# Novel Carbon–Carbon Bond Formation by Means of a Rhodium Acetate-catalysed Reaction of γ,δ-Unsaturated Diazoketone and Its Application to the Synthesis of 4-*epi*-Isovalerenenol

**Toshio Honda,*[a] Hirohide Ishige,[a] Masayoshi Tsubuki,[a] Koichi Naito[b] and Yukio Suzuki[b]**
[a] *Institute of Medicinal Chemistry, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan*
[b] *Research and Development of Horiuchi Itaro Co., Ltd., Kumegawa-cho 5-29-7, Higashimurayama-shi, Tokyo 189, Japan*

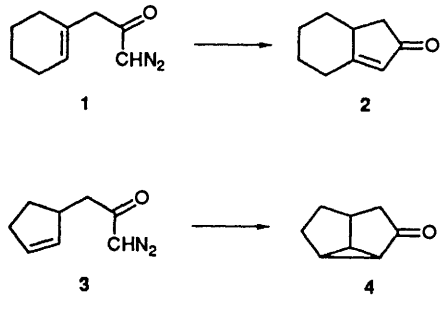
Rhodium acetate-catalysed decomposition of a γ,δ-unsaturated diazoketone gives novel carbon–carbon bond formation, a method used to synthesise 4-*epi*-isovalerenenol.

Carbenes or carbenoids react with olefins to provide a powerful synthetic tool for the formation of new carbon–carbon bonds in organic synthesis.[1] Recently we have helped to develop a reaction for carbon–carbon bond formation employing the rearrangement of sulphur ylides which are easily derived by preferential participation of divalent sulphurs and rhodium carbenoids.[2] As part of our continuing work on the utilisation of rhodium carbenoids as highly reactive species, we have initiated an investigation of the synthesis of the *trans*-perhydrindan ring system, often observed in natural compounds.

In 1984, Doyle and his co-worker reported[3] that the intramolecular cyclisation of the β,γ-unsaturated diazoketone **1** in the presence of catalysts such as $Cu(OTf)_2$ and $Rh_2(OAc)_4$, afforded the tetrahydroinden-2(1*H*)-one **2** in reasonable yield, whereas a similar reaction of the γ,δ-unsaturated diazoketone **3** brought about cyclopropanation to give the adduct **4** as a major product; with $BF_3$·$OEt_2$ in dichloromethane, however, compound **3** gave a complex mixture of products involving formation of **2** in low yield.

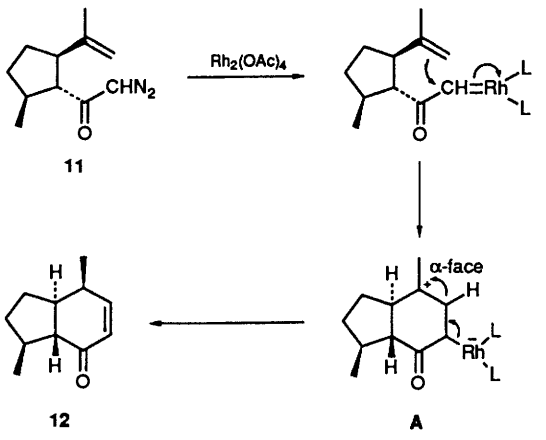
We applied this procedure to the chiral γ,δ-unsaturated diazoketone **11**, easily derived from (−)-carvone and discovered an interesting and useful method of forming a new carbon–carbon bond.

The starting material **11** was prepared as follows. Reduction of the ester **5**[4] with $NaBH_4$ in methanol gave the alcohol **6**, and this was converted into the xanthate **7** by methylation with carbon disulphide in *N*,*N*-dimethylformamide in the presence of 1,5-diazabicyclo[4.3.0]non-5-ene, followed by methylation with methyl iodide (93% overall yield). Deoxygenation of the xanthate **7** according to Barton's method[5] using tributyltin hydride and azoisobutyronitrile (AIBN) in refluxing toluene furnished the ester **8** (67%). After hydrolysis of **8** with aqueous sodium hydroxide, the resulting acid **9** was converted into the desired diazoketone **11** *via* the mixed anhydride **10**. Decomposition of the diazoketone **11** was carried out using various kinds of catalysts such as $BF_3$·$OEt_2$, $Cu(OTf)_2$, $Cu(acac)_2$, trifluoroacetic acid (TFA) and $Rh_2(OAc)_4$ and found that rhodium acetate was the best catalyst for carbon–carbon bond formation. The major isolated compound (40% yield from the acid **9**) was established, on the basis of

