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Catalysis of Mukaiyama Aldol Reactions by a Tricyclic Aluminum Alkoxide Lewis Acid

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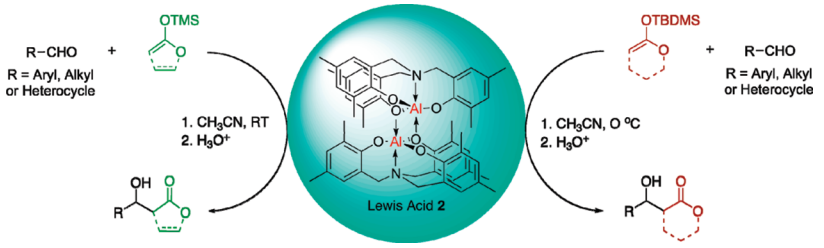

The Mukayiama aldol reaction of aldehydes is efficiently accomplished with a low concentration of the dimeric alumatrane catalyst **2** at mild or subambient temperatures. Our protocol tolerates a wide variety of electron-rich, neutral, and deficient aryl, alkyl, and heterocyclic aldehydes. A wide variety of enol silyl ethers are also tolerated. An intermediate that was isolated provides mechanistic information regarding the role of dimeric **2** in the Mukaiyama aldol reaction. Experimental evidence is presented for the stronger Lewis acidity of **5** compared with F_3B.

Introduction

Aldol reactions usually require electron deficient aldehydes and are often plagued by the formation of side products such as α,β-unsaturated esters. Despite these deficiencies, the Mukaiyama aldol reaction is one of the most versatile carbon−carbon bond forming reactions allowing access to synthetically challenging β-hydroxy carbonyl compounds.[1] Intensive efforts have been made to synthesize such compounds owing to the pivotal nature of the Mukaiyama aldol reaction in the synthesis of a variety of natural products.[2] Utilization of this transformation for the synthesis of β-hydroxy carbonyl compounds was a notable achievement attained through the development of the addition of a silyl enol ether to aldehydes and ketones. It may be noted that very few methodologies for catalytic aldol reactions of ketones have been developed compared with those for aldehydes.[3]

Because of the utility of β-hydroxy carbonyl compounds, many Lewis acid and Lewis base catalysts for their synthesis have been investigated. Lewis acids that activate the carbonyl moiety of an aldehyde or ketone in the Mukaiyama aldol reaction include bismuth(III) triflate,[2] lanthanum(III) bromide,[4] copper(I) fluoride,[5] $MgI_2 \cdot (OEt_2)_n$,[5] iron(II) chloride,[7] Me_3SiNTf_2,[8] and Zr(IV) compounds.[9] Common Lewis bases that activate the silicon atom of silyl enol ethers utilized in the Mukaiyama aldol reaction of aldehydes include *N*-heterocyclic carbenes,[10] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),[11] *N*-methylimidazole,[12] lithium benzylate,[13] and amines.[14] There

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(1) For a referenced list of known Mukaiyama aldol products, see the Supporting Information.

(2) Ollevier, T.; Bouchard, J.; Desyroy, V. *J. Org. Chem.* **2008**, *73*, 331–334.
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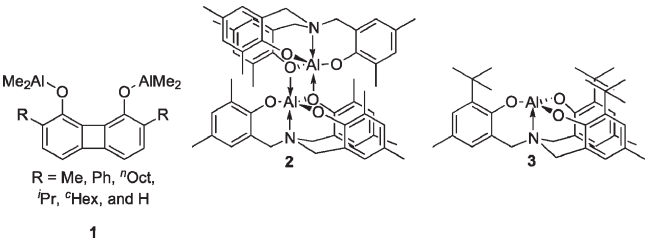
are also reports describing Lewis acids that have been grafted onto polymer supports for recyclability in Mukaiyama aldol reactions of aldehydes.[15] Lewis basic ionic liquids have also been shown to facilitate the synthesis of β-hydroxy carbonyl products from aldehydes,[16] and there are a few reports in which photochemistry has been employed in the Mukaiyama aldol reaction of aldehydes (although with the formation of oxetene as a byproduct[3d,17]).

Recent studies have centered on enolate substrates that supply Mukaiyama aldol products similar to those provided by the use of enol substrates. In 2006, Knochel and co-workers developed an elegant route to β-hydroxy esters via a Reformatsky reaction involving organozinc reagents instead of silyl groups. Advantages of organozinc reagents include their functional group tolerance, their stability in various solvents, and the ease with which they are synthesized.[18] β-Hydroxy esters are also obtainable by selectively opening epoxides in the presence of a cobalt catalyst under an atmosphere of carbon monoxide in methanol.[19] Instead of trimethylsilyl enol ethers Nakajima and co-workers used trichlorosilyl enol ethers in asymmetric aldol reactions carried out in the presence of a chiral phosphine oxide (*S*-BINAPO) to achieve high yields of the desired β-hydroxy esters with high functional group tolerance.[20] Scheeren and co-workers developed a method for synthesizing β-hydroxy esters from ketene acetals in the presence of 1 mol % of readily available inexpensive zinc chloride.[21] However, a drawback of this procedure is that ketene acetals are not commercially available and must be made from ortho esters in the presence of a sterically hindered aluminum alkoxide.[22]

