A study of base-catalyzed aldol reaction of trimethylsilyl enolates

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Mukaiyama-type aldol reaction of trimethylsilyl enolates with aldehydes in the presence of a base is a complicated reaction. It usually results in various products determined by the nature of base and reaction medium. The present study has been undertaken to understand these factors and design new Lewis base catalysts to optimize the yield of desired aldol product. It has been shown that mild Brønsted base with inbuilt hydrogen bonding sites are efficient catalysts for the reactions involving trimethylsilyl enolates. Based on the observed results, a mechanism is proposed to explain the reaction outcome.

Keywords: Aldol reaction, base catalyzed, carboxylate salts, lithium amides

The reaction of silyl enolates with aldehydes or ketones in the presence of a catalyst, the Mukaiyama aldol reaction, is a versatile C–C bond forming reaction. It has some significant advantages over the other aldol variants and hence has attracted interest for almost four decades. Due to weak nucleophilic character of silyl enolates, activation of electrophile or nucleophile is needed. Electrophilic activation using Lewis acids has been studied extensively in stoichiometric as well as catalytic protocols. Nucleophilic activation of silyl enolates is a more interesting option and offers several advantages over the former one. It may consist of formation of reactive metal enolates by transmetallation with metal salts or nascent enolates by nucleophilic cleavage of a Si–O bond with fluoride ions or phosphines. The third possibility is the formation of activated coordinate complexes of silicon with Lewis bases generating a hypervalent silicon in which the Lewis acidity of silicon gets enhanced by the formation of ‘3C-4e’ bonds. These complexes were studied in detail by Denmark, et al., who introduced phosphoramid derived Lewis bases. However the methodology is restricted to trichlorosilyl enolates. A much simpler enantioselective version of this reaction was reported by Nakajima, et al., using dilithium binaphtholate as catalyst and trimethoxysilyl enolates as substrates. Generation of chiral siliconium cations from both the trichloro- and trimethoxysilyl enolates results in a closed and ordered preassembly of enolate, aldehyde and chiral catalyst resulting in stereoselectivity.

There are several reports of racemic version of this reaction using trialkysilyl enolates in the presence of Lewis bases such as sodium phenoxide-phosphine oxide, quaternary ammonium dendrimers containing iodide counterions, DBU, lithium alkoxides, lithium acetate, lithium amides, N-oxides, N-methylimidazole, N-heterocyclic carbenes, proa-zaphosphatranes and the recently reported 4-nitrophenoxy-magnesium iodide. An enantioselective aldol reaction using these enolates was reported as a two step process in the presence of Lewis base (AcO) paired with chiral quaternary ammonium cation of chinchonidine where the selectivity arises from the silylation step. In majority of these studies TMS enolates of α-substituted ketones or α,α-disubstituted methyl ester were used as substrates. There are only a few reports describing the use of TMS enolates of ketones in pyridine or DMF as solvent. However the reaction of TMS enolates of a few esters proceed without catalysts in polar coordinating solvents such as DMF, DMSO, and ionic liquids. However, the reported mechanism does not describe the equilibrium of metal aldolate with metal enolate, which can lead to the formation of all possible products such as aldol, elimination or TMS acetal. As a part of the ongoing efforts to develop simple chiral Lewis base catalysts for the reaction of TMS enolates with aldehydes, all these aspects have now been examined.

Results and Discussion

The reaction of isobutyraldehyde was first explored with less reactive TMS enolate derived from acetophenone in common organic solvents such as THF, CH₂CN, Et₂O and toluene in order to have fewer background reactions.
Initially Lewis bases obtained from easily accessible chiral compounds like amino acids\textsuperscript{48}, ephedrines, binaphthyls\textsuperscript{49,50} and salen\textsuperscript{51} in the form of their lithium and sodium salts were used (Figure 1).

Our findings with the above listed salts were disappointing (Table I). One of the problems encountered was their low solubility in commonly used organic solvents like THF and CH\textsubscript{3}CN. On the other hand, polar solvents like DMF, DMSO and water, led to side reactions. The answer could be the use of some less acidic protic additives which can either increase the solubility or break aggregate structure of the catalyst in solution\textsuperscript{52}. Accordingly, various additives such as alcohols, diamines (both racemic and chiral), diols and water (catalytic as well as cosolvent) were examined. It was found that protic additives increased the solubility of these salts in common organic solvents and also suppressed the formation of elimination product B (e.g. Table I, entry 3 vs 2). However, not unexpectedly, these always led to substantial amount of hydrolysis product C.

