Tetrahedron Letters, Vol. 33, No. 13, pp. 1791-1794, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press Ltd

Catalytic Codimerization of α,β- with γ,δ-Unsaturated Ketones : Novel Stereoselective Method of the Synthesis of Functionalized 8-Oxabicyclo[3.2.1]octanes

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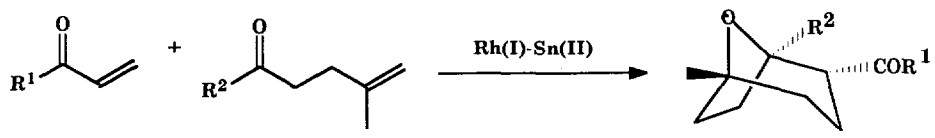
Abstract. Functionalized 8-oxabicyclo[3.2.1]octanes (**3a-e**) were obtained in one stage from vinyl ketones and 5-methylhex-5-en-2-one or 1-phenyl-4-methylpent-4-en-1-one in the presence of the catalytic system $[RhCl(C_2H_4)_2]_2$ - $SnCl_2$.

Numerous reports on the subject of homogeneous carbon-hydrogen bond activation by transition metal centers exist[1].

We reported recently that the system Rh(I) - Sn(II) catalysed carbon-carbon bond formation by carbon-hydrogen activation[2].

We report here a novel and unexpected stereoselective synthesis of functionalized 8-oxabicyclo[3.2.1]octanes by interaction α,β-unsaturated ketones **1** with γ,δ-unsaturated ketones **2** catalyzed by the $[RhCl(C_2H_4)_2]_2$ - $SnCl_2$ system.



1 **2** **3**

The reaction proceeds stereoselectively and gives only one *endo*-isomer with the carbonyl group in the equatorial position.

Substituted 8-oxabicyclo[3.2.1]octanes are used as a key intermediate for the synthesis of *Tromboxane* A_2 analogs[3].

Typically, a solution containing methyl vinyl ketone (9.26 mmol), 5-methylhex-5en-2-one (9.26 mmol), $[RhCl(C_2H_4)_2]_2$ (0.046 mmol), and $SnCl_2 \cdot 2H_2O$ (0.19 mmol) in 3 ml degassed acetone was heated in an argon atmosphere at 80°C in a sealed tube for 10h. Silica

gel column chromatography using hexane/ether (2/1) gave *endo*-2-(1,5-dimethyl-8-oxabicyclo[3.2.1]octyl)-ethan-2-one **3a**[4] in 39% yield. The results of the reaction **2** with other vinyl ketones using the rhodium(I)-tin(II) catalytic system are summarized in the Table 1.

Table 1. Synthesis of Substituted 8-Oxabicyclo[3.2.1]octanes Catalyzed by Rh(I)-Sn(II) System[a]

R^1	R^2	Conversion of **2**, %	Yield **3**[b]	
			to converted **2**, %	mol/g-at Rh
Me	Me	31	39 (**3a**)	12
Ph	Me	54	26 (**3b**)	11
t-Bu	Me	26	14 (**3c**)	4
5-(2-methylfuryl)	Me	47	33 (**3d**)	15
Me	Ph	94	13 (**3e**)	12

[a] α,β-unsaturated ketone (9.26 mmol), γ,δ-unsaturated ketone (9.26 mmol), $[RhCl(C_2H_4)_2]_2$ (0.046 mmol), $SnCl_2 \cdot 2H_2O$ (0.19 mmol), acetone 3 ml, 80°C, 10h;

[b] the yield of isolated products.