Reports of the use of aluminum Lewis acids in the Mukaiyama aldol reaction are quite limited. Maruoka et al. developed a bidentate organoaluminum Lewis acid **1** (R = Me) which, at the 1 equiv level, facilitated Mukaiyama aldol reactions in methylene chloride at low temperatures to produce high product yields.[23] Maruoka et al. expanded their methodology in 2007 by synthesizing several analogues of the bidentate aluminum Lewis acid analogues of **1** (R = Me), namely, R = Ph, ^{n}Oct, ^{i}Pr, ^{c}Hex, and H, in order to evaluate the reactivity of different substituents in the position ortho to the $OAlMe_2$ groups.[24] In that paper, it was postulated that the use of the bidentate Lewis acid **1** (R = Me) doubly activates substrate carbonyls to augment their reactivity and hence the selectivity of the carbonyl−Lewis acid complexes for formation of the aldol product. Again, however, one or more equivalents of **1** (R = Me) were required to obtain high yields of the desired product.[24]

Aluminum compounds that function as efficient promoters for the Mukaiyama aldol reaction would be advantageous owing to their relatively low cost and toxicity. Thus in view of the high concentrations required for **1** (R = Me), efforts to develop an aluminum Lewis acid able to operate in catalytic amounts are worthwhile. In 2006, we reported the synthesis of a novel tricyclic aluminum alkoxide (alumatrane dimer **2**) and showed that oxygen donor compounds and amines can split this dimer to form monomeric alumatranes.[25] Of particular interest in the present context is our observation that aldehydes rapidly split dimeric **2** to form monomeric alumatrane·aldehyde adducts. It was therefore speculated that **2** might serve as an advantageous catalyst in various Lewis acid-catalyzed reactions, and herein we explore this application of this novel catalyst in Mukaiyama aldol transformations.



Results and Discussion

Optimization Study of a Mukaiyama Aldol Reaction. The coupling of *o*-anisaldehyde with methyl trimethylsilyl dimethylketene acetal was conducted as a model screening reaction and the results are summarized in Table 1. The desired product was isolated after hydrolysis with 2 N aq HCl after 24 h. By using 10 mol % of **2** in toluene at room temperature, 40% of the desired product was obtained (Table 1, entry 1). Interestingly, when the mole percentage of alumatrane dimer **2** in toluene was decreased, the yield of the desired products increased from 52% to 68% (Table 1, entries 2−4). When the temperature was decreased from room temperature to 0 °C, using 5 mol % of **2**, the product yield increased from 52% (entry 2) to 63% (entry 5).

Typically, Mukaiyama aldol reactions require a polar solvent to obtain high yields. However, **2** in polar solvents such as tetrahydrofuran or diethyl ether, form soluble adducts whose ligands are quite stable to further reactions such as ether displacement by an aldehyde. On the other hand, when dimer **2** is stirred in acetonitrile for 24 h, no adduct formation is observed as shown by ^{1}H NMR spectroscopy and by visually observing that the alumatrane dimer **2** remains insoluble in this solvent as well as other solvents that do not form adducts with **2**.

When acetonitrile is used as the solvent for the screening reaction in Table 1, a 5 mol % catalyst loading of **2** leads to a nearly quantitative yield of product (entry 6). Upon lowering the loading of dimeric **2** to 2.5 mol % and 0.5 mol %, 94% and 84% yields of the desired product, respectively, were obtained (Table 1, entries 7 and 8). Since we observed higher product yields at lower loadings of **2** in toluene (entries 2−4), the screening reaction was carried out with a 50/50 mixture of acetonitrile/toluene containing 0.5 mol % of **2** in hopes of substantially increasing the product yield over 84% in

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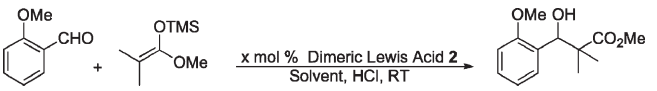
TABLE 1. Optimization of 2-Catalyzed Mukaiyama Aldol Reactions



entry	alumatrance (mol %)	solvent	yield (%)[a,b]
1	10	toluene	40
2	5	toluene	52
3	5	toluene	63[c]
4	2.5	toluene	60
5	0.5	toluene	68
6	5	CH_3CN	99
7	2.5	CH_3CN	94
8	0.5	CH_3CN	84
9	0.5	toluene/CH_3CN[d]	86
10	5	CH_3CN	74[e]

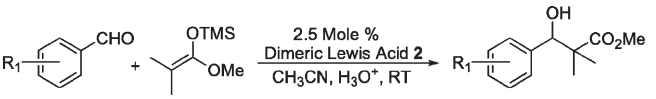
[a]Reaction conditions: 1 mmol of *o*-anisaldehyde, 1.2 mmol of enol silyl ether, 5 mL of solvent, rt, time: 24 h, then H_3O^+ treatment. [b]Average of two runs. [c]Reaction carried out at 0 °C for 3 days. [d]50/50 toluene/CH_3CN. [e]Alumatrane **3**[26] was used for this reaction.

