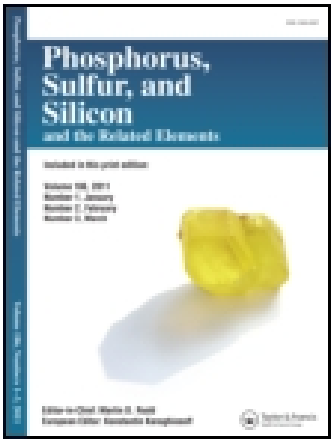

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MUKAIYAMA ALDOL REACTIONS CATALYZED BY A TRIMERIC ORGANO ALUMINUM(III) ALKOXIDE*

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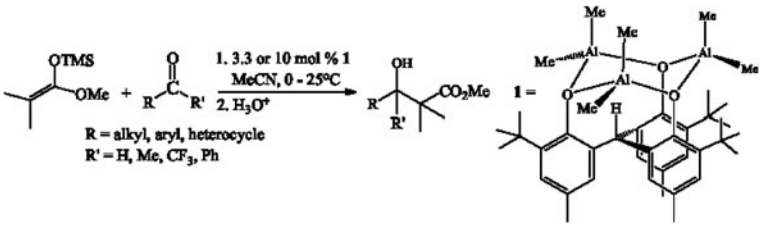
GRAPHICAL ABSTRACT



Abstract *Mukaiyama aldol reactions of enol ethers with a variety of aldehydes and ketones are efficiently catalyzed at 0–25 °C by the sterically bulky trimeric organo aluminum(III) alkoxide 1 synthesized via the reaction of 3 equiv of $AlMe_3$ with tripodal tris(2-hydroxy-3-tert-butyl-5-methylphenyl) methane and the elimination of 3 equiv of methane. Comparisons of its catalytic properties with the less sterically hindered analogue 2, the more sterically hindered analogue 3, a monomeric aluminum near-analogue 4, and a dimeric alumatrane 5 revealed that 1 possesses superior activity.*

Keywords Mukaiyama aldol reaction; trimeric; aluminum; tripodal ligand

INTRODUCTION

The Mukaiyama addition of a silyl enol ether to an aldehyde or ketone, leading to β-hydroxy carbonyl compounds, is one of the most important carbon-carbon bond formation reactions in classical organic synthesis.[1] The commercial importance of a variety of natural and synthetic products produced with this reaction has inspired considerable efforts to develop more effective Mukaiyama aldol catalysts.[2] In this regard, a variety of Lewis acids and bases have been tested, including $Bi(OTf)_3$,[3] lanthanide iodides [e.g,

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*Dedicated to Professor Dr. Louis D. Quin on the occasion of his 86th birthday.
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‡On Sabbatical Leave at Iowa State University.
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$SmI_2(THF)_2$],[4] $CuF{\cdot}3PPh_3{\cdot}2EtOH$,[5] $MgI_2{\cdot}(OEt_2)_n$,[6] $FeCl_2$,[7] Me_3SiOTf,[8] $Tf_2CHCH_2CHTf_2$ (a Bronsted acid precatalyst[9]), a Ti(IV) compound chelated by a chiral tridentate ligand and 3,5-di-tert-butylsalicylate,[10] Zr(IV) compounds with two modified chiral BINOL ligands,[11] N-heterocyclic carbenes,[12] DBU,[13] N-methylimidazole,[14] lithium benzylate,[15] and proazaphosphatranes.[16] Despite the numerous excellent catalysts for the Mukaiyama aldol reaction that have been reported, the search for new catalysts remains of current interest.

The authors recognize that Al, the key element in the catalyst whose properties are discussed in the present article, does not appear in the list of elements considered to be within the Journal's purview, namely, P, As, Sb, Bi; S, Se, Te; and Si, Ge, Sn. This list contains elements usually classified as metalloids (Si, Ge, As, Sb, Te) nonmetals (P, S, Se) and metals (Sn, Bi). Aluminum is usually classified as a metal because of its, metallic properties (e.g., high electrical and thermal conductivity, luster, malleability, and ductility).[17] However, because of several other properties which Al also possesses (e.g., directional bonding in the solid state,[18] covalent bonding in the majority of its compounds,[19] formation of anionic aluminates,[20] amphoterism of its oxide[21]), Al has sometimes been classified as a metalloid.[22] Based on the combination of metallic and metalloidal characteristics of this element, Al could be eligible for inclusion in the list of elements whose chemistry is appropriate for coverage in the Journal, particularly on the very special occasion of honoring Professor Louis Quin in this issue.

Although Lewis acidic properties of aluminum compounds and their usefulness in organic transformations are well-known, relatively few examples of such compounds [e.g., dimethylaluminum chloride,[23] (2,6-dimethylphenoxy)dimethylaluminum,[24] Me_2AlNTf_2,[25] chiral tethered bis(8-quinolinolato) aluminum halide (TBOx),[26] dimeric (2,7-disubsituted-1,8-biphenylenedioxy)bis(dimethylaluminum),[27] and monomeric/dimeric alumatrane complexes ligated by tris(2-oxy-3,5-dialkylbenzyl)amine[28,29]] have been reported to function as efficient promoters for the Mukaiyama aldol reaction. Interestingly, $AlCl_3$ does not function well as a catalyst for this reaction.[30] All previous use of aluminum compounds as catalysts for Mukayama reactions has focused on monomeric or dimeric aluminum systems;[23–30] however, an example of a trimeric aluminum complex as a catalyst for this reaction has to our knowledge not been reported.