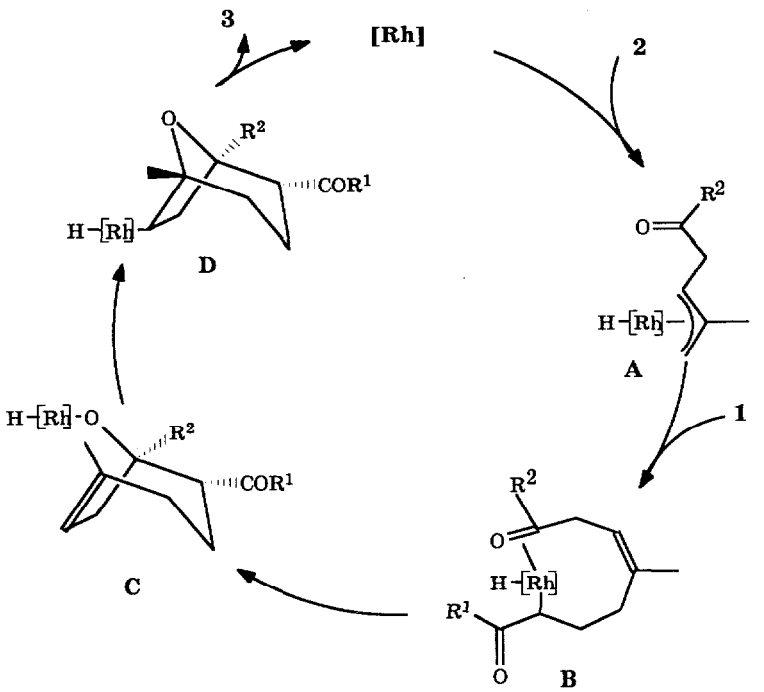
The formation of only one stereoisomer is observed in all cases, and it should be noted that the cycloheptane ring has the "bath" form in the bicyclic system.

The structures of (**3a-e**) have been proved by ^1H, ^{13}C and ^{17}O NMR using ^1H-^1H and ^1H-^{13}C correlation methods COSY and XHCORRD.

In particular, the ^1H NMR spectrum of **3a** shows two weakly connected 4- and 5-spin system H^2-H^5 and H^1, H^6-H^9. COMe group lies in the equatorial position as H^1 proton has large *aa* coupling constant with H^6 (12.67 Hz) and *ae* coupling constant with H^7 is 4.67 Hz. Availability of two *W* coupling constants $^4J_{H^1\text{-}H^5} = 0.92$ and $^4J_{H^3\text{-}H^8} = 1.62$ Hz indicated the "chair" conformation of the tetrahydropyran ring. Two signals with $\delta = 566.7$ ppm (C=O) and $\delta = 112.6$ ppm (-O-) have been found in ^{17}O NMR.

The supposed mechanism of the reaction is shown in Scheme 1. According to this mechanism the oxidative addition of the Rh-Sn[5] complex into the C-H bond with the formation of the allylhydride complex **A** takes place first. This is followed by insertion of a vinyl ketone molecule into the Rh-C bond, and reduction to oxallylhydride complex **B** (complexes of this type have been described already[6]). Subsequent nucleophilic addition to the C=O group gives complex **C**. Intramolecular attack on the C=C bond and reductive elimination leads to bicycle **3**.

Scheme 1



[Rh] = $L_nRh\text{-}SnCl_3$ (where L = Solvent or vinyl ketone)

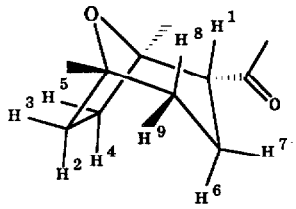
References and Notes

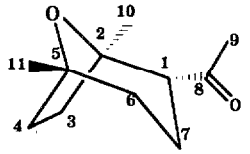
1. (a) Parshall, G.W. *Acc. Chem. Res.* **1975**, *8*, 113-117. (b) Muetterties, E.L. *Chem. Soc. Rev.* **1982**, *11*, 283-320. (c) Halpern, J. *Inorg. Chim. Acta*, **1985**, *100*, 41-48.