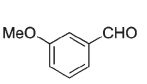
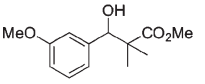
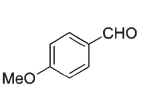
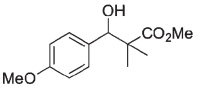
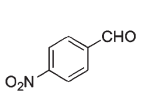
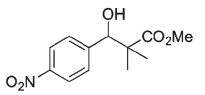
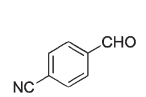
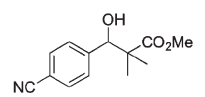
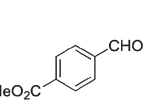
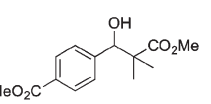
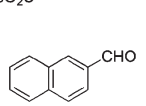
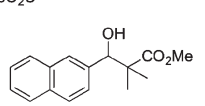
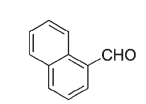
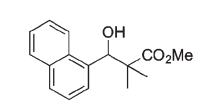
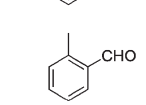
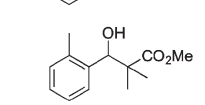
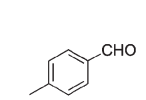
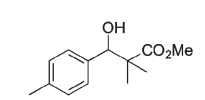
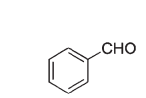
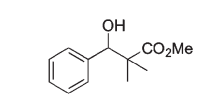
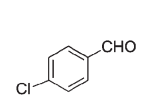
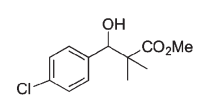
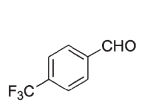
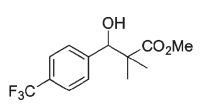
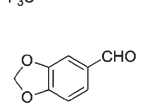
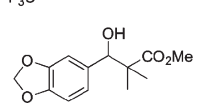
acetonitrile alone (entry 8) and 68% in toluene by itself (entry 4). However, the product yield rose to only 86%. The sterically more congested alumatrane monomer **3**[26] at 5 mol % loading was also screened, but the product yield was only moderate (Table 1, entry 10). For the scoping reactions discussed below, 2.5 mol % of **2** in acetonitrile was employed unless noted otherwise.

Mukaiyama Aldol Reactions of Aryl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal. With use of the optimized conditions in entry 7 of Table 1, the scope of our methodology was explored with a variety of aryl aldehydes (Table 2), including examples possessing activating or deactivating functionalities. *m*-Anisaldehyde and *p*-anisaldehyde when subjected to our protocol with methyl trimethylsilyl dimethylketene acetal resulted in 92% and 90% yields of the desired product (Table 2, entries 1 and 2, respectively) in relatively short reaction times. A previous description of this reaction with 5 mol % of $MgI_2 \cdot (OEt)_n$ in CH_2Cl_2 for 30 min resulted in only a 30% product yield.[6] Deactivating groups such as nitro, cyano, and ester functionalities were also compatible with our protocol (entries 3−5, respectively). Interestingly, dimer **2** prefers to cleave to form an adduct with an aldehyde carbonyl rather than an ester carbonyl as shown in entry 5, wherein a 92% isolated yield of the desired β-hydroxy ester is recorded. Sterically hindered aldehydes such as 1-naphthaldehyde and *o*-tolualdehyde provide the corresponding products in 88% and 91% isolated yield, respectively (Table 2, entries 7 and 8). Pleasingly, halogen-substituted aryl aldehydes are stable to hydrodehalogenation under our conditions (entry 11). *p*-Trifluorotolualdehyde reacted with methyl trimethylsilyl dimethylketene acetal in the presence of **2**, affording a 92% yield of the desired β-hydroxy ester (entry 12). The highest yield of this compound reported in the literature is 68%.[3]

Mukaiyama Aldol Reaction of Heterocyclic and Alkyl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal. With use of the optimized conditions in entry 7 of Table 1, 3-pyridinecarboxaldehyde was subjected to our protocol with 2.5 mol % of **2**. With methyl trimethylsilyl dimethylketene acetal in acetonitrile at room temperature, a 96% yield of the desired β-hydroxy ester was achieved (Table 3, entry 1). This yield is somewhat higher than the highest yield found in the literature for this compound, which was synthesized by combining 3-pyridinecarboxaldehyde and the appropriate enol

TABLE 2. Reactions of Aryl Aldehydes with Methyl Trimethylsilyl Dimethylketene Acetal

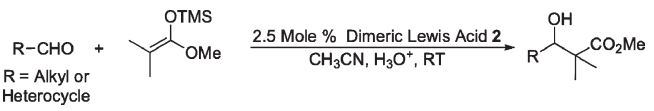


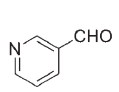
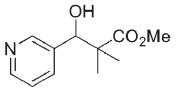
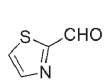
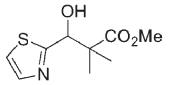
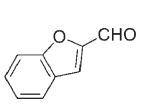
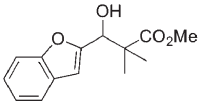
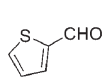
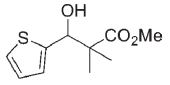
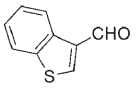
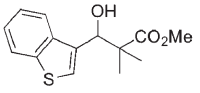
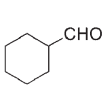
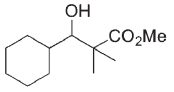
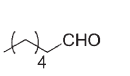
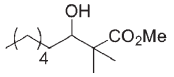
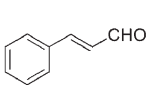
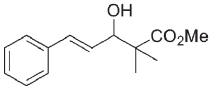
Entry	Aldehyde	Product	Time	Yield (%)[a,b]
1			2 h	92 (Lit: 30)
2			1 h	90 (Lit: 44-98)
3			7 h	95 (Lit: 32-100)
4			6 h	98 (Lit: 68-90)
5			6 h	92 (Lit: 99)
6			2 h	92 (Lit: 77-81)
7			2 h	88 (Lit: 82-97)
8			3 h	91 (Lit: 83)
9			3 h	85 (Lit: 79-99)
10			1 h	95 (Lit: 18-100)
11			4 h	93 (Lit: 60-94)
12			10 h	92 (Lit: 33-68)
13			2 h	98 (Lit: 98)

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mol % of dimeric **2**, 5 mL of CH_3CN, rt, 1−10 h, then H_3O^+ treatment. [b]Average of two runs. Yields in parentheses are literature yields (see the Supporting Information for references).