Tripodal tris(2-hydroxy-3,5-dimethylphenyl)methane and its derivatives containing various alkyl groups in the 3 and 5 positions of the phenyl rings are versatile ligands upon deprotonation of their hydroxyl groups owing to coordination of their three phenoxide oxygens to a variety of elements.[25] Although many main group and transition metal complexes containing such tripodal ligands[31] have been reported, including an Al complex of tris(2-oxy-3,5-di-tert-butylphenyl)methane,[31c] we found no reports describing their application as catalysts for organic synthesis. Here we report for the first time the synthesis and characterization of trimeric **1** and **2** and their efficacies as catalysts for the Mukaiyama aldol reaction in comparison to **3**–**5** (Figure 1).

RESULTS AND DISCUSSION

The synthesis of **1** in 98% yield was accomplished by treating 3 equiv of $AlMe_3$ with tris(2-hydroxy-3-tert-butyl-5-methylphenyl)methane at 0 °C in toluene. The axial and equatorial trios of methyl groups bound to the Al centers are separated by 1.51 ppm in the solution ^{1}H NMR spectrum of **1** owing to differential shielding effects by the aryl rings. In addition, despite a high quadrupolar relaxation rate for the ^{27}Al nucleus

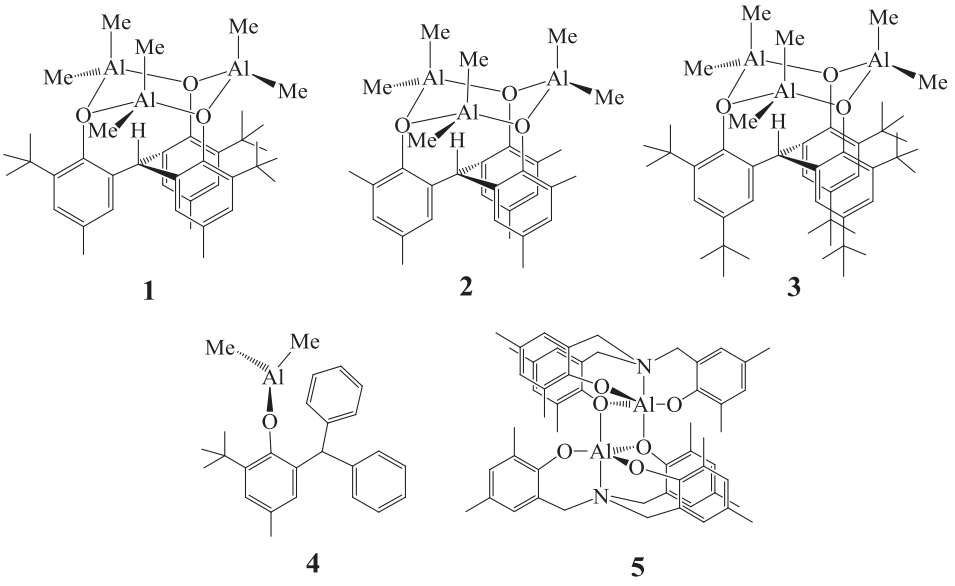


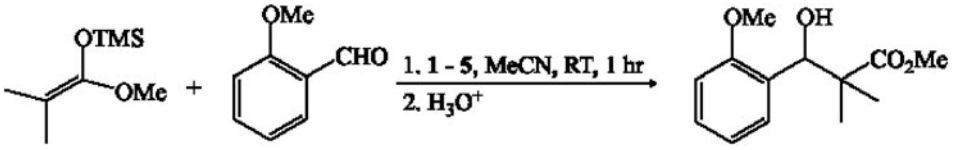
Figure 1 Al complexes studied in this work.

($I = 5/2$) and a broad background signal at about 60 ppm in the spectrum,[32] a single broad ^{27}Al NMR chemical shift was observed at 155.6 ppm, which is reasonably assigned to a tetracoordinated aluminum atom in solution.[33] Crystallographic studies that confirm the structure shown for catalyst **1** will be published separately in due course.

The sterically less hindered analogue of **1**, namely **2**, was synthesized analogously in 99% yield using tris(2-hydroxy-3,5-dimethylphenyl)methane in the presence of trimethyl aluminum. The sterically more hindered analogue **3** was synthesized via a literature procedure[31c] in 95% yield using tris(2-hydroxy-3,5-di-tert-buthylphenyl)methane and trimethyl aluminum. The monomeric near-analogue **4** was prepared *in-situ* in impure form [via the reaction of trimethyl aluminum with 2-benzhydryl-6-(tert-butyl)-4-methylphenol] and was used as such for catalytic screening. Evidence for the virtually quantitative conversion to **4** in its synthesis was the disappearance of the ^{1}H NMR peak corresponding to the hydroxyl proton of the ligand, and only small peaks assigned to impurities in its shifted and somewhat more complicated spectrum. Alumatrane dimer **5** was prepared according to our previous report.[34]

An evaluation of the relative efficacies of **1–5** in the room temperature aldol reaction of $Me_2C{=}C(OMe)OSiMe_3$ with o-anisaldehyde as a model reaction (Table 1) was carried out. Good to excellent isolated yields of aldol products were obtained after room temperature acid hydrolysis and purification by column chromatography. As shown in Table 1, 3.3 mol% of **1** (10 mol% Al) in MeCN was the best catalyst system among those we tested (entries 1–2) while catalysts **2–5** gave lower yields of reaction products (entries 3–10). Surprisingly, sterically crowded **1** facilitated higher yields (entries 1 and 2) than the sterically less encumbered analogue **2** (entries 3 and 4) while the lower yields observed with the sterically more hindered analogue **3** were expected (entries 5 and 6). In situ-generated monomeric **4** (which reasonably resembles one-third of a trimeric **1** molecule) and also the dimeric alumatrane **5** led to relatively poor product yields (entries 5–8). Catalysts **1–5** displayed

