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Diphenylboron perchlorate as an efficient catalyst for self- and cross-condensation reactions of aldehydes having α-active hydrogens

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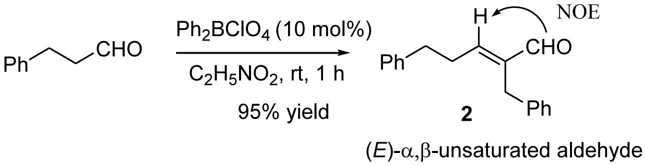
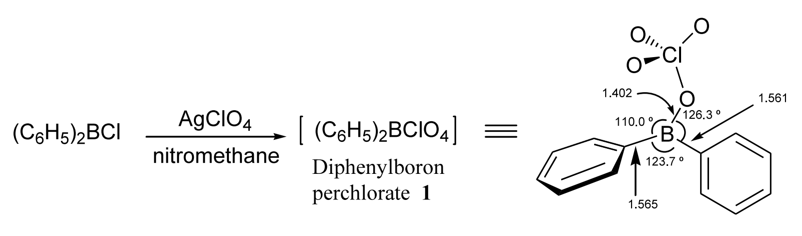
Abstract—Diphenylboron perchlorate very smoothly catalyzed self- and cross-condensation reactions of aldehydes at rt in nitroethane. The new catalyst provided novel behaviors owing to the characteristics of possessing a covalency in the boron–oxygen bond, compared with ionic perchlorates. © 2003 Elsevier Science Ltd. All rights reserved.

Diphenylboron perchlorate **1**,[1] prepared from Ph_2BCl and $AgClO_4$ in nitromethane, has a covalent character in the B–O bond, as investigated by the ^{11}B NMR and ab initio calculation (Scheme 1).[2] The perchlorate **1** was expected, therefore, to possess catalytic activities different from those of ionic trityl perchlorate.[3] Actually, the Mukaiyama aldol reaction of aldehydes with 1-phenoxy-1-trimethylsiloxyethene did not proceed in the presence of **1** (10 mol%) in nitroethane at −78°C for 3 h. This non-reactivity evidently reflects either the lack of Lewis acidity necessary for the aldol reaction or the existence of somewhat different actions in the reaction. When aldehydes having α-hydrogens to the carbonyl group were stirred at rt under similar conditions without silyl nucleophiles, the reaction led to the corresponding self-condensed α,β-unsaturated aldehydes in high yields.[4] Self-condensation reactions under classical conditions did not necessarily result in good yields of aldols and their dehydration products for a variety of aldehydes.[5] Recently, enolizable aliphatic aldehydes were reported to undergo self-condensation to the corresponding α,β-unsaturated aldehydes in the presence of a stoichiometric amount of titanium tetraalkoxide.[6] Studies on aldehyde condensations are under further development and are shifting to enantioselective cross-aldol reactions.[7] We disclose herein catalytic self- and cross-aldol reactions to (*E*)-α,β-unsaturated aldehydes by using a novel catalyst, Ph_2BClO_4 **1**.

Self-condensation reaction of hydrocinnamaldehyde took place very smoothly in the presence of 10 mol% of **1** in nitroethane at rt for 1 h to give selectively (*E*)-5-



Scheme 2. A catalytic self-condensation reaction of hydrocinnamaldehyde.



Scheme 1. Covalent character of the B–O bond of **1**.

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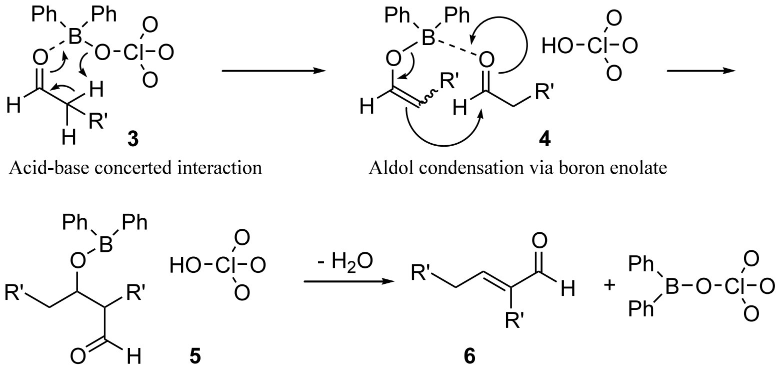
phenyl-2-(phenylmethyl)-2-pentenal **2** in 95% yield, as shown in Scheme 2.[8] The olefinic double bond of the compound was confirmed to be *E*-configuration by NOE experiments. Ketones and esters did not undergo the corresponding self-condensation under these conditions at all. The novel catalytic feature of **1** can be rationally explained with the geometrical selectivity to (*E*)-olefin, as follows: The structural characteristics are particularly attributable to the unique catalytic ability which induces an acid-base concerted interaction with an aldehyde having two hydrogen atoms α to the carbonyl group (Scheme 3).[9] Ph_2BClO_4 **1** might play the two roles of carbonyl group activation by the boron atom (as an acid) and hydrogen abstraction by the perchlorate oxygen atom (as a base) so as to convert the aldehyde to their *Z*-enol borinate, depicted in **A** of Scheme 3.[7a] The boron enolate obtained proceeds to the successive aldol condensation to afford *syn*-aldol[10] (in **B** of Scheme 3) which should be dehydrated to (*E*)-olefin **2** (in **C** in Scheme 3) along with regeneration of the catalyst **1**.

