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Chemoselective Aldol Reaction of Silyl Enolates Catalyzed by MgI$_2$ Etherate

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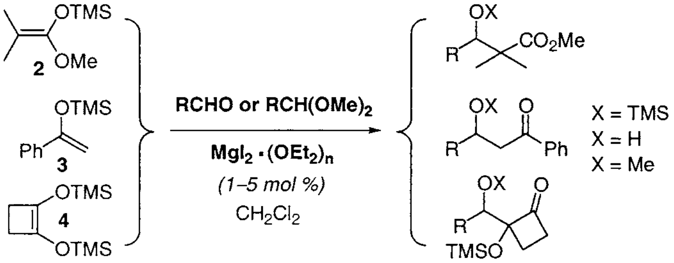
ABSTRACT



Mukaiyama-type aldol coupling of typical silyl enolates 2–4 with aryl or vinyl aldehydes and acetals was realized in the presence of 1–5 mol % of MgI$_2$ etherate (1) in a mild, efficient, and highly chemoselective manner. Iodide counterion, weakly coordinating peripheral ethereal ligands (Et$_2$O) of Mg(II), and a noncoordinating reaction media (i.e. CH$_2$Cl$_2$) are among the critical factors for the unique reactivity of this catalytic system.

Magnesium(II) species are widely used as Lewis acid catalysts in various functional transformations[1] and C−C bond-forming reactions[2] due to the high electrophilicity of the Mg^{2+} ion and its tendency to form a *multi*-coordinate (up to 5 or 6) complex.[3] Among them, magnesium halides are most frequently used. Revelation of the intriguing catalytic reactivity of magnesium halide-derived chiral Lewis acids by Corey et al.[4] has stimulated increased interest in the asymmetric catalysis of the C−C bond formation reaction by a Mg(II) complex.[5] However, the use of Mg(II) Lewis acids in aldol condensation has been rather limited so far.[6] We report here the preliminary results on the unique catalytic reactivity of MgI$_2$ *diethyl etherate* (**1**) for the mild, efficient, and chemoselective (Mukaiyama-type) aldol reaction of aryl aldehydes and acetals with silyl enolates. To the best of our knowledge, this is the first effective catalysis of Mukaiyama-type aldol *catalytic in magnesium halide*.[7] The Mukaiyama-

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(1) For examples, see: (a) Ohnishi, Y.; Kagami, M.; Ohno, A. *J. Am. Chem. Soc.* **1975**, *97*, 4766. (b) Meyers, A. I.; Oppenlaender, T. *J. Am. Chem. Soc.* **1986**, *108*, 1989. (c) Bolm, C.; Beckmann, O.; Cosp, A.; Palazzi, C. *Synlett* **2001**, 1461. (d) Bouzide, A. *Org. Lett.* **2002**, *4*, 1347. (e) Chowdhury, P. K. *J. Chem. Res., Synop.* **1990**, 192 and 390. (f) Chowdhury, P. K. *J. Chem. Res., Synop.* **1992**, 68. (g) Yamaguchi, S.; Nedachi, M.; Yokoyama, H.; Hirai, Y. *Tetrahedron Lett.* **1999**, *40*, 7363. (h) Jang, D. O.; Joo, Y. H. *Synth. Commun.* **1998**, *28*, 871. (i) Martinez, A. G.; Barcina, J. O.; del Veccio, G. H.; Hanack, M.; Subramanian, L. R. *Tetrahedron Lett.* **1991**, *32*, 5931. (j) Murakata, M.; Tsutsui, H.; Taksuchi, N.; Hoshino, O. *Tetrahedron* **1999**, *55*, 10295.

(2) For examples, see: (a) Sibi, M. P.; Porter, N. A. *Acc. Chem. Res.* **1999**, *32*, 163. (b) Yang, D.; Gu, S.; Yan, Y.-L.; Zhu, N.-Y.; Cheung, K.-K. *J. Am. Chem. Soc.* **2001**, *123*, 8612. (c) Li, C.-J.; Zhang, W.-C. *J. Am. Chem. Soc.* **1998**, *120*, 9102. (d) Rawat, D. S.; Zaleski, J. M. *J. Am. Chem. Soc.* **2001**, *123*, 9675. (e) Alper, P. B.; Meyers, C.; Lerchner, A.; Siegel, D. R.; Carreira, E. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 3186. (f) Lautens, M.; Han, W. *J. Am. Chem. Soc.* **2002**, *124*, 6312. (g) Bertozzi, F.; Gustafsson, M.; Olsson, R. *Org. Lett.* **2002**, *4*, 3147−3150. (h) Yang, D.; Gu, S.; Yan, Y.-L.; Zhao, H.-W.; Zhu, N.-Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 3014. (i) Yang, D.; Gao, Q.; Lee, C.-S.; Cheung, K.-K. *Org. Lett.* **2002**, *4*, 3271−3274.