Table 1 Survey of aluminum complexes in a Mukaiyama aldol reaction catalyzed by **1**–**5**.[a]



Entry	Catalyst	Catalyst (mol%)	Al (mol%)	Yield (%)[c]
1	1[a]	3.3	10	92
2		1.7	5.0	89
3	2[a]	3.3	10	84
4		1.7	5.0	78
5	3[a]	3.3	10	82
6		1.7	5.0	81
7	4[b]	10	10	64
8		5.0	5.0	42
9	5[a]	5.0	10	70
10		2.5	5.0	66

[a]Reaction conditions: 1 mmol *o*-anisaldehyde, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 5 mL acetonitrile, room temperature, 1 h.

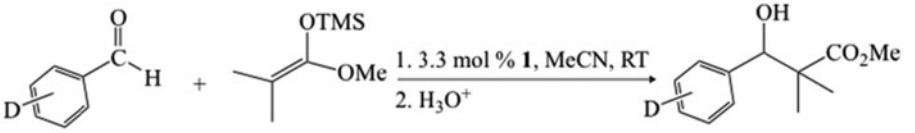
[b]Reaction conditions: in situ-generated **4**, 1 mmol o-anisaldehyde, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 1 mL toluene + 4 mL acetonitrile, room temperature, 1 h.

[c]Yields are averages of three runs.

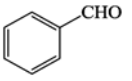
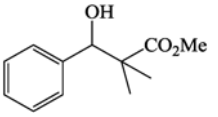
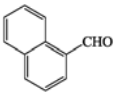
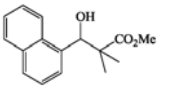
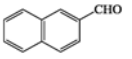
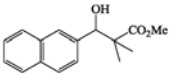
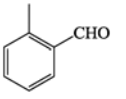
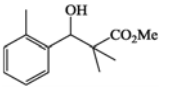
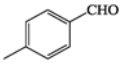
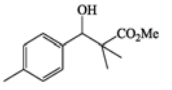
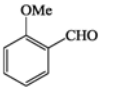
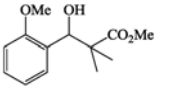
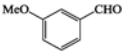
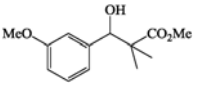
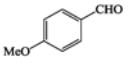
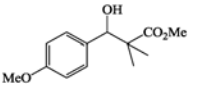
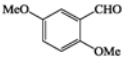
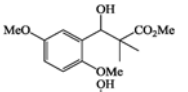
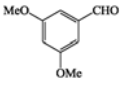
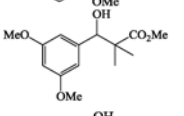
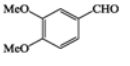
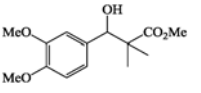
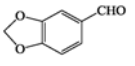
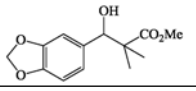
greater catalytic activity for our model reaction in acetonitrile than in toluene. Because **5** required more than 30 min to dissolve in acetonitrile, even with vigorous stirring, the 1-h reaction solution in Table 1 was created after **5** had dissolved. Because **4** is not soluble in acetonitrile but is soluble in toluene, the reactions in entries 7 and 8 of Table 1 were carried out in the solution that persisted after **3** had been dissolved in 1 mL of toluene followed by the addition of 4 mL of acetonitrile.

We next examined a variety of aldehydes using the best catalyst (**1**) in the Mukaiyama aldol reaction of $Me_2C{=}C(OMe)OSiMe_3$. As observed in Table 1, better yields and/or shortened reaction times for catalyst **1** than those for **5** were also observed in Tables 2–4. Both electron-neutral and electron-donating aldehydes reacted with a slight excess of $Me_2C{=}C(OMe)OSiMe_3$ to afford the desired aldol products in good to excellent yields within 30–180 min at room temperature (Table 2). Reaction times required for good product yields varied, depending on the aldehyde employed. Electron-neutral aryl aldehydes, such as benzaldehyde (entry 1), 1-naphthaldehyde (entry 2), and 2-naphthaldehyde (entry 3) underwent clean addition reactions with $Me_2C{=}C(OMe)OSiMe_3$ to give the expected aldol products in excellent yields. However, the reaction time for 2-naphthaldehyde was longer than for 1-naphthaldehyde to achieve a comparable yield of the corresponding aldol product. Aldehydes with electron-donating substituents, such as those in entries 4–12, provided good to excellent isolated yields of the corresponding aldol products. *p*-Tolualdehyde was more reactive than *o*-tolualdehyde (entries 4–5), while *o*-anisaldehyde and *p*-anisaldehyde showed similar reactivities (entries 6 and 8). Among the aldehydes in entries 6–8, *m*-anisaldehyde provided the highest yield under the same reaction conditions. All the di-substituted benzaldehydes investigated featured one methoxy group meta to the CHO functionality, and as the second methoxy group moved closer to the CHO position, better reactivity was observed (entries 9–11). Regardless of the acyclic or cyclic structures (entries