(26) Su, W.; Kobayashi, J.; Ellern, A.; Kawashima, T.; Verkade, J. G. *Inorg. Chem.* **2007**, *46*, 7953–7959.

TABLE 3. Hetero and Alkyl Aldehydes with Methyl Trimethylsilyl Dimethylketene



Entry	Aldehyde	Product	Time	Yield (%)[a,b]
1			7 h	96 (Lit: 47-95)
2			5 h	95 (Lit: 75)
3			5 h	91
4			6 h	96 (Lit: 57)
5			6 h	73 87[c]
6			2 h	86 (Lit: 48-89)
7			1 h	89 (Lit: 62-89)
8			12 h	52 (Lit: 55-99)

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mol % of dimeric **2**, 5 mL of CH_3CN, rt, 1−12 h, then H_3O^+ treatment. [b]Average of two runs. Yields in parentheses refer to literature yields (see the Supporting Information for references). [c]5 mol % of **2** was used.

silyl ether in water after stirring for 24 h.[27] A compound containing two hetero atoms (Table 3, entry 2) provided a 95% yield of the desired product. This compound was previously synthesized only once according to the literature, in a reaction using a PEG-supported ligand in the presence of 30 mol % of $Cu(OTf)_2$,[28] resulting in only a moderate yield (75%) of the desired product.

Oxygenated heterocycles are also amenable to our protocol and are apparently not vulnerable to adduct formation with **2** as is the case with THF.[25] Thus when 2-benzofurancarboxaldehyde was subjected to our protocol, 91% of the desired (but previously unreported) β-hydroxy ester in entry 3 was realized. 2-Furaldehyde when subjected to our protocol underwent >95% conversion to the trimethylsilyl-protected product as revealed by ^{1}H NMR spectroscopy. However, after hydrolysis, the desired product (which was shown to be present in the ^{1}H NMR spectrum of the crude product) decomposed to an intractable material upon attempted purification by column chromatography. Column chromatographic purification of the trimethylsilyl-protected product failed, owing to desilylation and subsequent decomposition.

The sulfur-containing heterocycles 2-thiophenecarboxaldehyde and thianaphthene-3-carboxaldehyde upon reaction with methyl trimethylsilyl dimethylketene acetal produced 96% and 73%, respectively, of the desired products (entries 4 and 5 in Table 2). However, the latter reaction in the presence of 5 mol % of dimer **2** increased the product yield to 87% (entry 5). Alkyl aldehydes in our protocol gave good product yields of 86% and 89% (entries 6 and 7, respectively). The vinylic aldehyde in entry 8 can be used in our procedure, but only a 52% yield of desired product was realized owing to the Michael addition product that also formed, as shown by the ^{1}H NMR spectrum of the crude reaction mixture. A higher loading of dimer **2** or a change of solvent did not improve the yield of the desired product.

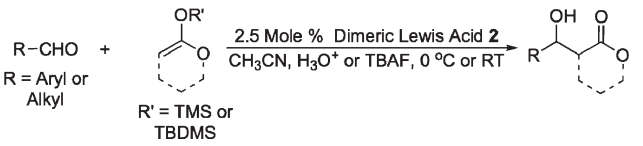
Mukaiyama Aldol Reaction of Various Aldehydes with 6-(*tert*-Butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran and 2-(Trimethylsiloxy)furan. 2-(Trimethylsiloxy)furan operates well in our protocol, undergoing coupling with *o*-anisaldehyde with use of the optimized conditions in Table 1, entry 7, to give 86% of the desired product (Table 4, entry 1). Although there is an opportunity for 1,2 addition to the aldehyde with this enol silyl ether, the only products obtained stemmed from the desired 1,4 addition process. During the course of our study, we discovered that for this reaction to occur, only aryl aldehydes with ortho substituents or aryl aldehydes with electron withdrawing substituents anywhere on the ring functioned satisfactorily in our procedure. When *m*-anisaldehyde was employed, 5 mol % of **2** was required to obtain a 51% yield of the desired product (Table 4, entry 2). However, when 4-cyanobenzaldehyde was used, 84% of the desired product was obtained in a 1/2 syn/anti ratio (Table 4, entry 3). 2-Fluorobenzaldehyde in our procedure gave a 93% product yield in a 1:1 syn:anti ratio (Table 4, entry 4) but the use of *o*-tolualdehyde provided only a 61% yield. However, when 5 mol % of dimeric **2** was used for the reaction of the latter aldehyde, the yield increased to 72% with a 1:4 syn:anti ratio (Table 4, entry 5).