Thus products A-C are formed in varying ratios depending on the nature of Lewis base and reaction medium used (Scheme I) while O-acylated product was not observed at all. The Brønsted basicity is responsible for the abstraction of acidic \(\alpha\)-proton from the intermediate after 1,3-silicon migration resulting in the elimination product B; while product C is formed due to the hydrolysis of the Lewis base activated TMS enolate. It indicated towards a proper balance between Lewis basicity and Brønsted basicity as well as the requirement that anhydrous reaction medium is a must to improve the yield of expected aldol product A.

It was interesting to observe that the carboxylate salts 1b and 1d, provided only the elimination product (Table I, entries 2 and 5) and their analogues with free

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**Table I** — Examination of mono and bimetallic salts of bidentate ligands as catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Time (hr)</th>
<th>Yield (%)\textsuperscript{a}</th>
<th>Temp (°C)</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
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<td>DMF/THF\textsuperscript{b}</td>
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<td>1b</td>
<td>THF</td>
<td>25</td>
<td>24</td>
<td>Elimination</td>
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</tr>
<tr>
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<td>1c</td>
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<tr>
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\textsuperscript{a}Isolated yield of A (in all cases \(ee\) was < 20\%, determined by comparison of optical rotation with literature value\textsuperscript{53}).

\textsuperscript{b}DMF:THF (1:9).

\textsuperscript{c}10 mol% of ethylene diamine as additive.

\textsuperscript{d}Mixture of A (predominant), B and C, judged by TLC.

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Figure 1 — Mono and bimetallic salts of bidentate ligands

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NH (1a and 1c) provided improved yield of the desired product. The lithium salts of binaphthyl derived ligands also showed similar behavior (Table I, entries 9 and 11 vs 10). These results indicated the involvement of hydrogen bonding interactions in the transition state similar to that reported for TMSCN additions to aldehydes. A possible mechanism has been hypothesized involving closed transition state as shown in the Figure 2. The proton present in the catalyst structure may be acting as hydrogen bonding site; balancing the Brønsted basicity of catalyst. However the catalyst without such features will not involve any extra stabilization in the transition state and hence display Brønsted basic character. Abstraction of α-proton from the aldolate after 1,3-silicon migration results in more of the elimination product B.

Lithium salts of ephedrine derivatives 2a and 2b even with an N-H proton gave substantial amounts of elimination product (Table I, entries 6 and 7). This is because of their strong Brønsted basicity as compared to carboxylates and phenoxides. A few bimetallic salts have also been evaluated as catalysts. However, these provided lower yield of the aldol product than monometallic salts. The elimination product B was formed predominantly (Table I, entries 12–14). Also the enantioselectivities were poor in all the cases. This could be attributed to the reaction proceeding through an open transition state with silicon fully saturated by chelation. These results differ from those with trimethoxysilyl reagent where one of the methoxy group leaves after the chelation of Lewis base forming siliconium cation.

Sodium salts of above listed ligands have also been employed but most of them have low solubility in THF and CH3CN while in a mixture of THF and DMF (1:9) they resulted in the formation of side products. Therefore, tetrabutyl ammonium salts of a few of the ligands were used but they always resulted in appreciable amounts of the elimination product. Several nonionic Lewis bases were used as catalysts for this reaction in THF e.g. tertiary amines, N-oxide, phosphine oxides, HMPA, etc. It was observed that as the Lewis basicity of these catalysts is too low; they do not catalyze the reaction. Based on these findings, lithium salts were used as catalysts for the rest of the study.

The present study indicated that hydrogen bonding sites like NH or OH present in the monometallic salts suppress the formation of elimination product. However, the salts of acids like hydroxy acids and amino acids are of little use as they present solubility problems. Also, as seen from Table I, the yields with mono metalic salts of binaphthyl derivatives were not impressive. An alternate option was therefore conceived which involved using the salts of monoamide derivatives (Figures 3 and 4). The required monoamides of symmetrical 1,2-diamine were prepared by modification of the procedure recently reported.