Table 2 Scope of the Mukaiyama aldol reaction of electron-neutral and electron-donating aryl aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ catalyzed by **1**[a]



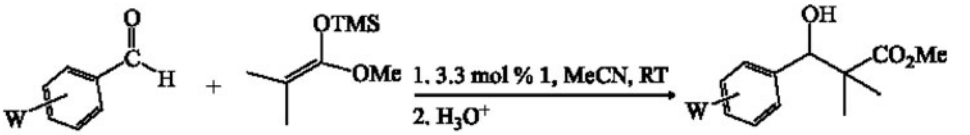
D = electron-neutral or electron-donating groups

Entry	Aldehydes	Product	Time (min)	Yield (%)[b]
1			30 60 (Lit: 60)	91 95 (Lit: 95)
2			90 (Lit: 120)	88 (Lit: 88)
3			120 (Lit: 120)	90 (Lit: 92)
4			60 180 (Lit: 180)	82 97 (Lit: 91)
5			60 (Lit: 180)	89 (Lit: 85)
6			30	81
7			30 (Lit: 120)	90 (Lit: 92)
8			30 60 (Lit: 60)	83 99 (Lit: 90)
9			30	98
10			60	91
11			60	86
12			60 120 (Lit: 120)	85 99 (Lit: 98)

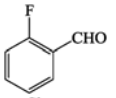
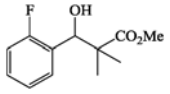
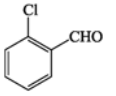
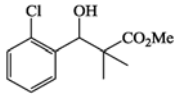
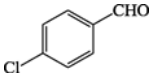
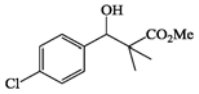
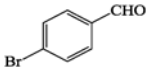
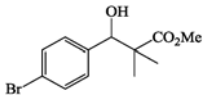
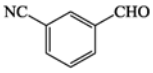
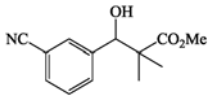
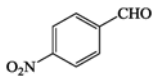
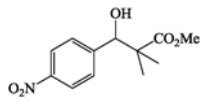
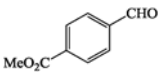
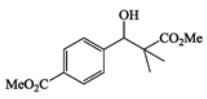
[a]Reaction conditions: 1 mmol aldehyde, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 3.3 mol% 1, 5 mL CH_3CN, room temperature.

[b]Isolated yields after silica gel column chromatography. Times and yields in parentheses are literature values associated with **5**.[22]

Table 3 Scope of the Mukaiyama aldol reaction of electron-withdrawing aryl aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ catalyzed by 1[a]



W = electron-withdrawing group

Entry	Aldehydes	Product	Time (min)	Yield (%)[b]
1			180	62
2			120	87
3			60 (Lit: 240)	96 (Lit: 93)
4			180	87
5			180	85
6			180 (Lit: 420)	92 (Lit: 95)
7			180 (Lit: 360)	91 (Lit: 92)

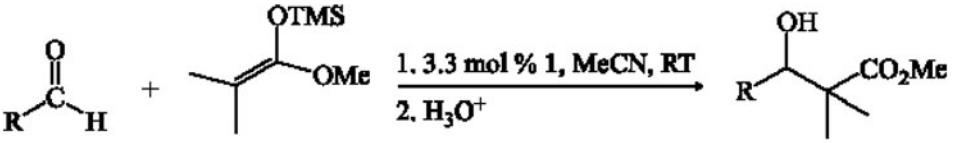
[a]Reaction conditions: 1 mmol aldehyde, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 3.3 mol% 1, 5 mL CH_3CN, room temperature.

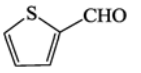
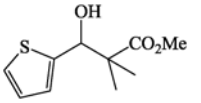
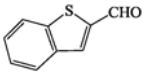
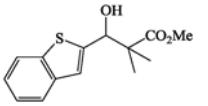
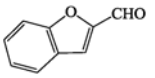
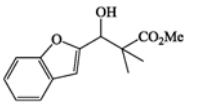
[b]Isolated yields after silica gel column chromatography. Times and yields in parentheses are literature values associated with **5**.[28]

11 and 12) product yields were similar. Interestingly, the best isolated product yield (98%) was realized in only 30 min for 2,5-dimethoxybenzaldehyde (entry 9). Enolizable aldehydes are apparently not favorable candidates under our conditions. Thus cinnamaldehyde did not provide the desired product under the reaction conditions given in Table 1.

A variety of aldehydes bearing electron-withdrawing groups were also screened with $Me_2C{=}C(OMe)OSiMe_3$ using **1** as the catalyst, and the results are summarized in Table 3. Except for 1-fluorobenzaldehyde (entry 1), all the other benzaldehydes in Table 3 provided good to excellent isolated yields of aldol products within 60–180 min. Interestingly, 2-chlorobenzaldehyde led to a better yield than 2-fluorobenzaldehyde despite the presence of a more electronegative fluoro group in the latter (entries 1–2), whereas 4-chlorobenzaldehyde gave a better yield than the less electronegative 4-bromobenzaldehyde (entries 3–4). The

Table 4 Scope of the Mukaiyama aldol reaction of heterocyclic aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ catalyzed by **1**[a]



Entry	Aldehydes	Product	Time (min)	Yield (%)[b]
1			180 (Lit: 360)	98 (Lit: 96)
2			180	91
3			180 (Lit: 300)	98 (Lit: 91)

[a]Reaction conditions: 1 mmol aldehyde, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 3.3 mol% 1, 5 mL CH_3CN, room temperature.