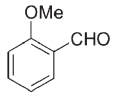
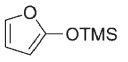
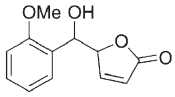
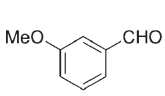
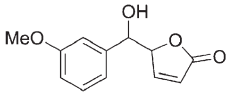
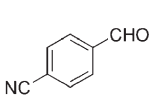
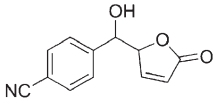
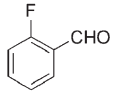
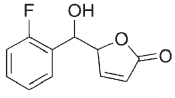
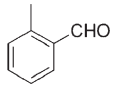
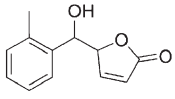
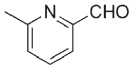
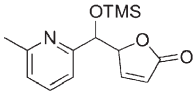
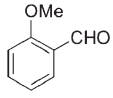
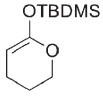
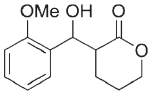
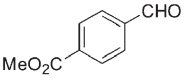
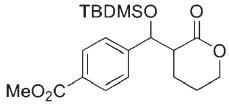
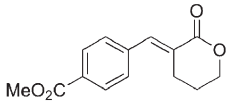
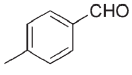
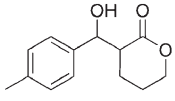
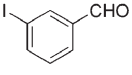
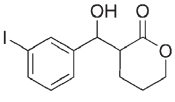
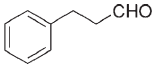
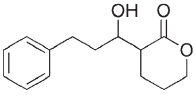
The heterocyclic aldehyde 6-methylpyridinecarboxaldehyde is compatible with 2-(trimethylsiloxy)furan. However, the desired product was isolated as the trimethysilyl-protected analogue because the hydrolyzed product decomposed on the chromatography column (Table 4, entry 6). The isomeric selectivity of the reactions with 2-(trimethylsiloxy)furan was not appreciably changed upon increasing the temperature from 0 to 70 °C.

Mukaiyama aldol reactions in which the β-hydroxy ester product possesses acidic protons are plagued by dehydration under basic conditions to produce the corresponding α,β unsaturated esters.[10,14] In an effort to expand the scope of our methodology, a variety of aldehydes were coupled with different silyl enol ethers to produce products with acidic protons. To this end, 6-(*tert*-butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran was coupled with *o*-anisaldehyde by using the optimized conditions in Table 1, entry 7. When the reaction was carried out at room temperature, the major product was the α,β unsaturated ester. Pleasingly, however, lowering the temperature to 0 °C afforded the desired

(27) Loh, T.; Feng, L.; Wei, L. *Tetrahedron* **2000**, *56*, 7309–7312.
(28) Maurizio, B.; Cinquini, M.; Franco, C.; Giuseppe, C. *Org. Biomol. Chem.* **2004**, *2*, 3401–3407.

TABLE 4. Various Aldehydes with 6-(tert-Butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran and 2-(Trimethylsiloxy)furan



Entry	Aldehdye	Enol Ether	Product	Time	Yield (%)[a]	Syn/Anti[d]
1				2 h	86[b] (Lit: 87)	1/6
2				3 h	35[b] 51[e] (Lit: 73-81)	1/2
3				1 h	84[b] (Lit 48)	1/2
4				2 h	93[b]	1/1
5				3 h	61[b] 72[e] (Lit: 90)	1/4
6				1 h	82[b]	Single Isomer
7				7 h	88[c]	1/1
8				6 h	91[c]	1/1
9				6 h	93[c]	
10				8 h	92[c]	1/1
11				13 h	83[c]	1/1
12				15 h	87[c] (Lit: 87)	1/2

[a]Average of two runs. [b]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mol % of dimeric **2**, 5 mL of CH_3CN, rt, 1−3 h, H_3O^+ treatment. [c]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mol % of dimeric **2**, 5 mL of CH_3CN, 0 °C, 6−15 h, then treatment with TBAF. Yields in parentheses are literature yields (see the Supporting Information for references). [d]Syn/anti ratio determined by either ^{1}H NMR spectroscopy or weight of separated isomer. [e]5 mol % of dimeric **2** was used.

β-hydroxy ester in 88% isolated yield after 7 h (Table 4, entry 7) with no dehydration product observed by ^{1}H NMR spectroscopy. ^{1}H NMR spectroscopy also revealed that the final product was obtained in a 1:1 syn:anti ratio. This result

demonstrates that our protocol not only tolerates trimethylsilyl-protected silyl enol ethers, but also *tert*-butyldimethylsilyl-protected silyl enol ethers which are more stable to normal hydrolytic workup.

Methyl 4-formylbenzoate, *p*-tolualdehyde, and 3-iodobenzaldehdye reacted with 6-(*tert*-butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran affording 91%, 92%, and 83% yields, respectively, of the desired products, each in a 1:1 syn:anti ratio (Table 4, entries 8−11). However, when 4-formylbenzoate was used, the silyl-protected product was isolated because on TBAF treatment, this product produced only the α,*β*-unsaturated ester (Table 4, entries 8 and 9). Enolizable hydrocinnamaldehyde gave an 87% isolated yield of product in a 1:2 syn:anti ratio (Table 4, entry 12).

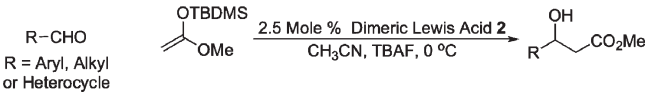
Mukaiyama Aldol Reaction of Various Aldehydes with 1-(*tert*-Butyldimethylsilyloxy)-1-methoxyethene. Since the use of monosubstituted silyl enol ethers produced satisfying results, we investigated a silyl enol ether lacking olefinic substitution, namely, 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene. At 0 °C, a variety of aldehydes reacted with this silyl enol ether in the presence of 2.5 mol % of dimer **2**, giving the corresponding *β*-hydroxy ester products in high yields with no dehydration products observable by ^{1}H NMR spectroscopy. Thus, *o*-anisaldehyde reacted with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene, leading to the desired *β*-hydroxy ester in 90% yield (Table 5, entry 1). We were able to find only one previous report of the synthesis of this compound, and its low yield (33%) emanated from a reaction with 10 mol % of DBU in THF at room temperature for 24 h.[11] 3,5-Dimethoxybenzaldehyde is also a viable substrate for our procedure, producing the expected (but heretofore unreported) product in 96% isolated yield (Table 5, entry 2).