It was found that by using THF as a solvent, monoaclylation can be achieved with free 1,2-diamine itself. Reactions performed with 1 equivalent of acylating agent provided the monoacylated products 6a and 7a at 0°C and the diacylated products 6c and 7d at 25°C. Ligands 7c and 7f were prepared by the
same procedure using trifluoroacetic anhydride. Unfortunately, these conditions were found to be unsuitable for monotosylation/mesylation of 1,2-diamines and monoacylation of BINAM. Therefore, monotosylate of (1R,2R)-cyclohexane-1,2-diamine 6b (Ref. 57), and monomesylate of (1S,2S)-1,2-diphenylethane-1,2-diamine 7b (Ref. 58) were prepared by the reported procedures. Monopivalamide of (R)-BINAM 8 was prepared using pyridine as the base. Ditosylate 6d and dimesylate 7e (Ref. 59) were also prepared to compare the behavior of their salts with those of salen and binaphthyl derivatives.

Further, to check the role of hydrogen bonding, 9 was prepared from 6a. Corresponding lithium salts were generated in situ from the aforementioned amides by the reaction with n-BuLi (Figure 4).

These amides 10-14 were then examined for the present Mukaiyama-type aldol reaction. In most cases good yields were realized in a short period of time, though the enantioselectivities were low (Table II).

It was interesting to find that salts of monoamides exhibited catalytic behaviour of amino acid carboxylates. For example 10a gave good yield while 10b promoted elimination reaction (Table II, entry 1 vs 3). This explains the desirable effect of hydrogen bonding site in the catalyst structure. Out of these, 11c with electron withdrawing fluorine atoms was found to be the best one (Table II, entry 9). In general, mono metallic salts were found to be better than the bimetallic ones. Some of the catalysts (10a, 10b, 11a and 12) were then used to study the substrate scope and solvent effects. These catalysts efficiently activated TMS

<table>
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<th>Entry</th>
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<th>Temp (°C)</th>
<th>Time (hr)</th>
<th>Yield (%)</th>
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</table>

*aIsolated yield of A (% ee was < 20% in most cases).
**Benzoaldehyde as electrophile53,60, i-PrOH:THF (1:4).
enolates of alkyl esters e.g. methyl isobutyrate while the TMS enolates of phenyl esters underwent cleavage to phenol along with the desired reaction. For this reaction, THF and DME were found to be the solvents of choice.

The present study helped to maximize the yield of aldol product A from the reaction of TMS enolate, however low enantioselectivities were obtained in all the cases. It is believed that the reaction proceeds through an open transition state unlike the mechanism that had been envisaged (Figure 2). Such a pathway can be explained by activation of the aldehyde followed by reaction with trimethylsilyl enolate which may or may not involve a hypervalent silicon.

In conclusion, Mukaiyama-type of aldol reaction is unique because it is catalyzed by Lewis acids, Lewis bases and also Brønsted acids. Each mode of catalysis has a different mechanistic pathway. The present study was undertaken to understand various factors that affect the Lewis base catalyzed mode of the reaction. It was found that the outcome of the reaction is controlled by Brønsted basicity of the catalyst which in turn is governed by structure of the ligand. This led to the design of Lewis bases with built-in OH/NH sites in the molecule. It has been shown that mild Brønsted bases with inbuilt hydrogen bonding sites are efficient catalysts for the reactions involving trimethylsilyl enolates. Further research will be needed to extend the present findings into an enantioselective protocol.

Experimental Section

All solvents and reagents were purified and dried according to the literature procedures. N-Methyl proline, binaphthyl derivatives, and salen were prepared according to literature reports. Ligands 6c (Ref.64) 7e (Ref. 65) and 7d (Ref. 66) are already reported and their data has been found in good agreement. TMS enolate of acetophenone was prepared by slight modification of the reported procedure. The reactions were monitored by TLC using silica gel 60 F254 pre-coated plates and were visualized either with UV, in an iodine chamber or with phosphomolybdic acid spray. The products were purified by column chromatography over silica gel (100-200 or 230-400 mesh). All melting points were recorded on a Büchi B-540 electro thermal melting point apparatus and are uncorrected. Optical rotations were measured on Bellimheam+Standley ADP220 digital polarimeter and IR spectra were recorded on a Shimadzu FTIR-8400 spectrophotometer. \( ^1\)H NMR spectra were recorded at 200 MHz with TMS as the internal standard and \(^{13}\)C NMR spectra were recorded at 50 MHz with CDCl\(_3\) (\(\delta\) 77) as the reference. Micro analysis was performed using a Carlo-Erba CHNS-0 EA 1108 elemental analyzer.