[b]Isolated yields after silica gel column chromatography. Times and yields in parentheses are literature values associated with **5**.[28]

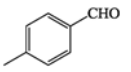
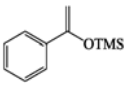
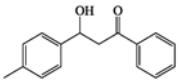
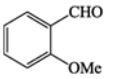
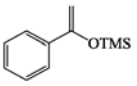
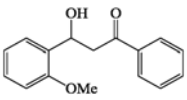
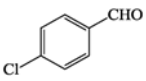
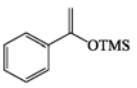
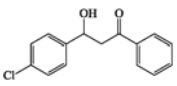
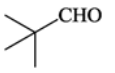
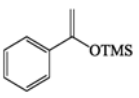
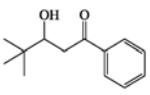
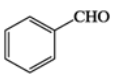
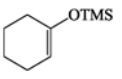
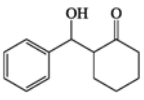
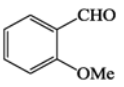
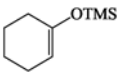
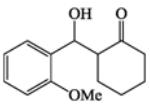
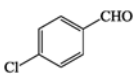
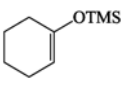
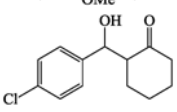
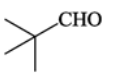
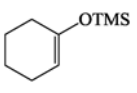
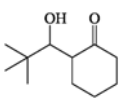
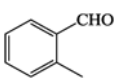
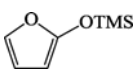
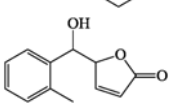
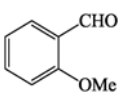
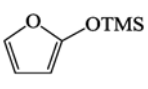
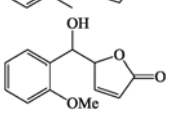
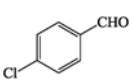
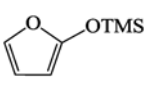
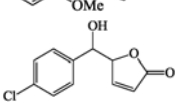
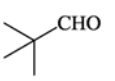
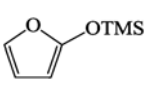
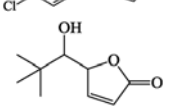
three electron-deficient benzaldehydes (entries 5–7) and ester-functionalized methyl 4-formylbenzoate underwent clean reactions giving good yields of products within 180 min (entries 5–7).

We then turned our attention to screening several heterocyclic aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ using catalyst **1**, and the results are summarized in Table 4. The 5-membered ring aldehydes bearing O or S heteroatoms afforded the expected aldol products in excellent isolated yields (91–98%) within 180 min.

We then screened aldehydes with $C_6H_5C(=CH_2)OSiMe_3$, $C_6H_9OSiMe_3$, and $(2\text{-}C_4H_3O)OSiMe_3$ in the presence of **1** as shown in Table 5. A benzaldehyde containing an electron-donating or electron-withdrawing substituent generally gave a good yield of product as did a sterically bulky aliphatic aldehyde. Although there is an opportunity for 1,2 addition to the aldehyde with 2-(trimethylsiloxy)furan, the only products obtained stemmed from the desired 1,4 addition process (entries 9–12).

It is interesting that aluminum catalysts for Mukaiyama reactions involving ketone substrates have not been reported.[23–30] We now disclose that Mukaiyama aldol additions of the enol ether $Me_2C{=}C(OMe)OSiMe_3$ to acetone, acetophenone, 2,2,2-trifluoroacetophenone, and benzophenone are very efficient in the presence of **1** as catalyst, although a longer reaction time (72 h), lower reaction temperature (0–5 °C) and a higher catalyst loading (10 mol%) are required than for aldehydes (Table 6). It is interesting that the reaction of $Me_2C{=}C(OMe)OSiMe_3$ with ketones afforded the corresponding hydrolyzed products after work up rather than TMS-protected species.

Table 5 Scope of the Mukaiyama aldol reaction of aldehydes with $C_6H_5C(=CH_2)OSiMe_3$,$C_6H_9OSiMe_3$, and $(2\text{-}C_4H_3O)OSiMe_3$ catalyzed by **1**[a]

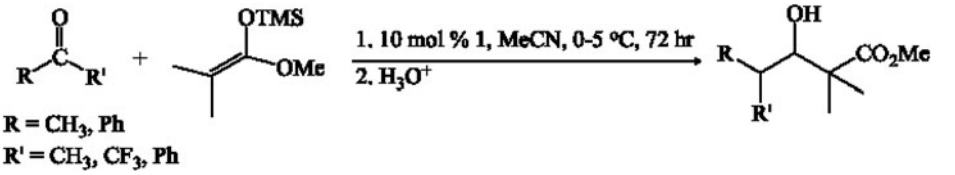
Entry	Aldehydes	TMS-enolate	Product	Yield (%)[b]
1				91
2				97
3				94
4				91
5				94
6				97
7				96
8				90
9				90
10				96
11				98
12				91

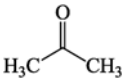
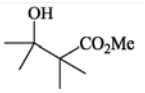
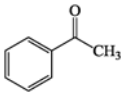
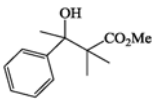
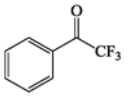
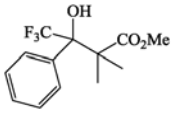
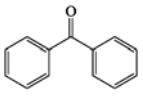
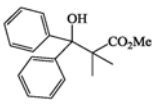
[a]Reaction conditions: 1 mmol aldehyde, 1.2 mmol TMS ether, 3.3 mol% 1, 5 mL CH_3CN, room temperature, 180 min.

