A Novel Carbocationic Species Paired with Tetrakis(pentafluorophenyl)borate Anion in Catalytic Aldol Reaction

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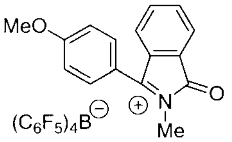
The aldol reaction of several aldehydes with silyl enol ethers proceeded smoothly to give the corresponding aldols in good to high yields at -78 °C by using 1.0 mol% of a novel cationic species with tetrakis(pentafluorophenyl)borate anion.

The reaction of silyl enol ethers which are stable and isolable carbon nucleophiles with activated carbonyl compounds is one of the most versatile synthetic tools for the carbon-carbon bond formation.[1] Although Lewis acids such as $TiCl_4$, $SnCl_4$, $BF_3{\cdot}OEt_2$, etc. are frequently employed in these reactions as useful promoters, it is still strongly desired to explore a new and effective catalyst which accelerates the reactions under essentially neutral conditions.

Previously, we had demonstrated that trityl salts such as triphenylmethyl perchlorate were unique and excellent catalysts in several synthetic reactions.[2] For example, the trityl salts effectively catalyzed the aldol reaction of silyl enol ethers with acetals or aldehydes to afford the desired aldols in good to high yields.[3] One of the most characteristic features was that these reactions were accelerated smoothly by using a catalytic amount (5–10 mol%) of the trityl salts because of their unique carbocationic properties. Existence of similar carbocationic species was proposed in 1970 by W. L. F. Armarego by preparation of several salts such as 1-oxoisoindolium hexachloroantimonate. They proposed that the salts existed as the stable cationic species in benzene by measuring their NMR, IR and mass spectroscopies.[4] Here, further development of a useful catalyst like trityl salts was tried based on those results, and a novel carbocationic species **1** having tetrakis(pentafluorophenyl)borate as a counter anion was found to be an effective catalyst in aldol reaction. In the present study, methoxy group was introduced onto the phenyl group located at 3-position because it would increase the stability of this cationic species. In this communication, we would like to report the catalytic aldol reaction of several aldehydes with silyl enol ethers or ketene silyl acetals by utilizing the novel and stable cationic species **1**.[5]



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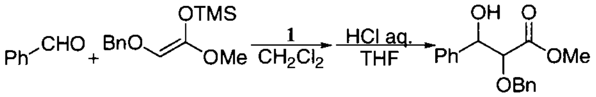
In the first place, several conditions were screened in order to optimize the amount of catalyst **1** in the aldol reaction. As shown in Table 1, only 0.1 mol% of **1** accelerated the reaction to give the desired aldol in a good yield. Thereafter, 1.0 mol% of **1** was used in the experiments in order to avoid any errors caused by the scale effect of the reaction.

Table 1.



Entry	1 / mol%	Yield / %	Time / h	Temp / ˚C
1	1.5	94.5	0.5	-78
2	1.0	94.5	0.5	-78
3	0.5	97.1	1.5	-78
4	0.1	83.2	21[a]	-78 - rt[a]

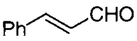
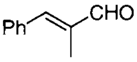
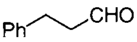
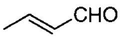
[a] Reaction was carried out at -78 ˚C for 4 h then rt for 17 h.

A typical procedure for the reaction of a silyl enol ether or a ketene silyl acetal with an aldehyde is as follows: **1** (0.005 mmol) was dissolved in 0.5 mL of dichloromethane, and to the solution, an aldehyde (0.5 mmol) in 1.0 mL of dichloromethane and a silyl enol ether or a ketene silyl acetal (0.75 mmol) in 2.0 mL of dichloromethane were added at -78 ˚C. The mixture was stirred for 30 min, followed by the addition of aqueous sodium hydrogencarbonate. The aqueous layer was extracted with ethyl acetate and the organic layer was evaporated. The residue was dissolved in tetrahydrofuran and 1 M hydrochloric acid was added to the solution. The mixture was stirred for 15 min at room temperature and then the reaction mixture was extracted with ethyl acetate. The organic layer was evaporated and the residue was purified by preparative TLC to give an aldol adduct. Several examples of the addition reactions are summarized in Table 2.

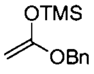
In almost all cases, the reaction proceeded smoothly to afford the desired aldol in a high yield. In case of using 3-phenylpropanal as a carbonyl component, however, the reaction was slow and the yield decreased even when the reaction was continued for over 2 h (Entry 17-19). As compared with trityl salt such as trityl tetrakis(pentafluorophenyl)borate,[6] the present catalyst **1** accelerated this reaction slightly more effectively (Entry 1 vs 2, Entry 4 vs 5 and Entry 6 vs 7). Thus, it is noted that **1** has better potential to accelerate the aldol reaction equally or slightly more effectively compared to that of trityl salts. The characteristic behavior was further demonstrated when cinnamaldehyde, an α,β-unsaturated aldehyde, was used (Entry 10 vs 11, Entry 12 vs 13); that is, the Michael adduct was obtained along with the aldol nearly in the same yields.[7] This is a little different from the general pattern of nucleophilic addition reaction which gives 1,2-adduct exclusively.[8]

