A Double Carbon-Carbon Bond Activation of 8-Quinolinyl Cyclopropyl Ketone by Chlorobis(ethylene)rhodium(I) Dimer

Dae-Yon Lee and Chul-Ho Jun*

Department of Chemistry, Yonsei University, Seoul 120-749, Korea
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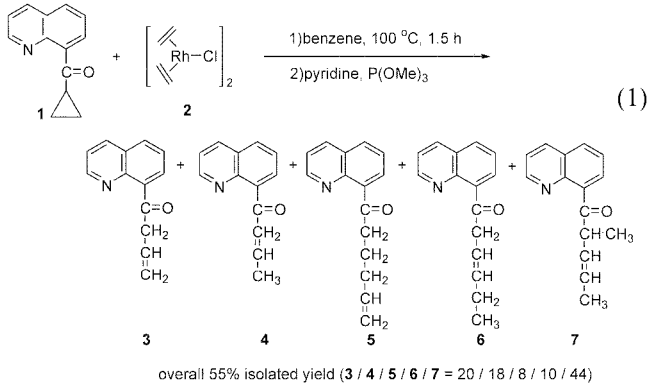
The activation of C-C bonds in organic molecules is one of current interests in organometallic chemistry especially due to its potential utility in synthetic method to form carbon skeleton, and a number of strategies have been devised in order to cleave C-C bond.[1] Among those strategies, it is the most common way to utilize the relief of ring strain energy of strained molecules such as cyclopropane, cyclobutane, and their derivatives.[2] Recently, a chelation-assistance protocol utilizing cyclometalation was developed to be regarded as one of the most promising ways as it could solve a problem concerning accessibility of metal complexes toward a C-C bond to be cleaved.[3] Quinoline derivatives are frequently used as cyclometalation models because they form very stable metal complexes,[4] and many preparation methods of quinolines are known.[5] In the course of our studies on a chelation-assisted C-C bond activation using 8-quinolinyl alkyl ketones, in which the C-C bond α to the carbonyl group could be easily cleaved by transition metal complexes,[4] we envisaged that a double C-C bond activation could be achieved when 8-quinolinyl alkyl ketone bearing a strained substituent such as cyclopropyl group was used as a substrate. In this communication, we wish to explain a consecutive chelation-assisted activation of the C-C bond α to the carbonyl group and a ring opening of cyclopropyl group using 8-quinolinyl cyclopropyl ketone.

In our experiment, cylcopropyl quinolin-8-yl methanone (**1**)[6] was allowed to react with a suspension of chlorobis-(ethylene)rhodium(I) dimer (**2**) in benzene at 100 °C for 1.5 h to give a dark brown precipitate. Since it was hard to isolate and identify the resulting reaction mixture due to complicated spectral data, the structures of these complexes were identified by those of ketones obtained through a ligand-promoted reductive elimination by pyridine and $P(OMe)_3$.



(1)

overall 55% isolated yield (**3** / **4** / **5** / **6** / **7** = 20 / 18 / 8 / 10 / 44)

After the reductive elimination, a mixture of (1-quinolin-8-yl)-but-3-en-1-one (**3**), (1-quinolin-8-yl)-but-2-en-1-one (**4**), (1-quinolin-8-yl)-hex-5-en-1-one (**5**), (1-quinolin-8-yl)-hex-3-en-1-one (**6**), and 2-methyl-(1-quinolin-8-yl)-pent-3-en-1-one (**7**)[7] was obtained in a 55% isolated yield with a ratio of 20 : 18 : 8 : 10 : 44 by column chromatographic isolation (eq. 1).

Among the products, 8-quinolinyl propenyl ketones, **3** and **4**, are derived from the ring opening of cyclopropyl group, and 8-quinolinyl pentenyl ketones, **5**, **6**, and **7**, are formed though the insertion of the ethylene into π-allylrhodium intermediate followed by isomerization.

Monitoring the ratio of products along the reaction revealed that the amount of 8-quinolinyl propenyl ketones (**3** and **4**) decreased while that of 8-quinolinyl pentenyl ketones (**5**-**7**) increased. Especially, the amount of **7** increased as reaction proceeded, and was the sole product after 48 h (Table 1). This result implies that precursor complexes of ketone **3** and **4** are the initial products, and then transform into those of **5**, **6**, and **7** as reaction proceeds.