Preparation of Ligands

N-((1R,2R)-2-Aminocyclohexyl)pivalamide, 6a

In an oven dried 10 mL round-bottomed flask, imidazole (450 mg, 6.6 mmol) was dissolved in anhydrous THF (5 mL). The solution was cooled to 0°C and pivaloyl chloride (0.37 mL, 3 mmol) was added dropwise to it. The resulting white suspension was stirred at 0°C for 30 min and then gradually warmed to RT. After stirring for 30 min, the precipitated imidazole hydrochloride was filtered under argon and washed with anhydrous THF (2 \(\times\) 5 mL). The filtrate and washings were combined and added slowly to the ice cold solution of (1R,2R)-cyclohexane-1,2-diamine (343 mg, 3 mmol) in anhydrous THF (5 mL). Stirring was continued at 0°C and the reaction was monitored by TLC. After completion (7 hr), solvent was evaporated on rotavapor and the residue was redissolved in DCM (20 mL). The solution was washed with water (10 mL) and brine (10 mL). It was dried over anhydrous Na\(_2\)SO\(_4\) and concentrated to get crude product, which was purified by flash column chromatography using methanol: dichloromethane (7:93) as eluent to get 6a (404 mg, 68%) as white solid. m.p. 96-97°C; R\(_f\) (10% methanol/dichloromethane): 0.4; \([\alpha]_D^{25} = -32.32^\circ\) (c 1.0, CHCl\(_3\)); IR (Nujol): 3344, 2922, 2856, 1634, 1207 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.03-1.44 (m, 13H), 1.67-1.80 (m, 4H), 1.90-2.04 (m, 1H), 3.42-3.52 (m, 1H); \(^13\)C NMR (CDCl\(_3\)): \(\delta\) 0.4; [\(\alpha\)]\(_D^{25}\) = -32.32° (c 1.0, CHCl\(_3\)); IR (Nujol): 3344, 2922, 2856, 1634, 1207 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\)): \(\delta\) 1.03-1.44 (m, 13H), 1.67-1.80 (m, 4H), 1.90-2.04 (m, 2H), 2.4 (dt, J = 10.48, 3.79 Hz, 1H), 3.42-3.52 (m, 1H), 5.56 (d, J = 6.82 Hz, 1H); \(^13\)C NMR (CDCl\(_3\)): \(\delta\) 24.9, 27.5, 32.2, 35.0, 38.6, 55.3, 55.7, 178.7. Anal. Cald. for C\(_{11}\)H\(_{22}\)N\(_2\)O: C, 66.62; H, 11.18; N, 14.13. Found: C, 67.06; H, 11.13; N, 13.94%.

N,N'-((1R, 2R)-Cyclohexane-1,2-diyl)bis(4-methylbenzenesulfonamide), 6d

In a 100 mL two necked round-bottomed flask equipped with a gas-outlet bubbler, cyclohexane-anediamine tartarate salt (1.32 g, 5 mmol) and K\(_2\)CO\(_3\) (2.073 g, 15 mmol) were suspended in methanol (30 mL). The mixture was cooled to 0°C and tosyl chloride (2.1 g, 11 mmol) was added portion wise. It was warmed to RT and monitored for evolution of CO\(_2\). After completion of the reaction (1.5 hr) as indicated by ceasing of CO\(_2\) evolution and TLC, solvent was evaporated and the residue was dried under vacuum. It was redissolved in
DCM (30 mL) and washed with brine (2 × 10 mL). The solution was dried over anhydrous Na₂SO₄ and concentrated to get crude product which was purified by recrystallization from toluene to yield 6d (1.56 g, 74%) as white solid. m.p. 168-169°C (Lit. 67 168-70°C); Rf (10% methanol/dichloromethane): 0.5; [α]₂⁰ = +2.9° (c 2.1, pyridine) [Lit. 67 +2.6° (c 2.33, pyridine)]; IR (Nujol): 3287, 2953, 2857, 1596, 1156, 1091 cm⁻¹; ¹H NMR (CDCl₃): δ 0.95-1.27 (m, 4H), 1.46-1.62 (m, 2H), 1.75-1.95 (m, 2H), 2.44 (s, 6H), 2.62-2.82 (m, 2H), 4.81 (bs, 2H), 7.32 (d, J = 8.09 Hz, 4H), 7.76 (d, J = 8.21 Hz, 4H).

