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A REGIO- AND STEREO-CONTROLLED SYNTHESIS OF α,β-UNSATURATED CARBONYL COMPOUNDS

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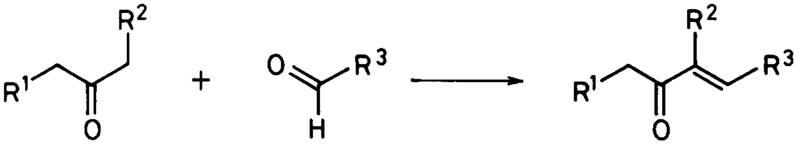
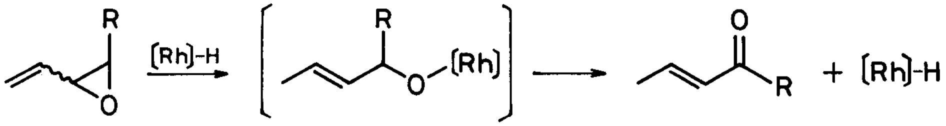
Summary: α,β-Unsaturated carbonyl compounds and butenolides are readily prepared by the rhodium(I) catalyzed isomerization of 1,3-diene monoepoxides and α-alkylidene-γ-butyrolactones, respectively. The former transformation is formally regarded as the equivalent of a regiospecific aldol condensation of an unsymmetrical ketone.

The regiocontrolled aldol condensation between two carbonyl compounds such as equation 1 is a highly useful synthetic operation in organic synthesis, however, there are very few reliable method in the regiodefined enolate formation of unsymmetrical ketone 1.[1] Thus, various new methods are reported in order to avoid the ambiguity.[2]



1 2 3 (1)

On the other hand, rhodium(I) hydride complexes are known as an efficient catalyst for isomerization of allyl alcohols to aldehydes or ketones under aprotic, homogeneous, and neutral conditions. Although the process can be elucidated by the addition and the subsequent elimination of rhodium hydride, we suggested an important role of Michael type interaction between $HRh(PPh_3)_4$ and α,β-unsaturated ketones in the formation of α-silyl ketones.[1a, 3a] The putative behavior of $HRh(PPh_3)_4$ stimulates us to apply it to a catalytic isomerization of other types of hydride acceptors like as equation 2.

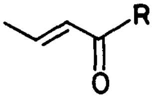
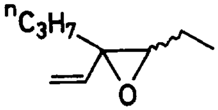
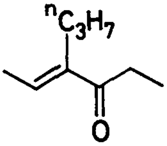
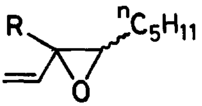
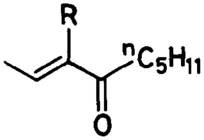
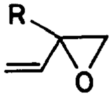
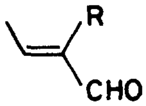
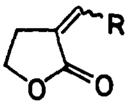
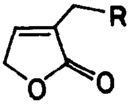


4 5 6 (2)

We describe herein the isomerization of 1,3-diene monoepoxide **4** and α-alkylidene-γ-butyrolactone **7** to form α,β-unsaturated carbonyl compound **6** and butenolide **8**, respectively.

When 1,3-diene monoepoxide **4** was treated with a catalytic amount (5 mol %) of $HRh(PPh_3)_4$ in benzene, α,β-unsaturated carbonyl compound **6** was obtained as a sole product. α-Alkylidene-γ-butyrolactone **7** was also isomerized to butenolide **8** by the assist of $HRh(PPh_3)_4$ in an excellent yield. Several examples are summarized in Table 1.

Table 1. Rh(I) Catalyzed reaction of 1,3-diene monoepoxides and α-alkylidene-γ-butyrolactones. [a]

Entry	Starting material		Product		Reaction time (h)	Yield (%)
1		**4a** R = $^{n}C_7H_{15}$		**6a**	18	83
2		**4b** R = $^{n}C_8H_{17}$		**6b**	17	91
3		**4c**		**6c**	15	83
4		**4d** R = Et		**6d**	17	78
5		**4e** R = $^{n}C_3H_7$		**6e**	23	83
6		**4f** R = $^{n}C_5H_{11}$		**6f**	19	89
7		**4g** R = Isopropyl		**6g**	20	70
8		**4h** R = Me		**6h**	3	35
9		**4i** R = $^{n}C_5H_{11}$		**6i**	21	75
10		**4j** R = 1-Ethylpropyl		**6j**	24	70
11		**4k**	no reaction		5	0
12		**7a** R = $^{n}C_8H_{17}$		**8a**	14	95
13		**7b** R = Cyclohexyl		**8b**	14	92