(3) (a) Tobe, M. L.; Burgess, J. *Inorganic Reaction Mechanisms*; Addison-Wesley Longman: New York, 1999, Chapter 7. (b) Wehmschulte, R. J.; Twamley, B.; Khan, M. A. *Inorg. Chem.* **2001**, *40*, 6004.

(4) (a) Corey, E. J.; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807. (b) Corey, E. J.; Wang, Z. *Tetrahedron Lett.* **1993**, *34*, 4001. See also: (c) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc.* **1991**, *113*, 728.

(5) Cf: (a) Bromidge, S.; Wilson, P. C.; Whiting, A. *Tetrahedron Lett.* **1998**, *39*, 8905. (b) Gothelf, K. V.; Hazell, R. G.; Jorgensen, K. A. *J. Org. Chem.* **1998**, *63*, 5483. (c) Desimoni, G.; Faita, G.; Mortoni, A.; Righetti, P. P. *Tetrahedron Lett.* **1999**, *40*, 2001. (d) Ichiyanagi, T.; Shimizu, M.; Fujisawa, T. *J. Org. Chem.* **1997**, *62*, 7937. (e) Sibi, M. P.; Asano, Y. *J. Am. Chem. Soc.* **2001**, *123*, 9708.

(6) For a few examples, see: (a) Corey, E. J.; Li, W.; Reichard, G. A. *J. Am. Chem. Soc.* **1998**, *120*, 2330. (b) Fujisawa, H.; Sasaki, Y.; Mukaiyama, T. *Chem. Lett.* **2001**, 190 and ref 7 therein. (c) Evans, D. A.; Tedrow, J. S.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2002**, *124*, 392. (d) Evans, D. A.; Downey, C. W.; Shaw, J. T.; Tedrow, J. S. *Org. Lett.* **2002**, *4*, 1127.

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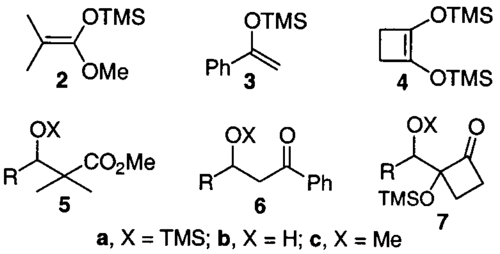


Figure 1. Typical silyl enolates and corresponding aldol adducts.

type aldol coupling[8] of aldehydes or acetals with typical silyl enolates **2**−**4**[9] was generally carried out in dry CH_2Cl_2 (as the solvent of choice)[10] in the presence of a catalytic amount (1−5 mol %) of freshly prepared **1** (0.2 M in Et_2O/benzene 1:2).[11] The resulting *homogeneous* reaction mixture was stirred under argon and monitored by TLC, and *silylated* adducts **5**−**7a** (of aldehyde) were usually obtained as major products after extractive workup and chromatography on silica gel. The reactions can be run simply at ambient temperature in most cases.

Of various carbonyl substrates screened,[12] aliphatic aldehydes are unreactive toward enol silanes **3** and **4**, only reacting with silyl ketene acetal **2** sluggishly. Aromatic aldehydes are reactive substrates toward **2**−**4**. Both aliphatic and aromatic ketones are inert. This interesting chemoselectivity was further evaluated by crossover experiments (Tables 1−3) of silyl enolates **2**−**4** with substituted aryl aldehydes, respectively. We have observed the following delicate electronic effects: (1) aryl aldehydes with an electron-donating substituent (i.e. *o*- or *p*-OMe, NMe_2) reacted *much faster* than benzaldehyde and (2) an electron-withdrawing substituent (i.e. Cl, NO_2, CF_3) *deactivated* aryl aldehyde remarkably. For example, *o*- and *p*-anisaldehyde are much more reactive than *m*-anisaldehyde and benzaldehyde (Table 1, entries 2, 3, 7, and 11). Furthermore, unsaturated aryl and vinyl aldehydes are highly reactive substrates and give aldol adduct predominately.[13] The discriminating ability of silyl enolates is inversely dependent on their relative nucleophilicity in the sequence **2** < **3** ∼ **4**. Similar electronic effects of Lewis acidic $Eu(dppm)_3$ were documented by Mikami and Nakai et al.[14] in chemoselective aldol and Michael reactions of aryl aldehydes with silyl enolate of type **2**.