[b]Isolated yields after silica gel column chromatography.

Acetone, acetophenone, 2,2,2-trifluoroacetophenone, and benzophenone were also screened with other silyl ethers such as $TBDMSC(-CH_2)OMe$, $(tert\text{-}Bu)C(-CH_2)OTMS$, $(2\text{-}C_4H_3O)OSiMe_3$, and $PhC(-CH_2)OTMS$ using **1** as the catalyst, and the results are summarized in Table 7. All the ketones in Table 7 provided excellent isolated yields of

Table 6 Scope of the Mukaiyama aldol reaction of ketones with $Me_2C{=}C(OMe)OSiMe_3$ catalyzed by **1**[a]



Entry	Ketones	Product	Yield (%)[b]
1			92
2			95
3			93
4			90

[a]Reaction conditions: 1 mmol ketone, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 10 mol% 1, 5 mL CH_3CN, 0–5°C, 72 h.

[b]Isolated yields after silica gel column chromatography.

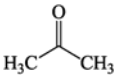
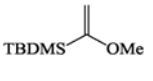
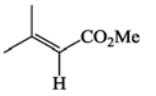
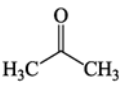
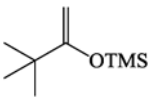
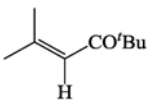
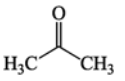
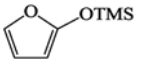
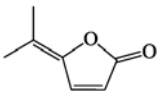
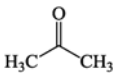
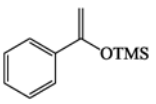
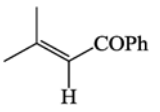
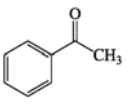
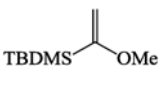
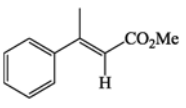
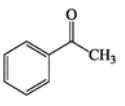
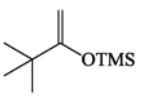
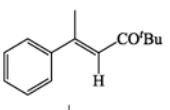
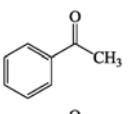
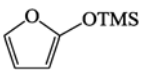
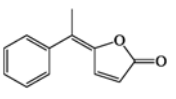
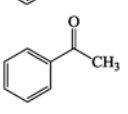
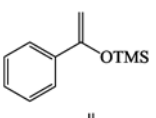
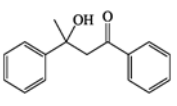
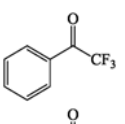
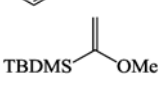
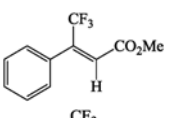
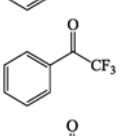
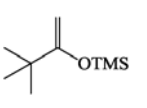
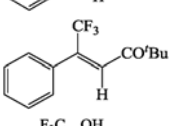
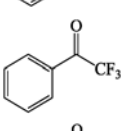
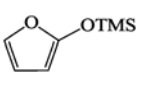
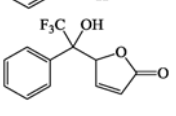
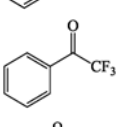
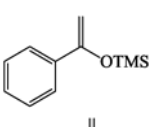
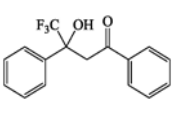
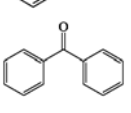
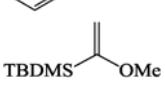
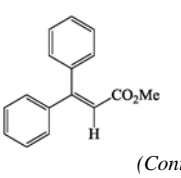
aldol products within 72 h at a reaction temperature of 0–5 °C. Except for entries 8, 11, 12, and 15, the reactions of ketones with silyl ethers provided the corresponding α,β-unsaturated ketones in excellent yield. It is not clear why elimination was not observed for at least some of the ketones investigated.

Earlier we reported that dimeric alumatrane **5** is insoluble in acetonitrile, but upon addition of benzaldehyde[29] or 2-methoxybenzaldehyde[28] to the mixture, a light yellow solution formed and an isolable monomeric alumatrane adduct containing benzaldehyde coordinated to the aluminum atom was obtained after workup. Similarly, an acetonitrile-d_3 solution of trimeric **2** became reddish orange upon benzaldehyde addition. In carrying out a similar experiment in an NMR tube, increasing the mole ratio of **2** beyond 1:1 induced broadening of the PhC(−O)H proton in its ^{1}H NMR spectrum, which supports formation of a 1:1 benzaldehyde adduct of **2**.