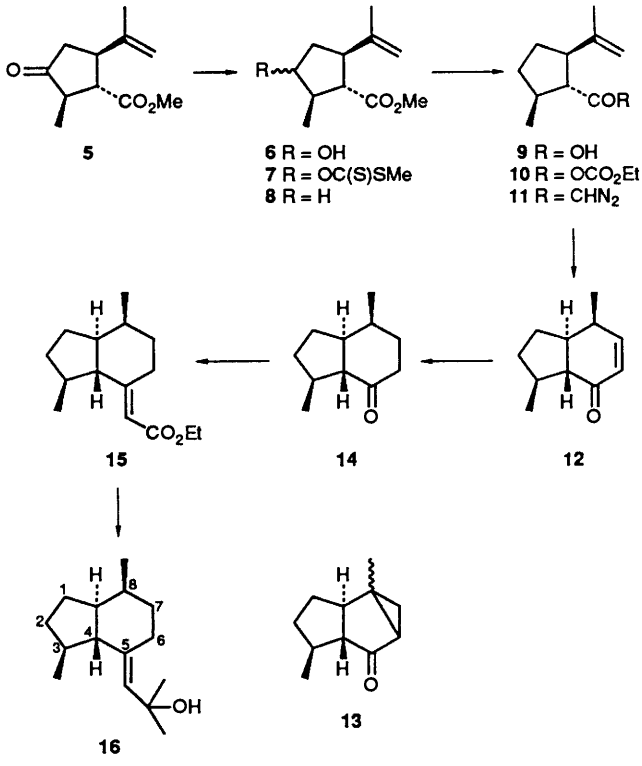



1 2 3 4

**Scheme 1**




Scheme 2




Scheme 3

spectroscopic evidence, as the cyclohexenone derivative **12**, together with a trace (<5%) of the cyclopropane derivative **13**. Although Doyle reported[3] that $Cu(OTf)_2$ was the most effective catalyst for this type of reaction, the decomposition of **11** with $Cu(OTf)_2$ in nitromethane gave **12** (19.8%) as a sole isolated product, other catalysts being found to be ineffective. It should be noted that the stereochemistry at the newly generated 8-position, was entirely controlled in this reaction. The observed stereoselectivity was rationalised by assuming that this reaction would proceed as shown in Scheme 2: thus, oxidative addition of the isopropenyl π-electron to the rhodium carbenoid gives the transition state **A** as the first step and this is followed by reductive elimination of the rhodium complex together with hydrogen migration to the carbocation centre from the less hindered side of the molecule to afford **12** stereoselectively.

The structure of **12** was unambiguously determined by its conversion into the ketone **14**, whose spectroscopic data were identical with those of an authentic specimen.[6] In exploring the utility of this new reaction we synthesised a valerenane type sesquiterpene having a perhydrindan ring system. Thus, a Horner–Emmons reaction of the ketone **14** with triethyl phosphonoacetate and sodium hydride in benzene provided, as the sole product (70%), the unsaturated ester **15**; this was then methylated with methyllithium in tetrahydrofuran to afford 4-*epi*-isovalerenenol **16** (66.5%). The *E* stereochemistry of the double bond of **16** was established on the basis of NMR evidence, in which a nuclear Overhauser effect between the olefinic proton and 3α-hydrogen was observed.

## Experimental

*Decomposition of the Diazoketone* **11** *with Rhodium Acetate.*— To a stirred solution of the acid **9** (500 mg, 2.98 mmol) and triethylamine (0.45 ml, 4.46 mmol) in $CH_2Cl_2$ (10 ml) was added ethyl chloroformate (0.71 ml, 7.44 mmol) at 0 °C and the reaction mixture was stirred for 30 min. The solution was washed with brine, dried ($Na_2SO_4$) and evaporated to give the mixed anhydride **10**. To a solution of the crude compound **10** in $CH_2Cl_2$ (5 ml) was added ethereal diazomethane (0.5 mol $dm^{-3}$; 17.9 ml, 8.95 mmol) at 0 °C and the mixture was allowed to stand overnight. Evaporation of the solvent afforded the diazoketone **11**, which was used for the next reaction without further purification. A mixture of crude compound **11** and rhodium acetate (130 mg, 0.29 mmol) in $CH_2Cl_2$ (25 ml) was stirred for 2 h at room temperature. Evaporation of the reaction mixture furnished a residue, which was purified by column chromatography on silica gel using hexane–AcOEt (99:1, v/v) as eluent to afford (1R,5R,6S,9S)-5,9-*dimethylbicyclo*[4.3.0]*non*-3-*en*-2-*one* **12** (0.2 g, 40%) as an oil; $[\alpha]_D^{25}$ +345.1° (*c* 1.32, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 1690; δ($CDCl_3$) 1.07 (3 H, d, *J* 7.3, Me),* 1.17 (3 H, d, *J* 6.1, Me), 1.2–2.26 (5 H, m), 2.62 (1 H, ddq, *J* 5.5, 5.5 and 7.3, 5-H), 5.87 (1 H, d, *J* 9.8, 3-H) and 6.84 (1 H, dd, *J* 5.5 and 9.8, 4-H); *m/z* 164 ($M^+$) (Found: $M^+$, 164.1194. $C_{11}H_{16}O$ requires *M*, 164.1200).

The second fraction furnished (1R,6S,9S)-5,9-*dimethyltricyclo*[4.3.0.$0^{3,5}$]*nonan*-2-*one* **13** (23 mg, 4.7%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1720; δ($CDCl_3$) 1.03 (3 H, d, *J* 6.1, Me), 1.02–1.16 (2 H, m), 1.25–1.94 (5 H, m), 1.32 (3 H, s, Me) and 2.15–2.46 (3 H, m); *m/z* 164 ($M^+$) (Found: $M^+$, 164.1194. $C_{11}H_{16}O$ requires *M*, 164.1200).

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* *J* Valves in Hz throughout.