The C−C Bond Activation and Skeletal Rearrangement of Cycloalkanone Imine by Rh(I) Catalysts

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The activation of the carbon−carbon bond by homogeneous catalysts is of current interest in organometallic chemistry.[1] However, a few examples of the homogeneous catalytic activation of the C−C bond by transition metal have been reported:[2−9] the decarbonylative cleavage of the C−C bond,[3] the β-alkyl elimination of the homoallyl alcohol,[4] the β-decarboxylative ring opening of cyclic carbonate,[5] the ring cleavage of *tert*-cyclobutanol,[6] and so on. Especially, ring-cleavages of cycloalkanones by transition metal catalyst have been limited to strained cyclic ketones such as cyclopropenone,[7] cyclobutenone,[8] and cyclobutanones[9] to take advantage of the release of the ring strain. On the other hand, catalytic C−C bond cleavages of large unstrained ring-sized cycloalkanones are rare. We recently reported on the new catalytic C−C bond activation of unstrained ketone compounds.[10] In this report, we wish to describe the ring-opening of an unstrained cycloalkanone imine and its skeletal rearrangement.

The reaction of cycloalkanoketimine **1**, prepared from cycloalkanone and 2-amino-3-picoline,[11] with 1-hexene (**2**, 1000 mol % based on **1**) was carried out in the presence of $[(C_8H_{14})_2RhCl]_2$ (**3**, 3 mol % based on **1**) and Cy_3P (6 mol %) to yield a mixture of the ring-opened alkenyl ketones **4** and 7-tridecanone (**5**) after hydrolysis (eq 1).[12]

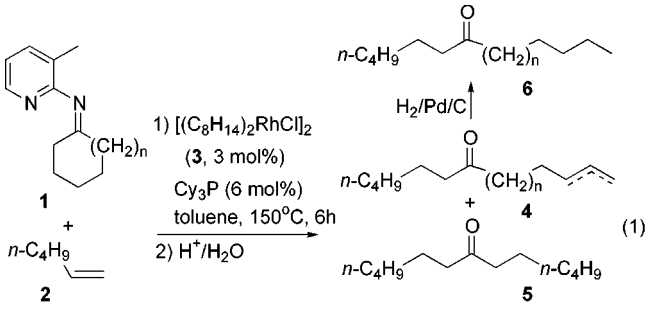


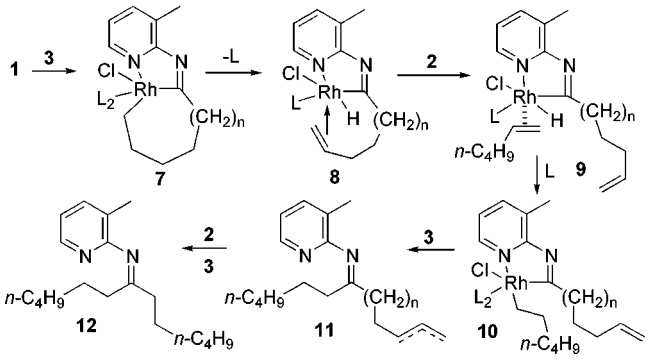
Table 1. C−C Bond Activation of Ketimine **1** with **2** by **3** and Cy_3P

entry	reactant **1** (n)	product(s)	ratio of **4**:**5** (ter:int of **4**)[a]	overall yield,[b] %
1	**1a** ($n = 0$)	**5**	0:100	9
2	**1b** ($n = 1$)	**5**	0:100	5
3	**1c** ($n = 2$)	**4c** + **5**	23:77 (52:48)	76
4	**1d** ($n = 3$)	**4d** + **5**	39:61 (13:87)	89
5	**1e** ($n = 5$)	**4e** + **5**	38:62 (15:85)	83
6	**1f** ($n = 7$)	**4f** + **5**	39:61 (22:78)	86
7	**1g** ($n = 10$)	**4g** + **5**	37:63 (16:84)	79

[a] The ratio of terminal olefin and internal olefin of **4** was determined by GCD. [b] Yields are determined by GCD.