Table 1. Crossover Aldol Coupling of **2** with Aryl Aldehydes[a]

$$\text{ArCHO} + \text{Ar'CHO} + \mathbf{2} \xrightarrow[\text{CH}_2\text{Cl}_2,\ \text{r.t.}]{\mathbf{1}\ (5\ \text{mol}\ \%)} \mathbf{5(a, b)} + \mathbf{5'(a, b)}$$

entry	Ar	Ar′	time (min)	ratio (**5**/**5′**)	yield (%)[b]
1	Ph	2-$NO_2C_6H_4$	120	80/20	98
2	Ph	2-$MeOC_6H_4$	10	<1/>99	99
3	Ph	4-$MeOC_6H_4$	10	<1/>99	98
4	Ph	2,5$(MeO)_2C_6H_3$	15	5/95	99
5	Ph	3-$MeOC_6H_4$	15	56/44[c]	99
6	Ph	4-MeC_6H_4	30	27/73[d]	80
7	2-$MeOC_6H_4$	3-$MeOC_6H_4$	15	>99/<1	99
8	4-$Me_2NC_6H_4$	4-$MeOC_6H_4$	10	>99/<1	98
9	4-$MeOC_6H_4$	4-$NO_2C_6H_4$	10	>99/<1	99
10	4-$MeOC_6H_4$	4-MeC_6H_4	20	80/20	96
11	4-$MeOC_6H_4$	4-ClC_6H_4	15	>99/<1	98
12	2-$MeOC_6H_4$	2-$NO_2C_6H_4$	10	>99/<1	99

[a] Reactions were run with a mixture of 0.5 mmol of each aldehyde, 0.5 mmol of silyl enolate **2**, and 5 mol % of MgI_2 etherate (**1**) (0.2 M solution in Et_2O/benzene (v/v 1:2)). [b] Isolated overall yield. [c] Ratio determined by ^1H NMR analysis. [d] Ratio determined by GC analysis.

Table 2. Crossover Aldol Coupling of **3** with Aryl Aldehydes[a]

$$\text{ArCHO} + \text{Ar'CHO} + \mathbf{3} \xrightarrow[\text{CH}_2\text{Cl}_2,\ \text{r.t.}]{\mathbf{1}\ (5\ \text{mol}\ \%)} \mathbf{6(a, b)} + \mathbf{6'(a, b)}$$

entry	Ar	Ar′	time (min)	ratio (**6**/**6′**)	yield (%)[b]
1	Ph	2-$NO_2C_6H_4$	120	>99/<1	87
2	Ph	2,5$(MeO)_2C_6H_3$	30	2/98	99
3	2-$MeOC_6H_4$	4-$MeOC_6H_4$	20	52/48[c]	99
4	4-MeC_6H_4	4-$MeOC_6H_4$	40	40/60	95
5	2-$MeOC_6H_4$	3-$MeOC_6H_4$	20	>99/<1	99
6	2-$CF_3C_6H_4$	2,5$(MeO)_2C_6H_3$	30	<1/>99	99

[a] Same reaction conditions as Table 1. [b] Isolated overall yield. [c] Ratio determined by ^1H NMR analysis.