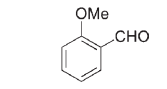
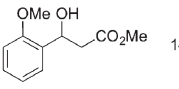
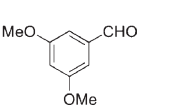
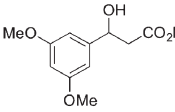
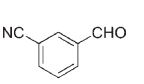
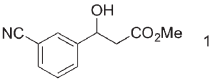
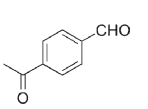
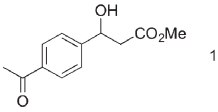
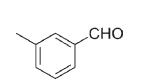
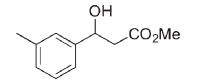
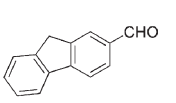
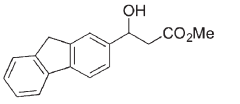
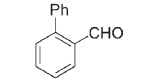
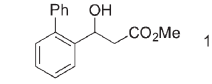
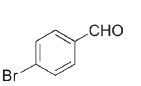
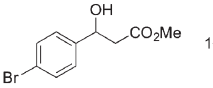
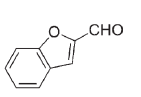
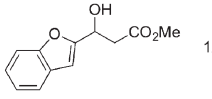
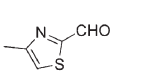
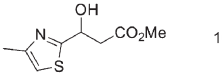
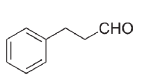
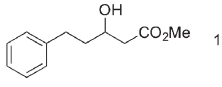
Electron-deficient aryl aldehydes bearing a cyano or acetyl group also function in our protocol (Table 5, entries 3 and 4, respectively) producing the desired (but unreported) products in both cases. Although the product yield was only 57% in the latter case, 5 mol % of **2** raised this yield to 89% (Table 5, entry 4). Electron-neutral aryl aldehydes also provided high yields of the desired *β*-hydroxy ester (Table 5, entries 5, 6, and 8).

Use of the sterically hindered aryl aldehyde 2-biphenylcarboxaldehyde facilitated a 94% product yield (Table 5, entry 7) and heterocyclic 2-benzofurancarboxaldehyde also led to an excellent product yield (95%, entry 9). The only reported method we were able to find for synthesizing the latter product was one in which the corresponding ketone was presynthesized by reacting 2-acetylbenzofuran with dimethyl carbonate in the presence of sodium hydride, affording an 87% yield of the α-ketone, which upon subsequent reduction with tartaric acid-modified Raney nickel in the presence of hydrogen gave 100% of the *β*-hydroxy ester.[29] Reaction of 4-methyl-2-thiazolecarboxaldehyde with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene gave the desired (but unreported) product in 81% isolated yield (Table 5, entry 10).

The alkyl aldehyde hydrocinnamaldehyde when reacted with 1-(*tert*-butyldimethylsilyloxy)-1-methoxyethene in the presence of 2.5 mol % of dimer **2** afforded a 90% yield of the desired product (Table 5, entry 11). Literature methods for synthesizing this product include alkylation of the dianion of methylacetoacetate with benzyl bromide,[30] and a seven-step synthesis beginning with a sulfinate that was allowed to react sequentially with carbon dioxide, benzyl bromide, and diazomethane in the presence of aluminum amalgam to

TABLE 5. Various Aldehydes with 1-(*tert*-Butydimethylsilyloxy)-1-methoxyethene



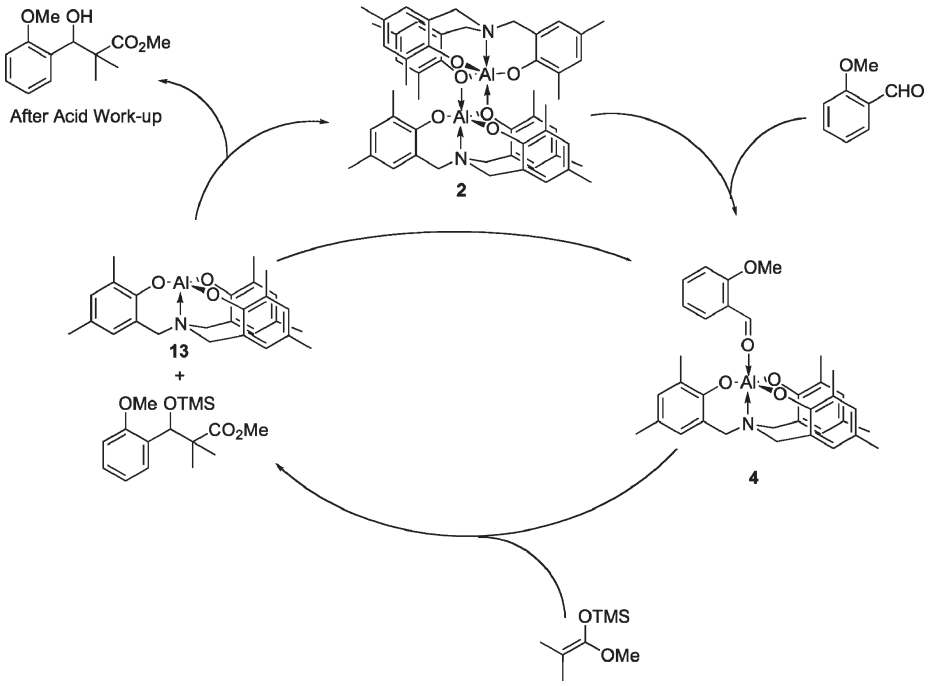
Entry	Aldehyde	Product	Time	Yield (%)[a,b]
1			14 h	90 (Lit: 33)
2			15 h	96
3			10 h	93
4			11 h	57 89[c]
5			8 h	92
6			6 h	93
7			10 h	94
8			16 h	83 (Lit: 87)
9			12 h	95 (Lit: 100)
10			10 h	81
11			13 h	90 (Lit: 16-87)

[a]Reaction conditions: 1 mmol of aldehyde, 1.2 mmol of enol silyl ether, 2.5 mol % of dimeric **2**, 5 mL of CH_3CN, 0 °C, 6−16 h, then treatment with TBAF. [b]Average of two runs. Yields in parenthesis refer to literature yields (see the Supporting Information for references). [c]5 mol % of **2** was used.