EXPERIMENTAL SECTION

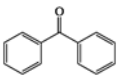
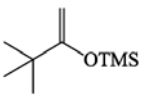
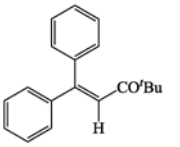
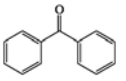
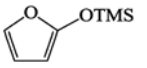
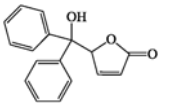
Synthesis of **1**. A 2.0 M solution of $AlMe_3$ in toluene (1.5 mL, 3.0 mmol) was added dropwise to a solution of tris(2-hydroxy-3-tert-butyl-5-methylphenyl)methane (0.50 g, 1.0 mmol) in toluene (30 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature over 1 h and then was stirred overnight. All volatiles were evaporated under reduced pressure, leaving a colorless solid, to which 10 mL of toluene were added. The solution was then filtered and stored at –20 °C in a refrigerator. Yield, 98% (0.66 g). ^{1}H

Table 7 Scope of the Mukaiyama aldol reaction of ketones with various enol ethers catalyzed by **1**[a]

Entry	Ketones	TMS-enolate	Product	Yield (%)[b]
1				90
2				91
3				92
4				96
5				95
6				98
7				94
8				97
9				91
10				90
11				93
12				99
13				92

(Continued on next page)

Table 7 Scope of the Mukaiyama aldol reaction of ketones with various enol ethers catalyzed by **1**[a] (Continued)

Entry	Ketones	TMS-enolate	Product	Yield (%)[b]
14				91
15				95

[a]Reaction conditions: 1 mmol ketone, 1.2 mmol $Me_2C{=}C(OMe)OSiMe_3$, 10 mol% 1, 5 mL CH_3CN, 0–5°C, 72 h.

[b]Isolated yields after silica gel column chromatography.

NMR (400.15 MHz, C_6D_6, ppm): δ 8.84 (s, 1H, C*H*), 7.74 (s, 3H, Ph*H*) 7.00 (s, 3H, Ph*H*), 2.05 (s, 9H, CH_3), 1.39 (s, 27H, C(CH_3)$_3$), 0.33 (s, 9H, Al-CH_3), −1.17 (s, 9H, Al-CH_3). $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6, ppm): δ 151.26, 139.81, 135.16, 128.85, 128.32, 127.29 (*Ph*), 35.70 (*C*(CH$_3$)$_3$), 32.27 (C(*C*H$_3$)$_3$), 27.83 (*C*H), 21.35 (*C*H$_3$), −5.72 (Al-*C*H$_3$), −7.96 (Al-*C*H$_3$). ^{27}Al NMR (104.2 MHz, C_6D_6, ppm): δ 155.6 ($\Delta\nu_{1/2} = 2082.9$ Hz). Anal. Calcd for $C_{40}H_{61}Al_3O_3$: C, 71.61; H, 9.17. Found: C, 71.92; H, 9.56.

Synthesis of **2**. This compound was prepared in 99% (0.54 g) yield by reacting $AlMe_3$ (1.5 mL, 3.0 mmol) with tris(2-hydroxy-3,5-dimethylphenyl)methane (0.376 g, 1.0 mmol) in toluene (30 mL) at 0 °C in a manner analogous to the procedure for **1**. ^{1}H NMR (400.15 MHz, C_6D_6, ppm): δ 8.84 (s, 1H, C*H*), 7.52 (s, 3H, Ph*H*), 6.54 (s, 3H, Ph*H*), 2.06 (s, 9H, CH_3), 1.99 (s, 9H, CH_3), 0.21 (s, 9H, Al-CH_3), –1.33 (s, 9H, Al-CH_3). $^{13}C\{^1H\}$ NMR (100.63 MHz, C_6D_6, ppm): δ 151.54, 135.31, 134.36, 130.85, 129.61, 126.47 (*Ph*), 29.23 (*C*H), 21.02 (*C*H$_3$), 17.12 (*C*H$_3$), −6.90 (Al-*C*H$_3$), −11.60 (Al-*C*H$_3$). ^{27}Al NMR (104.15 MHz, C_6D_6, ppm): δ 154.6 ($\Delta\nu_{1/2} = 1978.8$ Hz). Anal. Calcd for $C_{31}H_{43}Al_3O_3$: C, 68.37; H, 7.96. Found: C, 68.26; H, 8.13.

Synthesis of **4**. Sulfuric acid (1.66 mL, 30 mmol) was added dropwise to a solution of 2-tert-butyl-4-methylphenol (1.64 g, 10 mmol) and diphenylmethanol (1.84 g, 10 mmol) in glacial acetic acid (40 mL) at room temperature. The reaction mixture was stirred overnight and then 50 mL of distilled water was added. The aqueous layer was extracted twice with diethyl ether (30 mL), and the combined organic portions were dried over $MgSO_4$, filtered, and evaporated to dryness. After washing with 20 mL of *n*-hexane and drying, 2-benzhydryl-6-tert-butyl-4-methylphenol was obtained as a colorless powder. Yield, 94% (3.17 g). ^{1}H NMR (400.15 MHz, C_6D_6, ppm): δ 7.32–7.12 (m, 9H, CH(C$_6$*H*$_5$)$_2$), 7.00 (s, 1H, Ph*H*), 6.39 (s, 1H, Ph*H*), 5.57 (s, 1H, C*H*(C$_6$H$_5$)$_2$), 4.49 (s, 1H, O*H*), 2.15 (s, 3H, CH_3), 1.34 (s, 9H, C(CH_3)$_3$). $^{13}C\{^1H\}$ NMR (100.6 MHz, C_6D_6, ppm): δ 150.14, 142.06, 136.95, 130.62, 129.39, 128.84, 128.71, 128.50, 128.46, 126.93, 126.27, 126.24 (*Ph*, CH(*C*$_6$H$_5$)$_2$), 51.79 (*C*H(C$_6$H$_5$)$_2$), 34.54 (*C*(CH$_3$)$_3$), 29.87 (C(*C*H$_3$)$_3$), 21.11 (*C*H$_3$). HRMS m/z calcd for $C_{24}H_{26}O$ (M^+) 330.1984. Found 330.1980.

