and the acetoacetate support the above postulation.

The role of the aromatic aldehyde and the alkenyl ester function seemed to be crucial because no byproducts were obtained from the reactions with electron defficient aldehyde, for example 3-nitrobenzaldehyde, alkyl acetoacetates and alkyl aminocrotonates but 3-nitrobenzaldehyde with allyl acetoacetate gave the symmetric one[5]. 2,3-Dichlorobenzaldehyde with simply alkyl acetoacetates and alkyl 3-aminocrotonates also gave the byproducts. The extend researches are being undergone with various substituted aromatic aldehydes, alkyl or alkenyl aminocrotonates and acetoacetates. To avoid the formation of the minor side products the benzylidene intermediate should be applied[6].

Representative Procedure

The same molar amount (4.4 mmol) of 2,3-dichlorobenzaldehyde **1**, ethyl 3-aminocrotonate **2**, and 2-methyl-2-propenyl acetoacetate **3** was heated up to reflux in isopropyl alcohol with stirring for 6 hours. After cooling the solvent was removed in vacuo to give the oily product which was chromatographed on the silica gel with 30% ethyl acetoacetate in toluene.

The first running eluent (rf = 0.52) was collected and the solvent evaporated to give an oily product which was identified as di-2-methyl-2-propenyl 2,6-dimethyl-4 (2',3'-dichlorophenyl)-3,5-dicarboxylate **6** in 13.3% yield (by HPLC) [NMR($CDCl_3$) δ = 1.58, 1.70(each s, 3H,-CH_3), 2.80(s, 6H, -CH_3), 4.45(s, 4H, -OCH_2-), 4.65~4.90(m, 4H, =CH_2), 5.50(s, 1H, C_4-H), 5.66(b, 1H, =NH), 6.85~7.40(m, 3H, -Ph)]. The second eluent(rf = 0.49) was the major product which was turned out in NMR spectroscopy as ethyl 2-methyl-2-propenyl 2,6-dimthyl-4-(2',3'-dichlorophenyl)-3,5-dicarboxylate **4** in 72.6% yield (by HPLC) [NMR($CDCl_3$) δ = 1.20(t, 3H, -CH_3), 1.60 (s, 3H, -CH_3), 2.30(s, 6H, -CH_3), 4.07(q, 2H, -CH_2-), 4.45(s, 2H, -OCH_2-), 4.65~4.85 (m, 2H, =CH_2), 5.46(s, 1H, C_4 -H), 5.80(b, 1H, =NH), 6.85~7.35(m, 3H, -Ph)], The third eluent(rf = 0.45) was turned out as diethyl 2,6-dimethyl-4-(2', 3'-dichlorophenyl)-3,5-dicarboxylate **5** in 12.5% yield (by HPLC) [NMR($COCl_3$) δ = 1.18(t, 6H, -CH_3) 2.31(s, 6H, -CH_3), 4.07(q, 4H, -CH_2-), 5.46(s, 1H, C_4-H), 5.70(b, 1H, =NH), 7.06~7.32 (m, 3H, -Ph)].

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C-H Bond Activation and C-C Bond Activation: A New Synthesis of β,γ-Unsaturated Ketones *via* Acylrhodium(III) 1-Methylallyl Complexes Through a Hydride Insertion into Coordinated-Butadiene