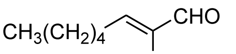
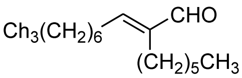
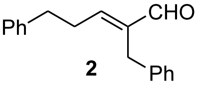
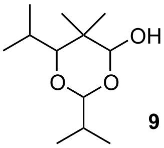
The higher homologs of aldehydes also underwent the self-condensation reaction to give the corresponding (*E*)-α,β-unsaturated aldehydes in good yields (entries 1 and 2 in Table 1). The reaction with a branched homolog resulted in the formation of an acetal, trapped with the starting aldehyde because the normal dehydration is impossible (entry 4). The cross-condensation reaction between aldehydes having α hydrogens (1 equiv.) and aryl aldehydes (4 equiv.) was realized to introduce (*E*)-α,β-unsaturated aldehydes in moderate yields with a small amount of the self-condensation products, as shown in Table 2. The reaction of



Scheme 3. A plausible mechanism of dimerization reaction catalyzed by diphenylboron perchlorate.

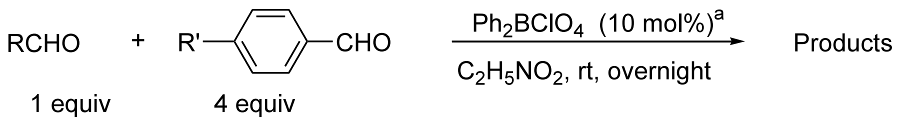
Table 1. Diphenylboron perchlorate-catalyzed self-condensation reaction of aldehydes

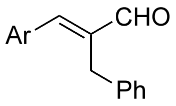
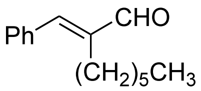
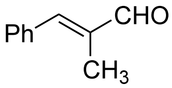
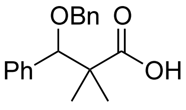
$$\text{RCHO} \xrightarrow[\text{C}_2\text{H}_5\text{NO}_2\text{, rt, 1 h}]{\text{Ph}_2\text{BClO}_4\text{ (10 mol\%)}^a} \text{Product}$$

Entry	R	Product	Yield (%)[b]
1	$CH_3(CH_2)_4$-	 $CH_3(CH_2)_4$ CHO $(CH_2)_3CH_3$ **7**	97
2	$CH_3(CH_2)_6$-	 $Ch_3(CH_2)_6$ CHO $(CH_2)_5CH_3$ **8**	95
3	$Ph(CH_2)_2$-	 Ph CHO Ph **2**	95
4	$(CH_3)_2CH$-	 OH O O **9**	54

[a] Diphenylboron perchlorate was prepared from Ph_2BCl (0.2 mmol) and $AgClO_4$ (0.2 mmol). [b] Yields were determined by ^1H NMR.

Table 2. Diphenylboron perchlorate-catalyzed cross-condensation reaction of aryl aldehydes and aldehydes having α-hydrogens



Entry	R	Product[b]		Yield (%)[c]
1	$Ph(CH_2)_2$-		**10** (R' = H)	90
			11 (R' = CH_3)	70
			12 (R' = Ph)	62
			13 (R' = MeO)	82
			14 (R' = NO_2)	33
2	$CH_3(CH_2)_6$-		**15** (R' = H)	76
3	CH_3CH_2-		**16** (R' = H)	57
4	$(CH_3)_2CH$-		**17** (R' = H)	69

[a] Diphenylboron perchlorate was prepared from Ph_2BCl (0.2 mmol) and $AgClO_4$ (0.2 mmol).

[b] The major product was obtained with a small amount of the corresponding self-condensation product. [c] Yields were determined by ^1H NMR.

butyraldehyde with benzaldehyde afforded an interesting compound, which was confirmed to be 3-benzyloxy-2,2-dimethyl-3-phenylpropanoic acid, in a good yield (entry 4 in Table 2).[8] Although Tishchenko reactions, coupled with aldol reactions, are frequently observed,[11] this is not the case. The formation of the carboxylic acid **17** can be accounted for by intramolecular oxidation of the terminal aldehyde, that is, an intramolecular Cannizzaro reaction, as depicted in Scheme 4.