The 2-benzhydryl-6-tert-butyl-4-methylphenol obtained was used for the in-situ synthesis of **4**. A 2.0 M solution of $AlMe_3$ in toluene (1.5 mL, 3.0 mmol) was added dropwise to a solution of tris(2-hydroxy-3,5-dimethylphenyl)methane (0.376 g, 1.0 mmol) in toluene

(6 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature over 1 h and then stirred overnight. The solution was used directly as a stock solution of **4**. The ^{1}H NMR spectrum of **4** is consistent with its proposed constitution.

Representative Procedure for Mukaiyama Aldol Reactions of $Me_2C{=}C(OMe)OSiMe_3$ with Aryl Aldehydes Catalyzed by **1**–**5**. To an oven-dried 10-mL vial equipped with a magnetic stirring bar and a septum was added acetonitrile (5 mL), 1 (0.03 mmol), and aldehyde (1.0 mmol). The mixture was stirred for 30 min at room temperature, followed by addition of $Me_2C{=}C(OMe)OSiMe_3$ (1.2 mmol). When the reaction was judged to be complete by TLC, the reaction was quenched by adding 2 *N* HCl (3 mL) solution followed by stirring the reaction mixture for an additional 3 h at room temperature. The reaction mixture was extracted with methylene chloride and dried over Na_2SO_4, the solution was filtered and dried on a rotavap apparatus, and then the crude product was purified by silica gel column chromatography (EtOAc:hexanes = 1:9).

Methyl 3-hydroxy-2,2-dimethyl-3-(2,5-dimethoxybenzene)propionate. (Table 2, entry 9): yellow oil. ^{1}H NMR (400.15 MHz, $CDCl_3$, ppm): δ 6.86 (s, 1H, Ph*H*), 6.76 (s, 2H, Ph*H*), 5.21 (s, 1H, C*H*OH), 3.73 (s, 6H, OCH_3), 3.69 (s, 3H, C(−O)COCH_3), 3.60 (br, 1H, O*H*), 1.13 (d, J = 17.6 Hz, 6H, C(CH_3)$_2$). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$, ppm): δ 178.10, 153.23, 151.20, 129.03, 114.96, 113.17, 111.45 (*Ph*), 73.94 (*C*HOH), 55.67 (O*C*H$_3$), 55.65 (O*C*H$_3$), 51.97 (C(=O)CO*C*H$_3$), 48.49 (*C*(CH$_3$)$_2$), 22.86 (C(*C*H$_3$)$_2$), 19.16 (C(*C*H$_3$)$_2$). HRMS m/z calcd for $C_{14}H_{20}O_5$ (M^+) 268.1311. Found 268.1306.

Methyl 3-hydroxy-2,2-dimethyl-3-(3,5-dimethoxybenzene)propionate. (Table 2, entry 10): yellow oil. ^{1}H NMR (400.15 MHz, $CDCl_3$, ppm): δ 6.43 (s, 2H, Ph*H*), 6.35 (s, 1H, Ph*H*), 4.79 (s, 1H, C*H*OH), 3.75 (s, 6H, OCH_3), 3.69 (s, 3H, C(=O)COCH_3), 3.08 (br, 1H, O*H*), 1.10 (d, J = 14.4 Hz, 6H, C(CH_3)$_2$). ^{13}C{^{1}H} NMR (100.63 MHz, $CDCl_3$, ppm): δ 178.06, 160.15, 142.42, 105.78, 99.52 (*Ph*), 78.73 (*C*HOH), 55.28 (O*C*H$_3$), 52.09 (C(=O)CO*C*H$_3$), 47.63 (*C*(CH$_3$)$_2$), 23.07 (C(*C*H$_3$)$_2$), 19.32 (C(*C*H$_3$)$_2$). HRMS m/z calcd for $C_{14}H_{20}O_5$ (M^+) 268.1311. Found 268.1305.

CONCLUSIONS

In summary, we have synthesized the novel bulky trimeric complex **1** in which an $(Me_2Al)_3O_3$ six-membered cyclohexanoid ring is axially bonded via the bridging phenoxide oxygens of a tris(2-oxy-3-tert-butyl-5-dimethylphenyl)methane ligand. Complex **1** is a potent catalyst at room temperature for Mukaiyama aldol reactions of $Me_2C{=}C(OMe)OSiMe_3$ with a diverse range of aryl aldehydes. As Table 1 reveals, the catalytic activity of **1** is superior to that of a less hindered trimeric analogue (**2**), a more hindered trimeric analogue (**3**), a monomeric near-analogue (**4**), and a dimeric alumatrane (**5**). The superior nature of **1** over **5** in the reactions reported here is accentuated by our reaction times and yields realized with **1** compared with those we reported earlier with **5**[28] for 13 of the reactions reported in Tables 2–4. Of those 13 reactions, **3** facilitated shorter times but greater yields, **5** facilitated shorter times and approximately the same yields, **2** facilitated equal times and greater yields and **3** facilitated ca equal times and yields. Under the same conditions (Table 5) **1** also showed excellent catalytic activity for the reactions of other enol ethers with aryl aldehydes and bulky trimethylacetaldehyde. As shown in Tables 6 and 7, the catalytic activity of **1** for the Mukaiyama addition of enol ethers to ketones was advantageously strong. However, compared with aldehydes, a longer reaction time, a lower reaction temperature, and a higher catalyst loading were required.

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