Alkenyl ketone **4**, consisting of terminal and internal olefins,[13] can be hydrogenated by 1 atm of H_2 on Pd/C to give saturated alkyl ketone **6**. Initially, the C−C bond in ketimine **1** is cleaved by rhodium(I) in **3** to give an (iminoacyl) rhodium(III) metallacyclic complex **7**, followed by β-hydrogen elimination to effect rhodium(III) hydride **8** (Scheme 1). In the presence of **2**, the olefin

Scheme 1



exchange of the ω-alkenyl group of **8** with **2** affords **9**. A hydride insertion in **9** and a reductive elimination of the resulting complex **10** produces **11**. Ketimines **11** undergo a further C−C bond activation to yield the symmetric dialkyl ketimine **12**.[14] The hydrolysis of **11** and **12** affords the corresponding ketones **4** and **5**.

As the size of the ring from cyclohexanoketimine to cycloheptanoketimine increases, the yields of the C−C bond cleaved products dramatically increase (Table 1). In case of cyclopentanoketimine **1a** and cyclohexanoketimine **1b**, small amounts (5−9% yields) of the C−C bond cleaved products were determined (Table 1, entries 1−2), while moderate yields (76−89%) of the C−C bond cleaved products were obtained in the reaction of cycloalkanoketimine larger than **1b** (entries 3−7). The reason

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(11) Cycloalkanoketimine was prepared by the reaction of cycloalkanone and *N*-lithium-2-amino-3-picoline, generated from 2-amino-3-picoline and *n*-BuLi in THF. See Supporting Information.

(12) In the C−C bond cleavage of ketimine, the catalyst **3** and Cy_3P shows the best catalytic activity among organotransition metal catalysts. Various olefins could be applied to this C−C bond activation reaction, and 1-hexene (**2**) was selected as a standard olefin.

(13) When the reaction of **1c** and **2** was carried out at 150 °C for 1 h under $(PPh_3)_3RhCl$ (3 mol %), **4c** bearing an exclusive terminal alkenyl group was obtained in a 13% yield along with **5** (5%). This result implies that the initial terminal olefin in ketimine is isomerized to internal olefin.

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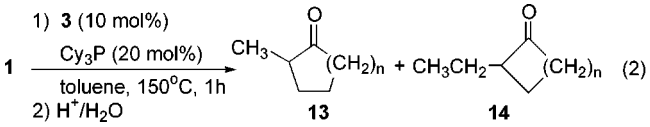
Table 2. Skeletal Rearrangement of Ketimine **1** by **3** and Cy_3P

entry	reactant **1** (*n*)	products	ratio of **13**:**14**	overall yield,[a] %
1	**1a** (*n* = 0)			0
2	**1b** (*n* = 1)	**13b**	100:0	21
3	**1c** (*n* = 2)	**13c** + **14c**	76:24	82
4	**1d** (*n* = 3)	**13d** + **14d**	33:67	12
5	**1h** (*n* = 4)			0

[a] Yields and the ratio of **13** and **14** were determined by GCD.

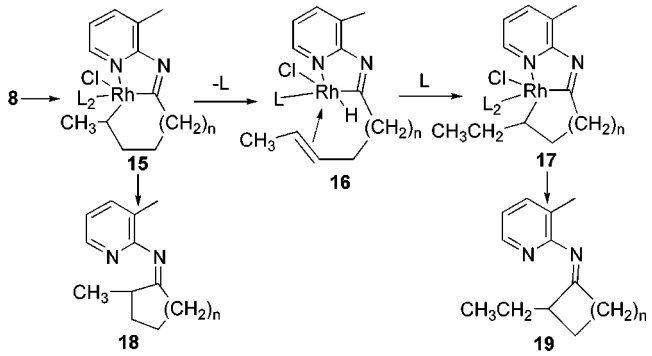
cycloalkanoketimines react differently according to size is not clear, but one speculation is that the cause may be the formation of metallacyclic complex **7**. To cleave the C−C bond of cycloalkanoketimine **1**, substrate should be flexible enough to form the unstrained metallacyclic complex **7**. Large-sized cycloalkanoketimines such as **1c**, **1d**, **1e**, and so on satisfy this requirement. However, the formation of **7** seems not to be facile for small-sized ketimines such as **1a** and **1b** due to the ring strain.