To examine the halide anion effect, halogen analogues of **1**, $MgCl_2$ etherate (**1a**) and $MgBr_2$ etherate (**1b**), were compared (see Table 6 of Supporting Information) with **1** under parallel reaction conditions (5 mol % of catalyst) in an aldol reaction of aryl aldehydes with enolates **2** or **4**. Etherate **1a** is practically inactive and **1b** is much less effective in terms of substrate conversion, yield, and

Table 3. Crossover Aldol Coupling of **4** with Aryl Aldehydes[a]

$$\text{ArCHO} + \text{Ar'CHO} + \mathbf{4} \xrightarrow[\text{CH}_2\text{Cl}_2,\ \text{r.t.}]{\mathbf{1}\ (5\ \text{mol}\ \%)} \mathbf{7(a, b)} + \mathbf{7'(a, b)}$$

entry	Ar	Ar′	time (min)	ratio (**7**/**7′**)	yield (%)[b]
1	Ph	2-$NO_2C_6H_4$	30	>99/<1	99
2	Ph	2,5$(MeO)_2C_6H_3$	20	4/96	99
3	Ph	2-$MeOC_6H_4$	15	<1/>99	99
4	Ph	4-$MeOC_6H_4$	15	<1/>99	99
5	Ph	4-MeC_6H_4	40	36/64[c]	96
6	2-$MeOC_6H_4$	2-$NO_2C_6H_4$	20	>99/<1	99
7	2-$CF_3C_6H_4$	2,5$(MeO)_2C_6H_3$	20	<1/>99	99
8	4-$MeOC_6H_4$	4-$NO_2C_6H_4$	20	>99/<1	99
9	4-$MeOC_6H_4$	4-MeC_6H_4	30	58/42	98
10	2-$MeOC_6H_4$	4-$MeOC_6H_4$	15	53/47[d]	99

[a] Same reaction conditions as Table 1. [b] Isolated overall yield. [c] Ratio determined by GC analysis. [d] Ratio determined by ^1H NMR analysis.

Table 4. Crossover Aldol Coupling of Aldehyde and Its Dimethyl Acetal with Silyl Enolates **2**−**4**[a]

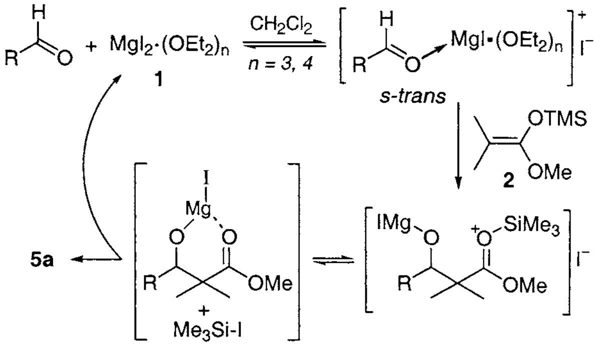
$$RCHO + R'CH(OMe)_2 + \mathbf{2–4} \xrightarrow[CH_2Cl_2,\ r.t.]{\mathbf{1}\ (5\ mol\ \%)} \mathbf{5–7(a)} + \mathbf{5–7(c)}$$

entry	R/R′	enolate/ time	ratio (**5-7a**/**5-7c**)	yield (%)[b]
1	n-C_7H_{15}	**2**/2 h	20/80[c]	97
2	$Ph/PhCH_2CH_2$	**2**/1 h	>99/<1	86
3	Ph	**3**/20 min	13/87[c]	99
4	$PhCH_2CH_2$	**3**/3 h	4/96[c]	95
5	PhCH=CH	**3**/0.5 h	40/60[c]	99
6	Ph	**4**/0.5 h	−/>99	99
7	PhCH=CH	**4**/0.5 h	−/>99	98

[a] Same reaction conditions as Table 1. [b] Isolated overall yield. [c] Determined by ^1H NMR analysis.

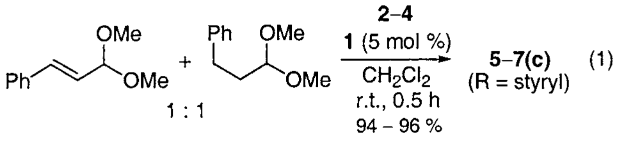
chemoselectivity. Apparently, the reactivity of aldehydes is principally dependent on the electron density of the formyl oxygen atom or the *coordinating* ability of the formyl group toward Mg(II), not the inherent *electrophilicity* of carbonyl,[15] which implies the formation of a coordination complex $[RCH{=}O{\rightarrow}MgI{\cdot}(OEt_2)_n]^+I^-$, in a favorable *s-trans* configuration,[16] presumably responsible for the effective activation of *electron-rich* aldehydic carbonyl. The cationic character[4a,c] of this more Lewis acidic Mg(II) coordinate with peripheral *ethereal* ligands (n = 3, 4) results from the dissociation of iodide ion in accordance with the coordination of the Lewis basic formyl group. The proposed catalytic cycle (Scheme 1) suggests that the transient iodotrimethylsilane (TMSI) may facilitate[17] the *irreversible* silylation of Mg-aldolate and regeneration of catalyst **1**.