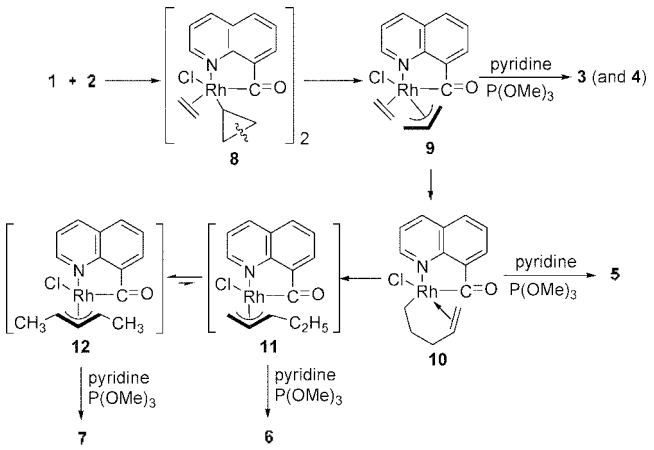
A plausible mechanism for the reaction is depicted in Scheme 1.

The first step of the reaction might be a chelation-assisted activation of the C-C bond α to the carbonyl group in **1** by **2** to give an acylrhodium(III) cyclopropyl complex **8**. Further ring opening of cyclopropyl group[2] in **8** generates an acylrhodium(III) π-allyl complex **9**, which gives **3** after the reductive elimination. This β,γ-unsaurated ketone **3** is so unstable that the terminal olefin is easily isomerized into internal olefin to afford the α,β-unsaturated isomer **4** during the reductive-elimination and/or chromatographic isolation

Table 1. The Reaction Profile for the C-C Bond Activation of 8-Quinolinyl Cyclopropyl Ketone (**1**) by Chlorobis(ethylene)rhodium(I) Dimer (**2**)[a]

Entry	Reaction time (h)	Ratio of products[b]					Isolated yield of products (%)
		3	**4**	**5**	**6**	**7**	
1	1.5	20	18	8	10	44	55
2	3	11	16	7	9	57	62
3	6	5	19	9	9	59	66
4	12	4	13	6	7	70	50
5	24	0	6	4	9	82	42
6	48	0	0	0	0	100	38

[a]The reaction was carried out in benzene at 100 °C, and then pyridine and $P(OMe)_3$ was added for a reductive elimination. [b]The ratio was determined by ^1H NMR after chromatographic isolation.



Scheme 1. A proposed mechanism of the reaction of 8-quinolinyl cyclopropyl ketone (**1**) and $[(C_2H_4)_2RhCl]_2$ (**2**).

processes. It is also possible that β-hydrogen elimination in **8** proceeds to form cyclopropene and acylrhodium(III) hydride, in which circumstance 8-quinolinyl ethyl ketone should be generated through an insertion of the coordinated ethylene and the reductive elimination.[8] However, 8-quinolinyl ethyl ketone was not observed, and it implies that β-hydrogen elimination in **8** does not take place because the formation of highly strained cyclopropene is not favored. A migratory insertion of the coordinated ethylene into acylrhodium(III) π-allyl complex **9** leads to the acylrhodium(III) 4'-pentenyl complex **10a**, which undergoes the reductive elimination to give **5**. There are very few examples of intermolecular insertion of olefin into the π-allyl-metal moiety[9] while this process is assumed as a key step in dimerization, oligomerizaiton or polymerization of diene.[10] The complex **10a** is easily transformed into a stable acylrhodium(III) η^3-1-ethylallyl complex **11**, which is further isomerized to more stable acylrhodium(III) η^3-1,3-dimethylallyl complex **12**. It was already reported that complex **11** is a kinetic product, and complex **12** is a thermodynamic product in the reaction of 8-quinolinecarboxaldehyde and chlorobis(1,4-pentadiene)rhodium(I) complex.[4a] A ligand-promoted reductive elimination of complex **11** and **12** produces the corresponding ketone **6** and **7**, respectively.