Contrastingly, when cycloalkanoketimine **1** was heated without **2** under Rh(I) catalyst, the ring-contracted products **13** and **14** were obtained (eq 2). For example, the reaction of cycloheptanoketimine **1c** at 150 °C for 1 h in the presence of **3** (10 mol % based on **1c**) and Cy_3P (20 mol %) affords a mixture of 2-methylcyclohexanone (**13c**) and 2-ethylcyclopentanone (**14c**) in an 82% yield in a 76:24 ratio after hydrolysis (Table 2, entry 3).[15] In a rearrangement of cyclohexanoketimine **1b**, only 2-methylcyclopentanone (**13b**) was determined in a 21% yield (entry 2): its not forming 2-ethylcyclobutanone (**14b**) was probably due to the instability of the strained cyclobutanone structure. With cyclooctanoketimine **1d**, a mixture of **13d** and **14d** was obtained in a 33:67 ratio in a 12% yield (entry 4). **1a** and **1h** did not show any skeletal rearrangement.[16]



Without additional olefins, a hydride inserts itself into the terminal olefin in **8** by Markovnikov's rule to generate **15**, which further undergoes β-hydrogen elimination and a hydride insertion in **16** to give **17** (Scheme 2). Reductive eliminations of **15** and **17** produce **18** and **19**, followed by hydrolysis to give **13** and **14**.

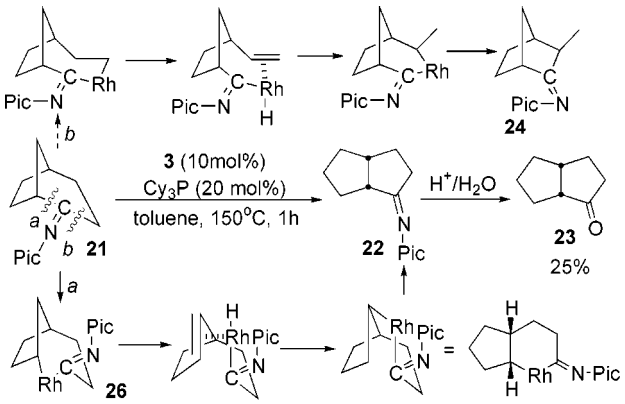
Scheme 2

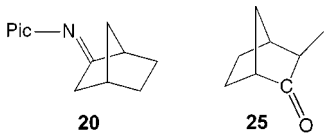


The product distribution seems to follow the thermodynamic stabilities of the rearranged products (**18** and **19**) compared with those of the starting cycloalkanoketimine **1**.

So far, the skeletal rearrangement has appeared to proceed toward the structures of cyclohexanone and cyclopentanone. This postulate was examined by performing a skeletal rearrangement of two bicyclic compounds, **20** and **21**, ketimines of norcamphor and bicyclo[3.2.1]octan-2-one. While ketimine **20**, consisting of cyclopentanone and cyclohexanone structures, does not show any reactivity for the skeletal rearrangement, the reaction of the ketimine **21** bearing cycloheptanone structure at 150 °C for 1 h leads to the bicyclic ketone **23** (25% yield) having two cyclopentyl structures exclusively after hydrolysis of **22** (Scheme 3). A significant observation is that the C−C bond cleavage occurs at *a* rather than at *b* even though *a* is a sterically more congested C−C bond than *b*.[17] If *b* were cleaved, **25** should have been formed after hydrolysis of **24**, but **25** was not determined.

Scheme 3





In this communication, we present C−C bond activations of various cycloalkanoketimines with and without 1-alkene by Rh(I) catalysts. Through the C−C bond activation by an Rh(I) catalysts, ring-opened alkenones are obtained with the addition of olefins, and skeletal-rearranged cycloalkanone derivatives are isolated without olefins.

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Supporting Information Available: Experimental procedures for preparation of cyclohexanoketimine **1b** and the catalytic C−C bond activation of **1c** with **2** and the skeletal rearrangement of **1c** by Rh(I) catalyst, including the characterization data for **1a**, **1b**, **1c**, **1d**, **1e**, **1f**, **1g**, **1h**, **4d**, **4e**, **4f**, **4g**, **6g**, **20**, and **21** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) The heating of cycloheptanone under $(PPh_3)_3RhCl$ (10 mol %) and 2-amino-3-picoline (100 mol %) at 150 °C for 48 h resulted in a mixture of **13c** and **14c** in a 27% yield (the ratio of **13c** and **14c** is 67:33).

(16) Ketimines of cycloalkanone larger than cyclononanone did not show any skeletal rearrangement either.

(17) If β-hydrogen elimination proceeds at the other side of a bridgehead as below, the starting intermediate **26** is regenerated through **27**. See: Olah, G. A. *Acc. Chem. Res.* **1976**, *9*, 41.