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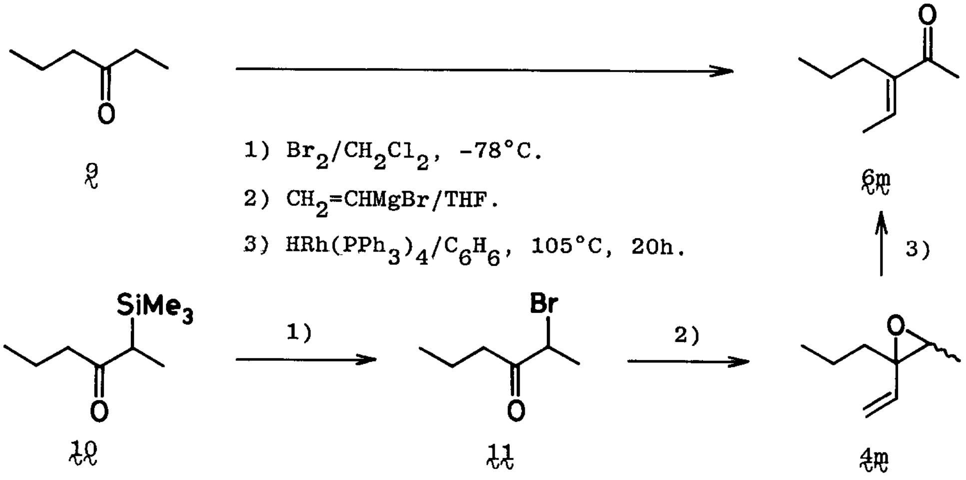
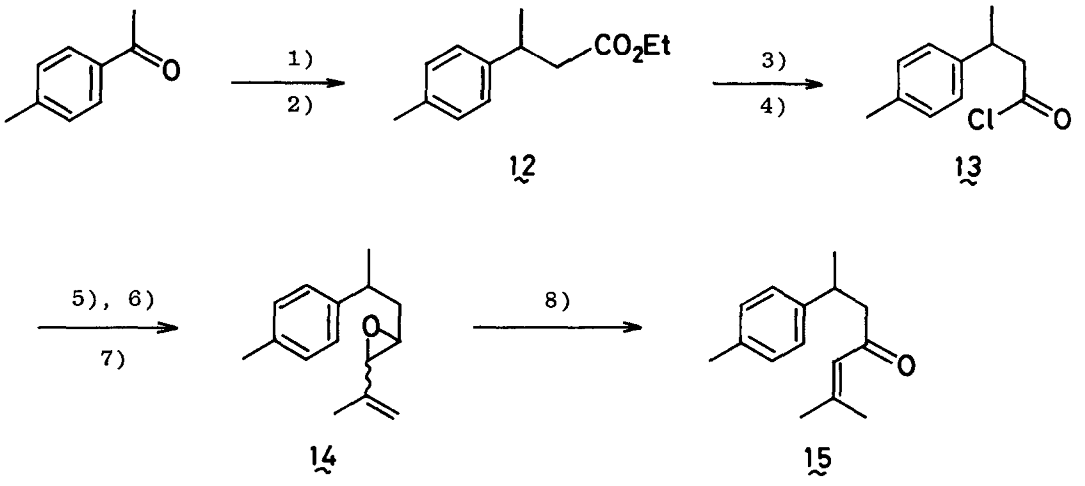
[a] The reaction was conducted on a 1 ∿ 3 mmoles scale in benzene at 105 °C under argon atmosphere using $HRh(PPh_3)_4$ as catalyst.

The catalytic isomerization of 1,3-diene monoepoxide possessing rather flexible structure proceeded to give **6** regiospecifically and *E*-selectively[4] (entry 1 ∿ 10). The resultant α,β-unsaturated aldehyde remained intact under the conditions (entry 8, 9, and 10). Cyclic 1,3-diene monoepoxide **4k** did not isomerize at all under the similar conditions (entry 11), whereas the cationic complex $[Rh(COD)(Ph_2PCH_2CH_2PPh_2)]^+PF_6^-$ effectively catalyzed the isomerization of **4k** to 3-cyclopenten-1-one in a 30 % yield. These two points, *E*-selectivity in **6** and inertness of catalyst to **4k**, contrast strikingly with the results of $[Rh(CO)_2Cl]_2$[6] or Pd(0)[7] catalyzed isomerization including cationic intermediate. In fact, geometrical mixture (*E*:*Z* = 81:19) of **6b** was obtained in a 55 % yield in the $[Rh(CO)_2Cl]_2$ catalyzed isomerization of **4b**. Thus, the nucleophilic interaction would be rather important than the electrophilic one in the $HRh(PPh_3)_4$ catalyzed isomerization.

Extremely restricted methods allow the regiospecific synthesis of α,β-unsaturated carbonyl compounds disconnected to an unsymmetrically substituted ketone.[2a, 2d] Therefore, the present approach promises an *E*-selective and regiospecific route. The regiospecificity can be readily attained by the intervention of α-trimethylsilyl ketone. The outline of the preparation of **6m** is delineated in the following. α-Trimethylsilyl ketone **10** is readily prepared[3] as the synthetic equivalent of **9** and leads selectively to α-bromo ketone **11**, which is converted to epoxide **4m** by the interaction of vinylmagnesium bromide. The overall transformation can be envisaged as a 1,2-carbonyl transposition of ketone **9** with concomitant introduction of an ethylidene group.



The present isomerization of 1,3-diene monoepoxide can be readily applied to the regiospecific synthesis of *ar-turmerone* **15**[8] as the key step demonstrated in the following scheme.



1) $\mathrm{Me_3Si\overset{\ominus}{C}HCO_2Et}$, THF, -78°C, 73%; 2) H_2, Pd-C, EtOH, room temp., 96%; 3) Me_3SiI, CCl_4, reflux, 72%; 4) $SOCl_2$, reflux, 85%; 5) $ClCH{=}C(CH_3)(CH_2SiMe_3)$, $TiCl_4$, CH_2Cl_2, -78°C, 92%; 6) $NaBH_4$, MeOH, room temp., 85%; 7) NaOH, aq. MeOH, room temp., 73%; 8) $HRh(PPh_3)_4$, 5 mol %, C_6H_6, 105°C, 86%.

References and notes

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