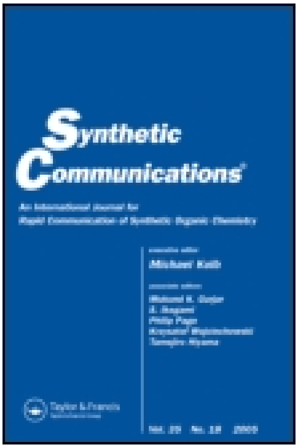

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ReBr(CO)$_5$-Catalyzed Knoevenagel Condensation

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ReBr(CO)$_5$-Catalyzed Knoevenagel Condensation

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ABSTRACT

The Knoevenagel condensation procedure has been efficiently promoted by using a catalytic amount of ReBr(CO)$_5$ to afford the corresponding dehydration coupling products in high yields.

Key Words: Rhenium complex; Knoevenagel condensation; Transition metal catalysis.

Knoevenagel condensations are especially important reactions for the synthesis of alkene compounds having electron-withdrawing groups such as

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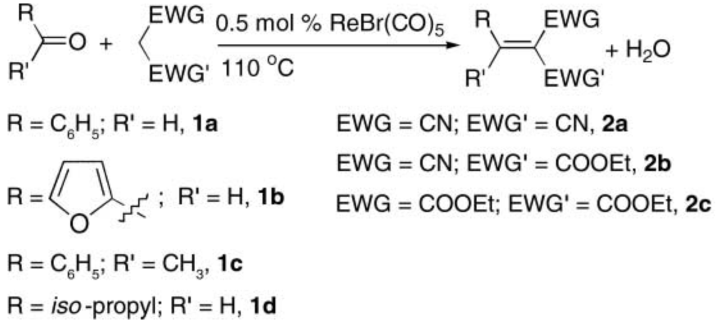
COR, CN, COOR, and NO_2. The reactions, which have been long known, are usually catalyzed by bases, acids, and solid catalysts, and the obtained alkenes are widely used as synthetic intermediates.[1] Recently, transition metal hydride ruthenium,[2] hydride and polyhydride rhenium,[3] and polyhydride iridium[3b]) complexes have been found to be the efficient catalysts for Knoevenagel condensation. However, the above mentioned transition metal hydride complexes are not easy to prepare. In addition, all of them are oxygen- and H_2O-sensitive, unstable compounds. Therefore, the catalytic reactions are required to be carried out under an inert atmosphere and using the prepurified reagents. In this paper, we report the development of Knoevenagel condensation catalyzed by $ReBr(CO)_5$ under an air atmosphere in the absence of solvent.



(1)

Aromatic and aliphatic aldehydes or aromatic ketones **1** readily reacted with active methylene compounds **2** in the presence of a catalytic amount of $ReBr(CO)_5$ to give the corresponding dehydration coupling products **3** in high yields (Eq. (1). The results of the representative Knoevenagel condensation are summarized in Table 1. $ReBr(CO)_5$-catalyzed Knoevenagel condensations were carried out in the absence of solvent by using equivalent amounts of **1** and **2** at 110°C.[a] In a typical experiment, a mixture of benzaldehyde **1a** (0.53 g, 5 mmol), malononitrile **2a** (0.33 g, 5 mmol), and $ReBr(CO)_5$ (11 mg, 0.025 mmol) was stirred at 110C for 1.5 hr. After cooling to room temperature, it solidified and then was treated with 5% aqueous ethanol. The crude 2-cyano-3-phenylacrylonitrile **3a** was obtained by filtration, washed with 5% aqueous ethanol, and dried in vacuum

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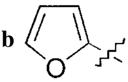
[a] All starting materials and $ReBr(CO)_5$ were analytic grade and used without further purification.

Table 1. ReBr(CO)$_5$-catalyzed Knoevenagel.[a]

Entry	R	R′	EWG	EWG′	Time (hr)	Yield (%)[b]
1	**1a** C_6H^5	H	**2a** CN	CN	1.5	**3a** 90
2			**2b** COOEt	CN	2	**3b** 88
3			**2c** COOEt	COOEt	5	**3c** 61
4	**1b** 	H	**2a**		2	**3d** 97
5			**2b**		3	**3e** 92
6	**1c** C_6H_5	CH_3	**2a**		50	**3f** 90
7[c]			**2b**		70	**3g** 45
8	**1d** iso-propyl	H	**2c**		4	**3h** 84

[a]Reactions were carried out at 110°C by using 5.0 mmol of **1**, 5.0 mmol of **2**, and 0.025 mmol of ReBr(CO)$_5$ in the absence of solvent.

[b]Isolated yields.

[c]Reaction was performed at 130°C.