N-((1S, 2S)-2-Amino-1,2-diphenylethyl)pivalamide, 7a. The procedure described above for preparation of 6a was followed using (1S,2S)-1,2-diphenylethlene-1,2-diamine (636 mg, 3 mmol). The crude product was purified by column chromatography using ethyl acetate: petroleum ether (1:3) as eluent to obtain 7a (660 mg, 74%) as white solid. m.p. 136-37°C; Rf (40% ethyl acetate/hexane): 0.5; [α]₂⁰ = −39.0° (c 1.23, CHCl₃); IR (Nujol): 3415, 3389, 3293, 2948, 2922, 2857, 1642, 1603, 1218, 1189 cm⁻¹; ¹H NMR (CDCl₃): δ 1.13 (s, 9H), 1.45 (bs, 2H), 4.47 (d, J = 2.91 Hz, 1H), 5.10 (dd, J = 7.70, 2.78 Hz, 1H), 7.07 (d, J = 7.20 Hz, 1H), 7.2-7.46 (m, 10H); ¹³C NMR (CDCl₃): δ 27.4, 38.6, 57.9, 59.1, 126.0, 126.3, 127.1, 127.4, 128.2, 128.5, 139.1, 140.7, 141.9, 177.6, 179.3. Anal. Calcd for C₁₀H₂₅N₂O: C, 76.99; H, 8.16; N, 9.45. Found: C, 77.24; H, 8.01; N, 9.43%.

N,N'-((1S, 2S)-1,2-Diphenylethene-1,2-diamine-2,2,2-trifluoroacetamide), 7f. The procedure described above for preparation of 6a was followed using (1S,2S)-1,2-diphenylethene-1,2-diamine (636 mg, 3 mmol), trifluoroacetic anhydride (0.84 mL, 6 mmol), imidazole (900 mg, 13.2 mmol) and after addition the reaction mixture was warmed to RT. After stirring for 2 hr at RT and solvent evaporation, the crude product was purified by column chromatography using ethyl acetate: petroleum ether (1:6) as eluent to get 7f (960 mg, 79%) as white solid. m.p 274-75°C; Rf (10% ethyl acetate/hexane): 0.2; [α]₂⁰ = +34.6° (c 1.01, MeOH); IR (Nujol): 3305, 2924, 2855, 1693, 1598, 1178 cm⁻¹; ¹H NMR (CDCl₃+DMSO-d₆): δ 5.25-5.38 (m, 2H), 6.90-7.07 (m, 10H), 9.31 (d, J = 7.32 Hz, 2H); ¹³C NMR (CDCl₃): δ 56.1, 125.8, 126.1, 126.7, 127.3, 136.7, 156.2, 157.0. Anal. Calcd for: C₁₈H₁₄F₃N₂O₂: C, 53.47; H, 3.49; N, 6.93. Found: C, 53.05; H, 3.42; N, 6.49%.

N-(R)²-Amino-[1,1'-binaphthalen]-2-yl)pivalamide, 8. A solution of BINAM (1.42 g, 5 mmol) and anhydrous pyridine (5 mL) in anhydrous DCM (20 mL) was cooled to 0°C. Pivaloyl chloride (0.61 mL, 5 mmol) was added dropwise to it. The yellow coloured solution was gradually brought to RT, stirred and the progress of reaction monitored by TLC. After completion of the reaction (8 hr), it was cooled to 0°C and neutralized with 2N HCl. The organic layer was separated and aqueous layer was extracted with DCM (2 × 20 mL). Combined organic extract was washed with saturated aqueous NaHCO₃ (10 mL) and brine (10 mL). It was dried over anhydrous Na₂SO₄ and concentrated to get the crude product, which was purified by flash column chromatography using ethyl acetate: petroleum ether (8:92) as eluent to yield 8 (530 mg, 29%) as white solid. m.p. 79-83°C; Rf (20% ethyl acetate/hexane): 0.4; [α]₂⁰ = +82.47° (c 1.19, CHCl₃); IR (Nujol): 3465, 3399, 3359, 2948, 2922, 2857, 1674, 1618, 1593, 1285 v/cm⁻¹; ¹H NMR (CDCl₃): δ 0.81 (s, 9H), 3.38-4.0 (bs, 2H), 6.89-7.00 (m, 1H), 7.09-7.48 (m, 7H), 7.68-8.05 (m, 4H), 8.67 (d, J = 9.09 Hz, 1H); ¹³C NMR (CDCl₃): δ 26.9, 39.5, 110.2, 117.9, 120.6, 122.7, 123.4, 124.9, 125.2, 126.8, 127.3, 128.0, 129.1, 130.3, 131.0, 133.3, 135.1, 142.7, 176.8. Anal. Calcd for C₂₅H₂₅N₂O: C, 81.49; H, 6.57; N, 7.60. Found: C, 81.12; H, 6.58; N, 7.14%.