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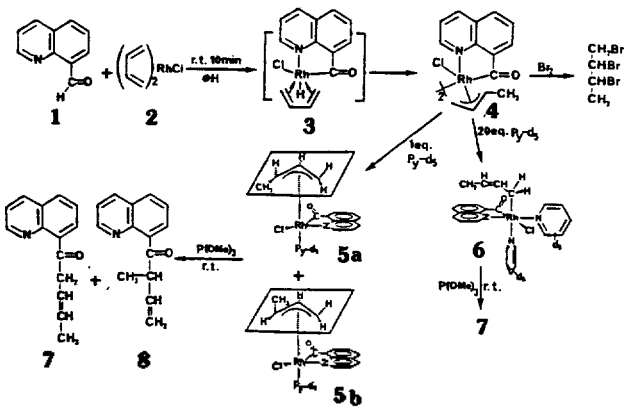
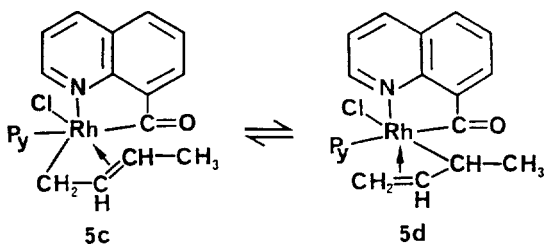
The activation of carbon-hydrogen bond[1] and carbon-carbon bond[2] by transition metal complexes has been one of the recent interests in organometallic chemistry. Especially a carbon-hydrogen bond of aldehyde can be easily broken by transition metals such as Wilkinson's catalyst, and subsequent decarbonylation gives alkanes[3]. This decarbonylation problem may be overcome through a cyclometallation to produce cyclopentanones since a five-membered ring is supposed to be a right size of a stable metallacycle complex[4]. The carbon-hydrogen bond of aromatic aldehydes can be activated by transition metals to give cyclometallated complexes without showing any decarbonylated products[5]. Also carbon-carbon bond activation in unstrained molecules having quinoline moieties has been reported[6]. Among them α,β-unsaturated ketones were not cleaved by rhodium(I) complexes even under vigorous conditions[7]. One of the target molecules to study is β,γ-unsaturated ketone since it was reported that the C-C bond of β,γ-unsaturated ketone is cleaved in a process of sigmatropic rearrangements in photochemical reactions via stable allyl radical species[8]. The synthesis of β,γ-unsaturated ketone is not facile[9]. This paper describes new synthesis of β,γ-unsaturated ketone through a C-H bond activation and a hydride insertion into butadiene coordinated to Rh(I) complex prepared by olefin exchange with bis-cyclooctene rhodium(I) chloride dimer[10].

8-quinolinecarboxaldehyde **1** reacted with a solution of $(C_4H_6)_2RhCl$ in benzene within 10 min to give an insoluble chlorine-bridged dimer **4**, which was isolated with pentane in 87% yield (scheme 1): decomp.>300 °C; Anal. Calcd for $C_{28}H_{26}Cl_2N_2O_2Rh_2$: C, 48.07; H, 3.72; N, 4.01. Found: C, 48.00; H, 4.08; N, 4.00. **4** can be solubilized by one equivalent of pyridine-d_5 to give the acylrhodium(III) 1-methylallyl complex **5**, five-coordinate species. η^3-1-methylallyl rhodium(III) complex **5** consists of two isomers, *anti*-η^3-1-methylallyl rhodium complex **5a** and *syn*-η^3-1-methylallyl rhodium complex **5b** in 62:38 ratio determined by ^1H NMR spectra: the methyl peaks of η^3-1-methylallyl group in **5a**; ^1H NMR($CDCl_3$) δ(ppm) 0.5(d, 3H J = 6.0Hz, CH_3), those of η^3-

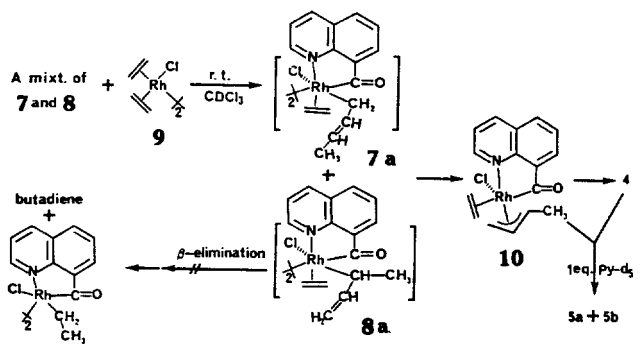


Scheme 1. Synthesis of β,γ-Unsaturated Ketones via C-H Bond Activation.

