scheme 8



propargyl acetate, and demonstrated that the intermediate vinylrhodium complex undergoes β-O elimination *via* both *syn* and *anti* modes, the latter being preferred.

Experimental Part

General. Column chromatography (CC)was carried out on 75/150 mesh silica gel (*Wako; Wakogel C-200*). NMR Spectra were measured in $CDCl_3$ on *Varian Mercury Plus 400* (^{1}H: 400 MHz) and *Gemini 2000* (^{13}C: 75 MHz) instruments. Chemical shifts (ppm) are referenced to residual signals of $CDCl_3$.

Rh-Catalyzed Reaction of 1-Ethylhex-2-ynyl Acetate (**4**) *with PhB(OH)$_2$*. A mixture of **4** (50.5 mg, 0.30 mol), $PhB(OH)_2$ (73.1 mg, 0.60 mmol), $NaHCO_3$ (50.4 mg, 0.60 mmol), $[RhCl(cod)]_2$ (2.2 mg, 1.5 mol%), and $P(OEt)_3$ (3.0 mg, 6 mol%) in MeOH (3 ml) was stirred at 70° under N_2 for 1 h. The mixture was cooled to r.t., and MeOH was removed *in vacuo*. Et_2O and H_2O were added to the residue, then the aq. layer was extracted three times with Et_2O. The combined org. layer was washed with H_2O and brine successively, and dried ($MgSO_4$). The org. layer was concentrated *in vacuo*, and the residue was purified by a short column of silica gel to afford *4-phenylocta-4,5-diene* (**12**, 43.0 mg, 77%) and *1-ethyl-2-phenylhex-2-enyl acetate* (**14**, 12.6 mg, 17%).

Data of **12**: ^{1}H-NMR: 0.94 (*t*, *J* = 7.2, 3 H); 1.02 (*t*, *J* = 7.2, 3 H); 1.48–1.57 (*m*, 2 H); 2.27–2.41 (*m*, 2 H), 5.48 (*m*, 1 H); 7.10–7.14 (*m*, 1 H); 7.22–7.27 (*m*, 2 H); 7.34–7.36 (*m*, 2 H). ^{13}C{^{1}H}-NMR: 13.5, 13.9; 21.2; 22.2; 32.1; 96.0; 106.1; 125.9; 126.3; 128.3; 137.8; 203.6. H-RMS: 186.1406 (C_4H_{18}; calc. 186.1409).

Data of **14**: ^{1}H-NMR: 0.78 (*t*, *J* = 7.2, 3 H); 0.92 (*t*, = 7.2, 3 H); 1.36–1.58 (*m*, 4 H); 1.63–1.74 (*m*, 2 H); 2.03 (s, 3 H); 2.19–2.35 (*m*, 2 H); 5.61 (*t*, *J* = 7.2, 1 H); 5.73 (*t*, *J* = 7.2, 1 H); 7.17–7.26 (*m*, 3 H); 7.29–7.32 (*m*, 2 H). ^{13}C{^{1}H}-NMR: 10.0; 13.8; 21.3; 22.9; 26.2; 30.1; 74.2; 126.8; 127.5; 128.3; 135.3; 138.7; 141.4; 170.5. Anal. calc. for $C_{16}H_{22}O_2$: C 78.01, H 9.00, found: C 78.08, H 8.92.

*(*R*)-Allene* **12**: Prepared from (*S*)-**4** according to a literature procedure [17]. $[\alpha]_{25D} = -128$ (*c* = 1.27, MeOH); 84% ee (^{1}H-NMR in CD_3OD at −60° in the presence of heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrine as a chiral shift agent; (*S*) δ 5.82, (*R*) δ 5.69 for C*H*=C=) [13].

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