Scheme 1. Proposed Catalytic Cycle of Aldehyde Aldol



Evans et al. recently reported[6c,d] an interesting magnesium halide-catalyzed *non-Mukaiyama* aldol reaction with TMSCl as the essential silylating agent for the turnover of catalytic magnesium halide in which a similar electronic effect for aryl and vinyl aldehyde substrates is apparent.[18] It is also evident[19] that the cationic coordinate of the resultant Mg-enolate might be involved. These facts underscore the uniqueness of Mg-catalyzed aldolization.

Cross-aldol coupling of acetals with silyl enolates **2**−**4** was studied (see Table 2 of Supporting Information) under the catalysis of **1** in comparison with their parent carbonyl substrates. We observed that (1) both aliphatic and aryl aldehyde acetals are reactive substrates, while ketone acetals are inert and (2) acetals are generally more reactive than the parent aldehydes. Notable reactivity trends (Table 4) include (1) acetalization activated unreactive aliphatic aldehydes (entries 1 and 4) and (2) acetal of unsaturated aryl aldehyde (i.e. cinnamaldehyde) or vinyl aldehyde to give aldol adducts exclusively (eq 1). In view of the importance of acetal functioning as a carbonyl equivalent for C−C bond cross-coupling,[20] we revealed here that **1** is a novel mild Lewis acid catalyst for effective and chemoselective acetal activation. The preferential activation of acetal over its parent



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(7) For Mukaiyama aldol reactions mediated by stoichiometric magnesium halides, see refs 6a and 6b. For magnesium halide-catalyzed *non-Mukaiyama* aldol reactions, see refs 6c and 6d.

(8) Mukaiyama, T. *Org. React.* **1982**, *28*, 203.

(9) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181.

(10) Although other *noncoordinative* solvents, i.e., benzene and toluene, can also be used, CH_2Cl_2 is found to be most effective (see Table 7 in Supporting Information). Strong coordinating solvents, i.e., THF and DMF, prohibited the reaction. Reaction in Et_2O is very sluggish and a *heterogeneous* mixture resulted probably due to the formation of polymeric MgI_2.

(11) Cf: Arkley, V.; Attenburrow, J.; Gregory, G. I.; Walker, T. *J. Chem. Soc.* **1962**, 1260. It is critical to use a freshly prepared *ethereal* solution of **1**; the use of an equal amount of commercially available MgI_2 (Aldrich) resulted in a *very slow* and sluggish reaction.

(12) See Table 1 in the Supporting Information.

(13) For example, cinnamaldehyde reacted with **2** in the presence of 5 mol % of **1** at −78 °C to yield 72% of aldol product along with 28% of Michael adduct, while geranial gave aldol product **5a** exclusively (entries 10−13, Table 1 in the Supporting Information).

(14) (a) Mikami, K.; Terada, M.; Nakai, T. *J. Org. Chem.* **1991**, *56*, 5456. (b) Hanyuda, K.; Hirai, K.; Nakai, T. *Synlett* **1997**, 31.

(15) For a mechanistic discussion, see: Asao, N.; Asano, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 3206 and references therein.

(16) Cf: Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1993**, *115*, 3133 and references therein. This *s-trans* activation complex would account for the observed comparable reactivity of *p*- and *o*-anisaldehydes (entry 3 of Table 2 and entry 10 of Table 3). Interestingly, (*S*)-α-*para*-(methoxy)-benzyloxypropanal reacted with silyl enolate **2** at −78 °C to give the corresponding syn adduct predominately (6:1) in 80% yield (entry 27, Table 1 in the Supporting Information), presumably via a favorable *chelative* complex due to the weak-coordinating (less Lewis basic) aliphatic carbonyl. In sharp contrast, remarkably chemoselective allylstannation of *o*-anisaldehyde over *p*-anisaldehyde catalyzed by $B(C_6F_5)_3$ and Me_3Al was reported by Maruoka et al., see: Ooi, T.; Uraguchi, D.; Kagoshima, N.; Maruoka, K. *J. Am. Chem. Soc.* **1998**, *120*, 5327. For recent accounts on the activation mode of this reaction other than *chelative*, see: (a) Blackwell, J. M.; Piers, W. E.; Parvez, M. *Org. Lett.* **2000**, *2*, 695. (b) Blackwell, J. M.; Piers, W. E.; McDonald, R. *J. Am. Chem. Soc.* **2002**, *124*, 1295.