2. Nikishin, G.I.; Klimova, T.E.; Ignatenko, A.V.; Kovalev, I.P. *Tetrahedron Lett.***1991**, *32*, 1077-1080.

3. (a) Bowers, K.G.; Mann, J.; Walsh, E.B.; Howarth, O.W. *J. Chem. Soc., Perkin Trans. I.***1987**, 1657-1666. (b) *New Synthetic Routes to Prostaglandins and Tromboxanes;*Roberts, S.M.; Scheinmann, F. Eds.; Academic press, 1982.

4. All new compounds were fully characterized by NMR (^1H, ^{13}C, ^{17}O), IR, mass spectrometry and elemental analysis.





3a: NMR ^1H (δ, ppm, CD_3CN): 2.37 (m, $^4J_{H^1\text{-}H^5}$ = 0.92, $^3J_{H^1\text{-}H^6}$ = 12.67, $^3J_{H^1\text{-}H^7}$ = 4.67,H^1), 1.78 (m $^2J_{H^2\text{-}H^3}$ = -12.34, $^3J_{H^2\text{-}H^4}$ = 10.16, $^3J_{H^2\text{-}H^5}$ = 4.94, $^4J_{H^2\text{-}H^9}$ = 0.30, H^2), 1.61 (m, $^3J_{H^3\text{-}H^4}$ = 5.00, $^3J_{H^3\text{-}H^5}$ = 13.09, $^4J_{H^3\text{-}H^8}$ = 1.62, H^3), 2.34 (m, $^2J_{H^4\text{-}H^5}$ = -12.99, H^4), 1.45 (m, H^5), 1.71 (m, $^2J_{H^6\text{-}H^7}$ = -13.77, $^3J_{H^6\text{-}H^8}$ = 13.63, $^3J_{H^6\text{-}H^9}$ = 5.20, H^6), 1.78 (m, $^3J_{H^7\text{-}H^8}$ = 5.33, $^3J_{H^7\text{-}H^9}$ = 1.77, H^7), 1.46 (m, $^2J_{H^8\text{-}H^9}$ = -13.00, H^8), 1.50 (m, H^9), 2.12 (d, ^4J = 0.47 Hz, C(O)Me), 1.22 (s, 2Me); NMR $^{13}C\{^1H\}$ (δ, ppm, CD_3CN): 23.40 (C^7), 25.84 (C^{10}), 26.85 (C^{11}), 31.80 (C^9), 33.82 (C^3), 36.89 (C^4), 37.05 (C^6), 57.98 (C^1), 81.14 (C^5), 82.23 (C^2), 212.29(C^8); NMR $^{17}O\{^1H\}$ (δ, ppm, $CDCl_3$): 112.6 (-O-), 566.7 (C=O); IR (ν, cm^{-1}): 1706 (C=O); MS, m/z 182(M^+), 124, 111, 97, 81, 69, 55, 43 (base), 27; Found: C, 72.21; H, 9.82%. $C_{11}H_{18}O_2$ requires C, 72.49; H, 9.95%.

5. The formation of the Rh-Sn bond under catalysis by $[RhCl(C_2H_4)_2]_2$ - $SnCl_2$ system has been demonstrated : Kovalev, I.P.; Kolmogorov, Yu.N.; Strelenko, Yu.A.; Ignatenko, A.V.; Vinogradov, M.G.; Nikishin, G.I. *J. Organomet. Chem.* **1991**, *420*,125-133.

6. (a) Milstein, D. *J. Amer. Chem. Soc.* **1982**, *104*, 5227-5228; (b) Vinogradov, M.G.; Kovalev, I.P.;Nikishin, G.I. *Usp. Khim. (Russ. Chem. Rev.)*, **1986**, *55*, 1979-2007; (c) Kovalev, I.P.; Evdakov, K.V.;Vinogradov, M.G.; Polyakov, A.V.; Yanovsky, A.I.; Struchkov, Yu.T. *Metalloorg. Khim.* **1989**, *2*, 673-676.

(Received in UK 16 January 1992)