1-methylallyl group in **5b**; ^{1}H NMR($CDCl_3$) δ(ppm) 1.6(d, 3H, J = 5.7Hz, CH_3)[11]. The carbonyl IR bands in **1** at 1690 cm^{-1} were shifted to 1640 cm^{-1} in **5**. Treatment of the chlorine-bridged dimer **4** with Br_2 generated 1,2,3-tribromopropane identified by ^{1}H NMR spectra. Trimethylphosphite caused facile ligand-promoted reductive elimination[2] of **5a** and **5b** to two different β,γ-unsaturated ketones in 73% yield, **7** and **8** in 80:20 ratio determined by ^{1}H NMR spectra after purification by column-chromatography with an identical R_f value: **8**; ^{1}H NMR($CDCl_3$) δ(ppm) 1.4(d, 3H, CH_3), 4.65(m, 1H, CH), 5.1(m, 2H, $=CH_2$), 5.7(m, 1H, -CH=), 7.3-8.3(m, 5H, quinoline ring protons), 8.9(dd, 1H, quinoline C-2 proton): TLC R_f = 0.42, hexane:ethylacetate = 5:2, SiO_2. η^3-1-methylallyl rhodium(III) complexes, **5a** and **5b**, are fluxional on the NMR time scale: η^1-methylally attached to a metal by a metal-carbon σ-bond undergoes intramolecular rearrangements as shown in scheme 2[13a]. Therefore generations of **7** and **8** can be explained by reductive elimination of **5c** and **5d** respectively. On increasing the concentration of pyridine-d_5(twenty-fold excess), two diastereotropic protons appear at 2.4 ppm (td, 1H) and 3.1 ppm (td, 1H), those of a six-coordinate species **6**. It can be explained that excess pyridine not only cleaves the chlorine-bridged dimer in **4** but also displaces the olefinic pi-bond in η^3-1-methylallyl group to hold the 18 electron rule[13b]. Ligand-promoted reductive elimination with trimethylphosphite of **6** and chromatic isolation gave only **7** in 87% yield: IR(neat) 3010, 2910, 1685, 1560, 1490, 970, 830, 790 cm^{-1}; ^{1}H NMR($CDCl_3$) δ(ppm) 1.6(d, 3H, CH_3), 4.1(d, 2H, CH_2), 5.7(m, 2H, -CH=CH-), 7.3-8.3(m, 5H, quinoline ring protons), 8.9(dd, 1H, quinoline C-2 proton): Anal Calcd for $C_{14}H_{13}NO$: C, 79.62; H, 6.16; N, 6.63. Found: C, 78.80; H, 6.31; N, 6.43.



Scheme 2. Fluxional System for η^3-1-Methylallyl Rhodium(III) Complex.



Scheme 3. C-C Bond Activation of β,γ-Unsaturated Ketones, 7 and 8.

When $[(C_2H_4)_2RhCl]_2$ and **7** was reacted at room temperature for 30 min in $CDCl_3$, initially the red solution was formed, and became an insoluble yellow chlorine-bridged dimer **4**. The red solution is supposed to be **10** since it is a soluble monomer and addition of pyridine-d_5 caused evolution of ethylene coordinated to the rhodium complex (Scheme 3). Addition of one equivalent of pyridine-d_5 to each of **10** and **4** gave the same ratio of **5a** and **5b**. Primary alkyl ketone **7** and secondary alkyl ketone **8** showed different reactivities at room temperature for C-C bond activation with **9**. When a mixture of **7** and **8** reacted with **9** at room temperature, ^{1}H NMR peaks of **8** had disappeared through 48 hrs while those of **7** were lost in 30 min to form **5a** and **5b** with treatment of pyridine-d_5. The difference of reaction rates between **7** and **8** may be due to a steric hindrance toward **9**: the C-C bond of the primary alkyl ketone **7** must be of access more readily to a rhodium metal center of **9** than that of secondary alkyl ketone **8**. **7a** and **8a** can be counted as intermediates of C-C bond activation in **7** and **8**. Still there is a possibility for **8a** to undergo β-elimination forming butadiene and the rhodium hydride which should have been trapped by ethylene leading to ethylation[14]. However any of these species was not observed in the reaction products. Heating **4** in toluene-d_8 did not show any β-eliminated product even at 100 °C. This confirms that η^3-1-methylallyl rhodium(III) complex **4** is thermodynamically very stable compared with saturated n-alkyl rhodium complexes which is used to decompose through β-elimination.