[0.69 g, yield: 90%; purity: 98% by gas chromatography (GC)] (entry 1).[b] If the reaction was performed at 90°C, the yield of **3a** was decreased greatly ($<$10%).

The reaction of **1a** with ethyl cyanoacetate **2b** afforded selectively the corresponding condensation product ethyl (*E*)-2-cyano-3-phenylpropenoate **3b** in 88% yield (entry 2). The dehydration of **1a** with diethyl malonate **2c** at 110°C for 5 hr gave ethyl 2-(ethoxycarbonyl)-3-phenylpropenoate **3c** in 61% yield (entry 3). Similarly, 2-furaldehyde **1b** reacted with **2a** and **2b** to give products 2-cyano-3-(2-furanyl)-acrylonitrile **3d** and ethyl (*E*)-2-cyano-3-(2-furanyl)propenoate **3e** in 97% and 92% yields, respectively (entries 4 and 5). Contrast to aromatic aldehydes **1a** and **1b**, under the same conditions, ketone displayed low reactivity. For example, the dehydration coupling reactions of phenylacetone **1c** with **2a** required a prolonged reaction time to achieve the satisfactory yield of 1,1-dicyano-2-phenyl-propene **3f** (50 hr, 90%, entry 6). The reaction of **1c** with **2b** at 130°C for 70 hr afforded the dehydration products 2-cyano-3-phenyl-2-butenoate **3g** in 45% yield as a mixture of stereoisomers (E/Z = 3/2). The use of an excess of amount of **1c** or **2b** did not improve the yield (entry 7). In addition, ReBr(CO)$_5$ also catalyzed the dehydration of aliphatic aldehydes with active methylene compounds. In the

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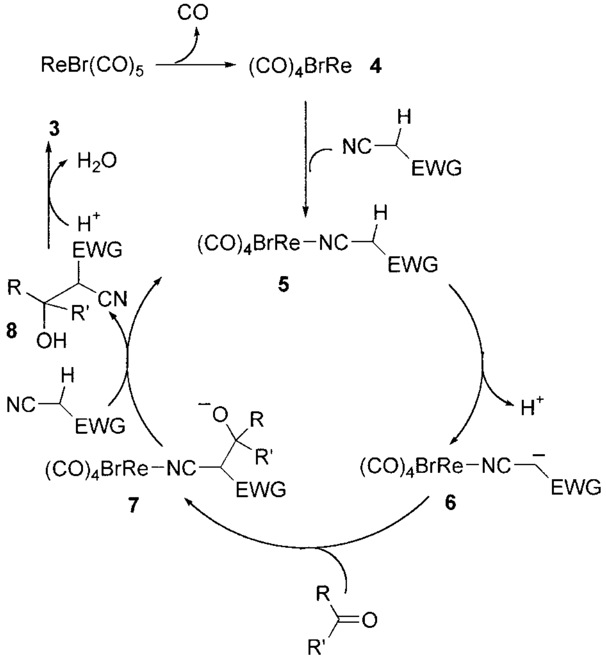
[b]The solid products were further purified by recrystallization from ethanol or aqueous enthanol, and the oil products were obtained by distillation in vaccum. All products obtained are known compounds and were confirmed by ^{1}H NMR and melting points by comparison with data reported in the literature.



Scheme 1. Proposed catalytic mechanism.

case of the reaction of isobutyraldehyde **1d** with **2c**, after heating for 4 hr, the expected product ethyl 2-(ethoxycarbonyl)-4-methylpentenoate **3h** was obtained in 84% yield (entry 8).

Other rhenium complexes such as $ReCl(CO)_5$ and $Re_2(CO)_{10}$ showed very low catalytic activity for the Knoevenagel condensation.

Although the detailed mechanism for $ReBr(CO)_5$-catalyzed Knoevenagel condensation remains to be elucidated, a proposed mechanism for the reactions of nitriles with carbonyl compounds is illustrated in Sch. 1. The reaction initiates by the decarbonylation of $ReBr(CO)_5$ to give 16-electron of intermediate $ReBr(CO)_4$ **4**, which has been reported to be generated from $ReBr(CO)_5$ in refluxing toluene.[4] The coordination of the nitrile to **4** would give complex **5**, which might undergo deprotonation to give the carbanion intermediate **6**.[c] The addition reaction of carbanion to C=O bond

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[c] One reviewer proposed that the carbanion in the intermediate **6** might be generated by deprotonation from **5** by a base, such as H_2O.

to give **7**,[3] which affords **8** and regenerates **5**. Compound **8** undergoes dehydration to afford alkene **3**.

In conclusion, we have developed a new transition metal complex $ReBr(CO)_5$-catalyzed Knoevenagel condensation to afford the dehydration coupling products in good yields. Further investigations on the application of this commercial complex on other catalytically synthetic reactions are in progress.

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