(29) Haruna, N.; Acosta, D. E.; Nakagawa, S.; Yamaguchi, K.; Tai, A.; Okuyama, T.; Sugimura, T. *Heterocycles* **2004**, *62*, 375–386.

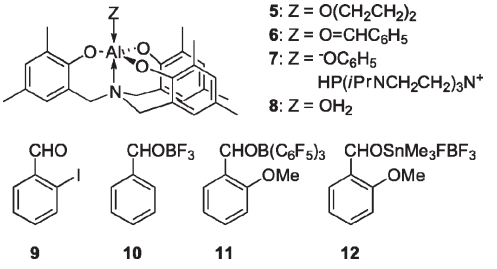
(30) Kamal, A.; Krishnaji, T.; Khanna, G. B. R. *Tetrahedron Lett.* **2006**, *47*, 8657–8660.

SCHEME 1. Suggested Pathway of the Mukaiyama Aldol Reaction of *o*-Anisaldehyde with Alumatrane Dimer 2



desulfinate the final product, resulting in an overall 80% isolated yield.[31] Product yields in the literature for this compound ranged from 16% to 87%.

Structural and Mechanistic Considerations. Earlier we reported that alumatrane dimer **2** is insoluble in acetonitrile, but upon addition of benzaldehyde to the mixture, a light yellow solution is formed. The same observation for the various aldehydes employed in the present study is consistent with splitting of dimeric **2** by the aldehydic oxygen to form adducts such as **4** in Scheme 1. Adduct **4** was synthesized and



crystals suitable for X-ray analysis were grown from a 10:1 mixture of pentane:toluene (Figure 1). As shown in this figure, the methoxy group appears to be quite free of steric encumbrance by any of the three neighboring methyl groups on the alumatrane moiety.

A comparison of some of the major X-ray crystallographic structural parameters of **4** with the corresponding ones in **5**−**12** is of interest. Because such a comparison is not of particular relevance to the thrust of the present work, however, this discussion can be found in the Supporting Information.

Earlier in this paper it was noted that although 2-substituted aryl aldehydes functioned well in our protocol, 2,6-dimethylbenzaldehdye and 2,6-dimethoxybenzaldehdye failed to produce detectable amounts of product (as shown by ^{1}H NMR spectroscopy) even though adduct formation was indicated by the solubility of dimer **2** in acetonitrile when either of these aldehydes was added. It would thus appear that the bulk of the second ortho substituent in combination with that of the alumatrane moiety increases the steric shielding of the carbonyl carbon to the point where nucleophilic attack by the double bond of the silyl enol ether is prevented, even though coordination of the aldehyde oxygen to the aluminum might render the aldehyde carbon sufficiently electrophilic.

If attack of **4** by an enol silyl ether is able to occur (Scheme 1) it appears that the alumatrane monomer moiety **13** is then released from the adduct to immediately form an adduct with another aldehyde before reforming dimer **2**. This assumption is based on our observation that no solids were formed during the reaction until all of the aldehyde is consumed. At the point in the reaction where insoluble dimer **2** began to form, a 2 M solution of aq HCl was added to the reaction mixture to hydrolyze the silylated penultimate product to the final aldol product. To demonstrate that the precipitate was indeed **2**, it was filtered under inert atmosphere immediately after its formation (before hydrolytic workup) and reused successfully in a duplicate reaction. Additional evidence that the precipitate is **2** came from our observation of similar recyclability of precipitated **2** in experiments involving the addition of TMSCN to aldehydes.[32]

Lewis Acidity of 13. The existence of a N → Al dative bond in monomeric **2** (as represented by **13**) might be expected to diminish its Lewis acidity sufficiently to preclude its usefulness in transformations such as the Mukaiyama aldol reaction. In a previous publication we reported calculational

(31) Fujisawa, T.; Fujimura, A.; Sato, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1273–1279.

(32) Raders, S. M.; Verkade, J. G. Manuscript in progress.

results indicating that **13** is more Lewis acidic than BF_3.[26] In the present work we provide experimental support for this conclusion. Herein we measured the ^{31}P NMR chemical shifts of **13**·O=PEt_3 (61 ppm) and F_3B·O=PEt_3 (78 ppm) in C_6D_6, and we also characterized the former compound by single-crystal X-ray crystallography (Figure 3). (Crystals of **13**·O=PEt_3 were grown from a concentrated solution of toluene in a freezer for 2 days.) Both of the aforementioned ^{31}P chemical shifts are downfield of the 55 ppm we measured for O=PEt_3 in the same solvent. However, the relative magnitudes of these deshieldings cannot be taken to be indicative of the relative Lewis acidities of **13** and BF_3, owing to differences in paramagnetic effects of the boron and aluminum nuclei. We then added 1 equiv of triethyl phosphine oxide to a mixture of 1.1 equiv of BF_3·OEt_2 in toluene to form the BF_3·O=PEt_3 adduct whose ^{31}P NMR spectrum was then taken (Scheme 2). The BF_3·O=PEt_3 adduct was then dried under reduced pressure leaving a white solid to which a 0.5 mol equiv of the alumatrane dimer **2** was added to determine if the dimer was capable of removing $OPEt_3$ from the BF_3·O=PEt_3 adduct. Consistent with the greater Lewis acidity of **13**, the ^{31}P NMR spectrum of the reaction mixture revealed only the ^{31}P chemical shift of **13**·O=PEt_3 (Figure 2).