In conclusion, a double C-C bond activation of 8-quinolinyl cyclopropyl ketone, a consecutive chelation-assisted activation of the C-C bond α to the carbonyl group and the ring opening of cyclopropyl group, was achieved by chlorobis(ethylene)rhodium(I) dimer. An insertion of the coordinated ethylene into the resulting acylrhodium π-allyl complex afforded 8-quinolinyl pentenyl ketones through the subsequent isomerization.

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6. Compound **1** was prepared from the reaction of cyclopropanecarboxaldehyde and 8-lithio quinoline derived from *sec*-butyl lithium and 8-bromoquinoline, followed by Swern oxidation of resulting alcohol. **1**: ^{1}H NMR (250 MHz, $CDCl_3$): δ (ppm) 8.98 (dd, J = 4.2, 1.7 Hz, 1H), 8.17 (dd, J = 8.3, 1.7 Hz, 1H), 7.89 (m, 2H), 7.55 (m, 1H), 7.42 (m, 1H), 3.57 (m, 1H), 2.98 (m, 1H), 1.39 (m, 2H), 1.10 (m, 2H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ (ppm) 206.7 (CO), 151.1-121.8 (Cs of quinoline ring), 23.6 (α-carbon to CO), 13.2 (β-carbons to CO); IR (neat): 3074, 3006, 1675, 1574, 1497, 1447, 1380, 1253, 1059, 970, 830, 803, 767 cm^{-1}; MS *m/z* (% relative intensity): 197 (13.2, M$^+$), 169 (100), 156 (9.7), 128 (21); HRMS (EI) *m/z*: calcd for $C_{13}H_{11}NO$ 197.079594, found 197.079411.
7. A typical prodedure (eq.1): A screw-capped pressure vial (3 mL) was charged with 20.0 mg (0.0102 mmol) of **1**, 19.7 mg (0.058 mmol) of **2**, and 2 mL of benzene. The reaction mixture was stirred for 1.5 h in an oil bath preheated to 100 °C. After the reaction, the mixture was cooled to room temperature, and 150 mg of pyridine and 120 mg of $P(OMe)_3$ were added. After stirred for overnight, the reaction mixture was purified by column chromatography (SiO_2, *n*-hexane : ethyl acetate = 5 : 2) to afford 12.0 mg (55%) of a mixture of 8-quinolinyl alkenyl ketones **3**, **4**, **5**, **6**, and **7** in a ratio of 20 : 18 : 8 : 10 : 44 (determined by ^{1}H NMR). Among the products, **3** was inseparable as it is readily isomerized to more stable **4** during isolation processes. Therefore, compound **3** was identified by ^{1}H NMR and GC-MS. **3**: ^{1}H NMR (250 MHz, $CDCl_3$) δ(ppm): 8.98 (dd, J = 4.2, 1.7 Hz, 1H), 8.17 (dd, J = 8.3, 1.7 Hz, 1H), 7.89 (m, 2H), 7.55 (m, 1H), 7.42 (m, 1H), 6.12 (m, 1H), 5.18 (m, 2H), 4.20 (d, J = 6.9 Hz, 2H); MS m/z (% relative intensity): 197 (6.9, M$^+$), 182 (78.4), 169 (100), 156 (29.1), 154 (42.9), 128 (38.4). **4**: ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 8.98 (dd, J = 4.2, 1.7 Hz, 1H), 8.17 (dd, J = 8.3, 1.7 Hz, 1H), 7.89 (m, 2H), 7.55 (m, 1H), 7.42 (m, 1H), 6.80 (m, 2H), 1.95 (m, 3H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ (ppm): 196.5 (CO), 150.7-121.5 (Cs of quinoline ring and α,β-carbons to CO), 18.6 (CH_3); IR (neat): 2906, 2927, 2869, 1726, 1662, 1621, 1572, 1446, 1382, 1285, 1128, 1071, 967, 826, 796 cm^{-1}; MS *m/z* (% relative intensity): 197 (3.2, M$^+$), 182 (100), 168 (25), 156 (16), 154 (34.8), 128 (21.5). Other products, **5**, **6**, and **7** have already been reported (see ref. 4(a)).
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