Compound **1** was prepared from phthalic anhydride by 4 steps procedure (Scheme 1). Namely, phthalic anhydride was treated with 4-methoxyphenylmagnesium bromide in tetrahydrofuran to give the benzoic acid derivative **6**. According to the procedure reported by Stoll,[9] it was transformed to **7** with intramolecular cyclization followed by a simple amidation of

Table 2.[a,b]

Entry	Aldehyde	Nucleophile	Yield / %, (ratio)[d]
1	PhCHO	**2**	88.4
2[c]		**2**	80.1
3		**3**	83.6
4		**4**	94.5[e]
5[c]		**4**	79.9[e]
6		**5**	72.7
7[c]		**5**	51.7
8		**2**	90.5 (100 : 0)
9		**3**	84.1 (58 : 42)
10		**4**	82.3 (55[f] : 45[g])
11[c]		**4**	49.4 (100[h] : 0)
12		**5**	83.1 (89 : 11)
13[c]		**5**	69.6 (92 : 8)
14		**2**	86.1 (100 : 0)
15		**3**	76.9 (94 : 6)
16		**4**	88.7 (95[i] : 5[j])
17		**2**	58.4
18		**3**	42.2
19		**4**	40.8[j]
20		**2**	81.0 (97 : 3)
21		**3**	83.6 (75 : 25)
22		**4**	79.1 (69[k] : 31[l])

[a] Reaction Conditions: See text. [b] Relative configulations of all diastereomers in this table were not determined. [c] Trityl tetrakis(pentafluorophenyl)borate was used instead of **1**. [d] The values in parenthesis is the ratio of aldol adduct : Michael adduct. [e] Diastereomeric ratio(Dr); 50 : 50. [f] Dr; 75 : 25. [g] Dr; 77 : 23. [h] Dr; 72 : 28. [i] Dr; 82 : 18. [j] Dr; not determined. [k] Dr; 72 : 28. [l] Dr; 72 : 28.



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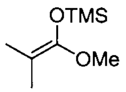

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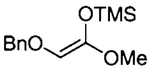

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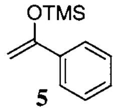

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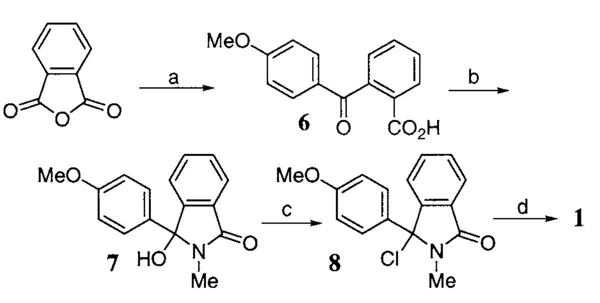
the caboxyl group, and the resulting lactam **7** was in turn transformed into the corresponding chloride **8** on treatment with thionyl chloride in dichloromethane. This intermediate was treated with lithium tetrakis(pentafluorophenyl)borate in boiling pentane and dichloromethane to form **1**.[6]



Reagents and conditions: a. 4-MeO-PhMgBr / THF, 73.6%; b. $SOCl_2$, $MeNH_2$ / THF, 92.1%; c. $SOCl_2$ / CH_2Cl_2; d. $LiB(C_6F_5)_4$ / pentane, CH_2Cl_2, 57.9% from **7**.

Scheme 1.

Several derivatives of **1** were easily prepared by this protocol involving the Grignard reaction and simple amidation. For example, sterically hindered carbocationic species can be prepared when isopropylamine was used instead of methylamine in step b. The 4-methoxyphenyl moiety was converted to any other functional groups by using various appropriate Grignard reagents. Unlike trityl salts having limited substituents, these results indicated that functionalized carbocationic species are possibly available.

It is noted that a tetrakis(pentafluorophenyl)borate anion stabilized novel carbocationic species **1** was synthesized and only 1.0 mol% of **1** accelerated the reaction of aldehydes with silyl enol ethers or ketene silyl acetals to give the aldol adducts in good to high yields. It should also be noted that both aldols and Michael adducts were obtained in nearly the same yields when α,β-unsaturated aldehydes were treated with nucleophiles **3**, **4** and **5**.[8] Further study on this topic is now in progress.

References and Notes

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4 W. L. F. Armarego and S. C. Scarma, *J. Chem. Soc., C*, **1970**, 1600.

5 Crystal data for **1**; yellow prismatic crystals, formula: $C_{40}H_{14}BNO_2F_{20}$, formula weight: 931.34, P1(#2), a = 11.038(2) Å, b = 17.475(3) Å, c = 10.134(1) Å, α = 105.77(1)°, β = 94.42(1)°, γ = 82.12(2)°, V = 1861.7(6) $Å^3$, Z = 2, D_{calc} = 1.661 g cm^{-3}, μ(Cu Kα) = 15.47 cm^{-1}, diffractometer: Rigaku AFC7R, measured reflections: 8137, unique reflections: 6778, observed reflections: 6397, calculations: teXsan Crystal Structure Analysis Package (Molecular Structure Corporation), $R(R_w)$ = 0.072(0.243).

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7 Previously, it was shortly described that the addition reaction between silyl enol ethers and α,β-unsaturated aldehydes using triphenylmethyl perchlorate as a catalyst gives a mixture of 1,2 and 1,4 adducts; S. Kobayashi, M. Murakami, and T. Mukaiyama, *Chem. Lett.*, **1985**, 953.

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