N-((1R,2R)-2-(Dimethylamino)cyclohexyl)pivalamide, 9. A 10 mL round-bottom flask equipped with reflux condenser, was charged with 12a (198 mg, 1 mmol) and cooled to 0°C. A 90% solution of formic acid (0.21 mL, 5 mmol) followed by 30% solution of formaldehyde (0.185 mL, 2.2 mmol) was added to it. The mixture was gradually brought to 70°C. After completion of the reaction (3 hr) as indicated by TLC, it was cooled to room temperature. The reaction mixture was neutralized by cautious addition of NaHCO₃ solution and saturated with brine. It was extracted with DCM (3 × 15 mL), dried over anhydrous Na₂SO₄ and concentrated to get crude product. Further purification was achieved through column chromatography using methanol: dichloromethane (3:97) as eluent to yield 9 (220 mg, 97 %) as white solid. m.p. 60-62°C; Rf (5% methanol/dichloromethane): 0.3; [α]₂⁰ = −74.14° (c 1.16, CHCl₃); IR (Nujol): 3374, 2933, 2857, 2826, 2781, 1638, 1532, 1209 cm⁻¹; ¹H NMR (CDCl₃): δ 0.92-1.37 (m, 13H), 1.60-1.73-1.91 (m, 3H), 2.22 (s, 6H), 2.27-2.57 (m, 2H), 3.30-3.47 (m, 1H), 8.52 (bs, 1H); ¹³C NMR (CDCl₃): δ 21.2, 24.5, 25.3, 27.5, 32.5, 38.7, 39.6, 51.3, 66.3, 179.1. Anal.
Calcd for C_{13}H_{20}N_{2}O: C, 68.98; H, 11.58; N, 12.38. Found: C, 68.82; H, 11.49; N, 11.98%.

**Preparation of salts**

Carboxylate salts 1a–d were prepared by reacting 1 mmol of carboxylic acid with exactly 1 mmol of corresponding metal hydroxide in methanol (2 mL) at RT. After completion of the reaction (30 min) as indicated by TLC, solvent was evaporated and the residue was dried under vacuum. These salts are stable and can be stored indefinitely in a desiccator. The salts of ephedrine derivatives, binaphthyls, salen and amides were generated in situ using standard solution of n-BuLi.

**Preparation of TMS enolates**

**TMS enolate of acetophenone**

An oven dried 500 mL two necked round-bottomed flask was charged with chlorotrimethylsilane (18.75 mL, 150 mmol) and anhydrous DMF (40 mL). Triethylamine (33.45 mL, 240 mmol) was then introduced gradually. To the resulting pale yellow suspension, acetophenone (11.66 mL, 100 mmol) was added dropwise and stirred vigorously at RT for 15 hr. It was then stirred at 60°C and the reaction was monitored by IR. After completion of reaction (18 hr), it was cooled to RT and diluted with petroleum ether (300 mL). To the resulting brown slurry ice cold water (100 mL) was added and organic layer was separated. It was washed with cold brine (5 mL) and dried over anhydrous Na_{2}SO_{4}. It was concentrated to get crude product which was purified by flash column chromatography using ethyl acetate: petroleum ether as eluent. The purified product was characterized by IR and 1H NMR and the data has been found to be in good agreement with the reported ones.

**General procedure for Mukaiyama-type aldol reaction**

In an oven dried 10 mL side armed flask, 0.2 mmol of catalyst was dissolved in appropriate solvent under argon atmosphere. The solution was cooled to 0°C and enolate (2 mmol, 0.4 mL) followed by aldehyde (2 mmol, 0.2 mL) was added dropwise. The reaction mixture was stirred at 0°C and monitored by TLC. (If not showing any progress at 0°C then brought to RT). After completion of the reaction, it was quenched with aqueous NH_{4}Cl (2 mL). The solvent was removed on rotary evaporator and the residue was extracted with ethyl acetate (3 × 5 mL). Combined organic layer was washed with brine (5 mL) and dried over anhydrous Na_{2}SO_{4}. It was concentrated to get crude product which was purified by flash column chromatography using ethyl acetate: petroleum ether as eluent. The purified product was characterized by IR and 1H NMR and the data has been found to be in good agreement with the reported ones.

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**References**