Other C-H bond activation and C-C bond activation with olefin-coordinated rhodium complexes is under investigation.

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Synthesis of Chain-Extended Nucleosides

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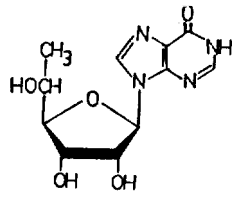
As a group of compounds, nucleosides have few rivals in the vast realm of the natural products, with regard to diversity in biological function. A great number of synthetic nucleosides have been reported and their biological activities have been tested. Recent extensive studies on antiviral drugs have further promoted synthesis of new types of nucleosides one of which is the chain-extended nucleosides. For example, C-5′ modified nucleoside **1** strongly inhibit purine nucleoside phosphorylase.[1] Another chain-extended nucleoside **2**, which is a carboxyl analog of adenosine 5′-phosphate, is the substrate of AMP metabolizing enzymes.[2] Arabinonucleosides **3** and **4** are active against herpes simplex virus type I.[3] 4′-Homoara-C, **5**,[4] ethylenic nucleoside **6**,[5] and acetylenic nucleoside **7**[6] have also antiviral and antileukemic activities. Despite of the promising biological activities of the chain-extended nucleosides, their synthetic and biological studies are yet rather scarce compared with other types of modified nucleosides.

Herein we report the synthesis of several new chain-extended nucleosides as potential antiviral agents. We expected that heptofuranose nucleoside **8** would be readily obtained from nucleoside aldehyde **9** with ylide **10**. Suprisingly, however, Howgate and coworkers[7] have reported that no reaction occurred between **9** and **10**. We reinvestigated the reaction of **9** with **10**. Oxidation of **11** with dimethyl sulfoxide and dicyclohexylcarbodiimide afforded aldehyde **9**. Without isolation of **9**, it was allowed to react with ylide **10** for 24h at room temperature to afford pure **8** in 75% yield after chromatography. The reason for Howgate's failure to obtain **8** is not clear but we speculate that Howgate and co-workers might not detect and, therefore, could not isolate the desired produt actually generated in the reaction mixture because we found R_f value of the starting aldehyde **9** and that of the product **8** were same on the TLC plates using various eluents.



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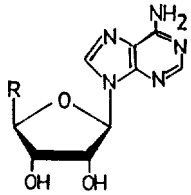
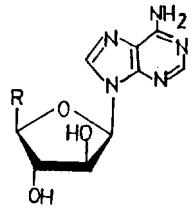
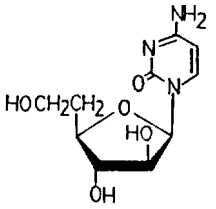


2 R=$-CH_2CH_2CO_2H$
6 R=$-CH{=}CH_2$



3 R=$-CH_2CH_2CH_2OH$
4 R=$-CH_2CH_2CONH_2$



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Hydrolysis with formic acid and subsequent catalytic hydrogenation of **8** gave another heptofuranose nucleoside **12** in 80% yield. Conversion of **8** to **13** was troublesome. Thus, reduction of **8** with lithium aluminum hydride at room temperature gave a complex mixture of products and the reaction was very slow at lower temperature. Lithium borohydride, however, nonselectively reduced **8** to **14** in 60% yield. But slow addition of DIBAL-H into the solution of **8** in THF at −78 °C afforded **13** in 65% yield and the subsequent hydrolysis of isopropylidene group of **13** with formic acid afforded **15** in 90% yield. In order to obtain a bicyclic nucleoside **17**, lactonization of **12** under various conditions and with several reagents were attemp-