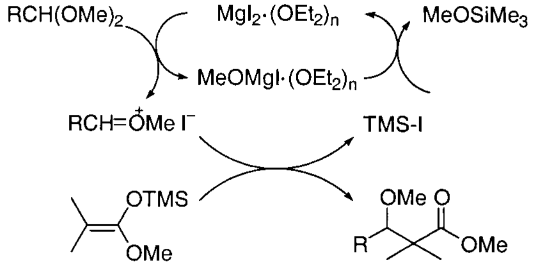
(17) The reaction is *not likely* catalyzed by TMSI since no observable transmetalation between silyl enolate and MgI_2 occurred (cf. ref 6b). Moreover, the chemoselectivity (vide infra) of TMSI-catalyzed Mukaiyama aldol is distinctly different from that of MgI_2 etherate. We thank one of the Reviewers for reminding us of this issue.

(18) Cf: ref 6c, higher yields and *drs* were documented for aldol products of aryl aldehydes substituted with an electron-donating group (i.e. *p*-MeO).

(19) Cf: ref 6c, for experimental procedure B, $NaSbF_6$ (up to 30 mol %) is required as an additive to drive the aldol reaction of *less* reactive *p*-nitrobenzaldehyde to completion, which is assumed to dissociate the chloride ion from the Mg(II) metal center.

(20) For a review, see: Mukaiyama, T.; Murakami, M. *Synthesis* **1987**, 1043.

Scheme 2. Proposed Catalytic Cycle of Acetal Aldol

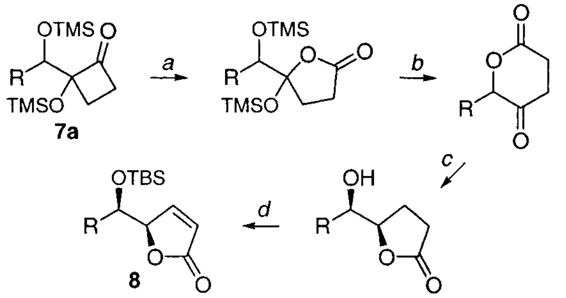


aldehyde may be attributed to the *fast* and *irreversible* silylation of MeOMgI etherate by transient TMSI to regenerate **1** and expel TMSOMe as the thermodynamically favored byproduct as shown in the proposed catalytic cycle (Scheme 2).

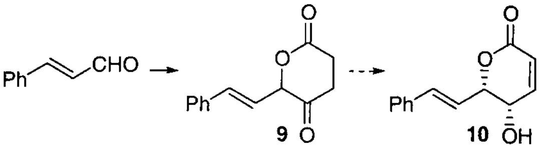
Commonly used strong Lewis acids, i.e., $TiCl_4$, $AlCl_3$, $SnCl_4$, and $BF_3{\cdot}OEt_2$, etc., are usually nonchemoselective or poorly chemoselective.[20] Trimethylsilyl triflate (TMSOTf),[21] TMSI,[22] and trityl perchlorate ($TrClO_4$)[23] are reported to selectively activate both aldehyde and ketone acetals but not their parent carbonyl compounds in aldol condensation with silyl enolates. The catalytic reactivity of **1** is opposite to some extent that of Lewis acidic organotin catalysts[24] which selectively activate the aldehydic carbonyl over its acetal, while differentiating ketone acetal over aldehyde acetal. Bidentate bis(phenoxyaluminum) Lewis acids recently have been developed as efficient Lewis acid catalysts for chemoselective activation of carbonyl over acetal function.[25] Thus, etherate **1** represents a novel type of main group Lewis acid catalyst, which selectively activates aldehyde acetals and electron-rich aldehydic carbonyls over ketone or its acetal equivalent. The uniqueness of **1** is attributed to the dissociative character[4a,6a,2e] of the iodide counterion, which is cooperating with the coordination of the Lewis basic oxygen atom of the formyl or acetal function with Mg(II) leading to a more Lewis acidic cationic Mg-coordinate as a result of Lewis base activation of Lewis acid.[26] The presence of ethereal solvent (Et_2O) as peripheral ligands of MgI_2 in noncoordinating media is also critical for the high catalytic reactivity of **1**.[10,11]