Diphenylboron perchlorate **1** turned out to be an efficient catalyst for self- and cross-condensation reactions of aldehydes having α-active hydrogens. The effectiveness of **1** for aldehyde condensations presumably arises from its binary characteristics of an acid and a base owing to the structural feature of a covalent boron-oxygen bonding of **1**. For the purpose of direct comparison of the reactivity depending on the bonding mode, study of the diphenylboron cation expected to be ionic is now in progress by changing the counter anion.

Acknowledgements

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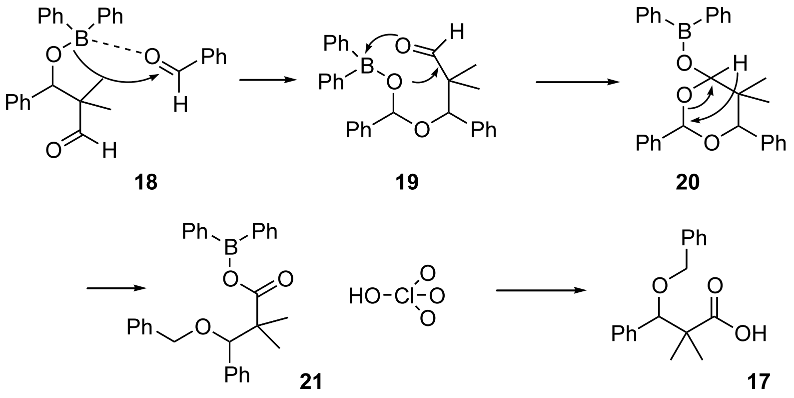

Scheme 4. A plausible pathway to **17** via an intramolecular Cannizzaro reaction.

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4. Ph_2BCl did not undergo the self-condensation. When $AgClO_4$ alone was used, the cyclic trimer of aldehydes was obtained in high yields.
5. (a) Nielsen, A. T.; Houlihan, W. J. *Organic Reaction*; John Wiley & Sons: New York, 1968; Vol. 16, pp. 1–438: Catalysts reported; NaOH, $POCl_3$, $SOCl_2$, H_2SO_4, KOH, $NaOCH_3$, $K[B(OCH_3)_4]$, K_2CO_3, $Al(OC_3H_7)_3$, ion-exchange resin, NaHg, C_2H_5OMgCl, CaO, $Zn(C_2H_5)_2$, and $(C_6H_5CO_2)_2Cu$; (b) House, H. O. *Modern Synthetic Reactions*; W. A. Benjamin: Menlo Park, 1972; pp. 629–653: A variety of catalysts were reported for the reactions between two molecules of the same aldehyde and between two different aldehydes to give aldols and/or their dehydration products under equilibrium.
6. (a) Mahrwald, R.; Schick, H. *Synthesis* **1990**, 592; (b) Mahrwald, R.; Costisella, B.; Gündogan, B. *Tetrahedron Lett.* **1997**, *38*, 4543: The reaction aldehydes with large excess of $TiCl_4$ and TMEDA gave *syn*-3-hydroxyaldehydes.
7. (a) Denmark, S. E.; Ghosh, S. K. *Angew. Chem., Int. Ed.* **2001**, *40*, 4759; (b) Northrup, A. B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2002**, *124*, 6798.
8. (*E*)-5-Phenyl-2-(phenylmethyl)-2-pentenal **2**: To a stirred solution of Ph_2BCl (0.2 mmol, 40 mg) in nitroethane (2 mL) was added a solution of $AgClO_4$ (0.2 mmol, 41 mg) in nitroethane (3 mL) at rt under Ar. After stirring for 1 h at this temperature, hydrocinnamaldehyde (2.0 mmol, 260 μL) was added. After 1 h, the excess of nitroethane was removed. The crude product was purified by flash column chromatography to give the α,β-unsaturated aldehyde (250 mg, 95% yield). IR (KBr) 2926, 1685 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.69–2.79 (m, 4H), 3.58 (s, 2H), 6.61 (t, $J=6.8$ Hz, 1H), 7.09–7.31 (m, 10 H), 9.44 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 29.6, 31.0, 34.4, 126.1, 126.4, 128.2, 128.3, 128.5, 128.6, 139.0, 140.4, 142.8, 154.7, 194.5. 3-Benzyloxy-2,2-dimethyl-3-phenylpropanoic acid **17**: IR (KBr) 2974, 1705 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 1.15 (d, $J=2.2$, 6H), 4.31 (d, $J=11.6$, 1H), 4.51 (d, $J=11.6$, 1H), 4.62 (s, 1H), 7.25–7.39 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 18.7, 23.0, 47.8, 71.1, 85.3, 127.5, 127.6, 128.0, 128.1, 128.5, 137.0, 138.0, 182.5. After evaporation of the nitroethane solvent, the self- and cross-condensation reactions of aldehydes in dichloromethane took place smoothly with nearly the same level of yield. In the cross-condensation the use of 4 equiv. of aromatic aldehydes is appropriate for lowering the yield of the corresponding self-condensation products.
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