It is worthy to note that the efficient and chemoselective aldol coupling of strained cyclic enolsilane **4** with aryl aldehydes or acetals was realized by using **1** as a mild Lewis acid catalyst.[27] The synthetic value of this aldol process was demonstrated by converting **7a** to the corresponding butenolide derivative **8** (Scheme 3). Cinnamaldehyde was analogously transformed to the δ-lactone intermediate **9** (eq 2), a potential synthetic precursor for styryl lactone natural products,[28] i.e., 5-hydroxygoniothalamin (**10**).

Scheme 3[a]



[a] Conditions and yields: (a) CH_3CO_3H, NaOAc, reflux or *m*CPBA, $NaHCO_3$, $CHCl_3$ (70%-90%); (b) i. TFA, THF−H_2O; ii. cat. *p*-TsOH, PhH, 80 °C (50%-78%); (c) $NaBH_4$, THF, RT (90%-98%); (d) i. TBSCl, imidazole, DMF, RT; ii. LDA, PhSeCl, −78 °C; iii. H_2O_2, THF, RT (65%). (R = phenyl, piperonyl, or styryl.)

 (2)

In summary, we have demonstrated the unique catalytic reactivity of **1** in the chemoselective Mukaiyama-type aldol coupling of aryl aldehydes and acetals with silyl enolates. This magnesium-catalyzed silyl enolate addition is mild, efficient, and operationally simple. The selective activation of electron-rich aldehyde and acetal function is attributed to the pre-formation of a cationic Mg(II) complex. Iodide counterion, weakly coordinating peripheral ethereal ligands for Mg(II), and a noncoordinating reaction media are critical factors for the unique reactivity of this catalytic system. Further investigation of the catalytic reactivity of **1** in other C−C bond constructing reactions is underway.

Acknowledgment. Dedicated to Professor E. J. Corey. This work was supported by the National Science Foundation (Distinguished Youth Fund 29925204). The Cheung Kong Scholars Program is gratefully acknowledged.

Supporting Information Available: Typical experimental procedures, Tables 1−7, and product characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) (a) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248. (b) Murata, S.; Suzuki, M.; Noyori, R. *Tetrahedron* **1988**, *44*, 4259.

(22) Sakurai, H.; Sasaki, K.; Hosomi, A. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3195.

(23) (a) Mukaiyama, T.; Kobayashi, S.; Murakami, M. *Chem. Lett.* **1984**, 1759. (b) Mukaiyama, T.; Kobayashi, S.; Murakami, M. *Chem. Lett.* **1985**, 447. (c) Mukaiyama, T.; Iwakiri, H. *Chem. Lett.* **1985**, 1363.

(24) (a) Sato, T.; Otera, J.; Nozaki, H. *J. Am. Chem. Soc.* **1990**, *112*, 901. (b) Chen, J.; Otera, J. *Synlett* **1997**, 29. (c) Chen, J.; Otera, J. *Tetrahedron* **1997**, *53*, 14275.

(25) Ooi, T.; Tayama, E.; Takahashi, M.; Maruoka, K. *Tetrahedron Lett.* **1997**, *38*, 7403.

(26) Cf: (a) Denmark, S. E.; Stavenger, R. A. *Acc. Chem. Res.* **2000**, *33*, 432. (b) Denmark, S. E.; Wynn, T. *J. Am. Chem. Soc.* **2001**, *123*, 6199.

(27) Cf: (a) Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 961. (b) Shimada, J.-I.; Hashimoto, K.; Kim, B. H.; Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1759. (c) Crane, S. N.; Jenkins, T. J.; Burnell, D. J. *J. Org. Chem.* **1997**, *62*, 8722 and references therein.

(28) Cf: (a) Harris, J. M.; O'Doherty, G. A. *Org. Lett.* **2000**, *2*, 2983. (b) Tsubuki, M.; Kanai, K.; Nagase, H.; Honda, T. *Tetrahedron* **1999**, *55*, 2493.