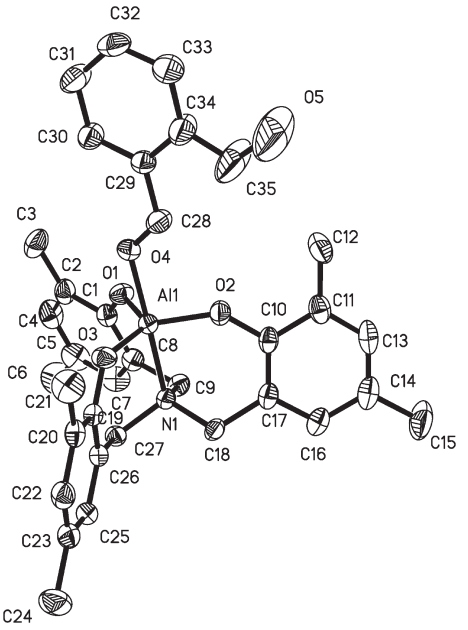


FIGURE 1. Computer drawing of the molecular structure of **4** at the 50% probability level. Hydrogen atoms are omitted for clarity. Major bond distances: Al−N, 2.101(3) Å; avg Al−O_{eq}, 1.751(3) Å; Al−O_{ax}, 1.986(3) Å; C=O, 1.216(3) Å. Major bond angles: avg N−Al−O_{eq}, 92.76(13)°; avg O_{eq}−Al−O_{eq}, 119.77(12)°; avg O_{eq}−Al−O_{ax}, 87.26(13)°.

In a further effort to substantiate these results, the product yields of the reaction of *o*-anisaldehyde and methyl trimethylsilyl dimethylketene acetal in the presence of dimer **2** and BF_3·OEt_2 were compared (Table 6). The reactions were carried out in acetonitrile with 2.5 mol % of dimeric **2** and 5 mol % of BF_3·OEt_2, and after 1 h, the reactions were quenched with 2 N aq HCl. As depicted in Table 6, the alumatrane dimer **2** provided a 97% yield of the desired product (entry 1), whereas BF_3·OEt_2 led to only a 35% product yield (entry 2). This contrast in efficacy of **2** compared with BF_3·OEt_2 is made the more striking because energy is required to split dimer **2** into **13**, the Lewis acidic species needed for carbonyl activation. These results are

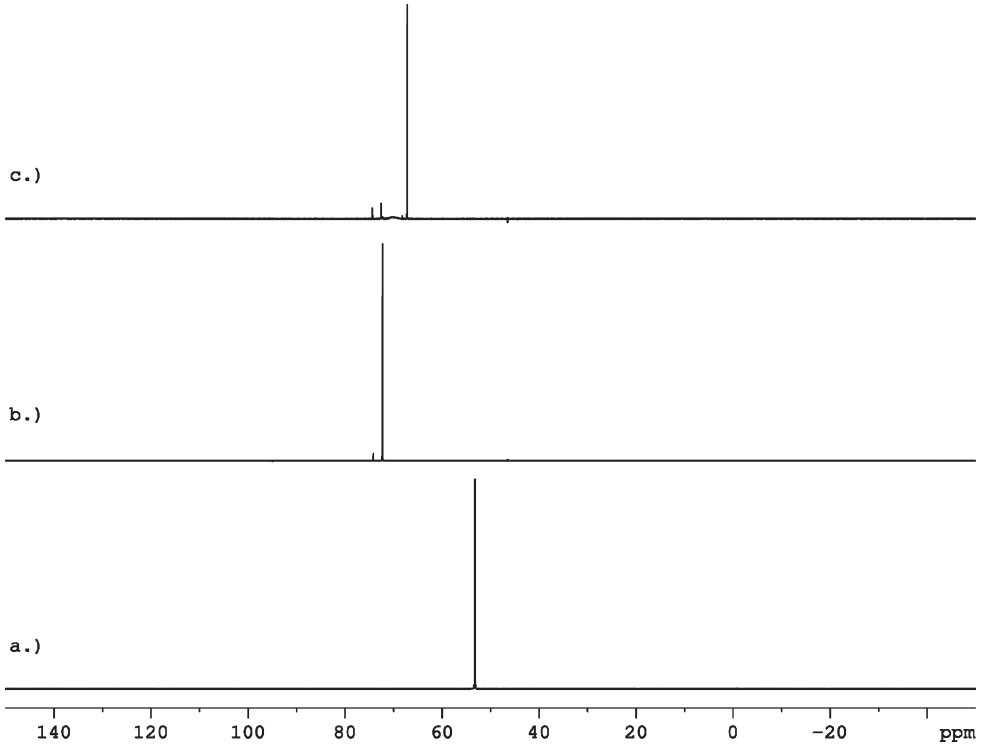


FIGURE 2. (a) ^{31}P NMR of O=PEt_3 in C_6D_6. (b) ^{31}P NMR of BF_3·O=PEt_3 in C_6D_6. (c) ^{31}P NMR after addition of alumatrane dimer **2** to BF_3·O=PEt_3.

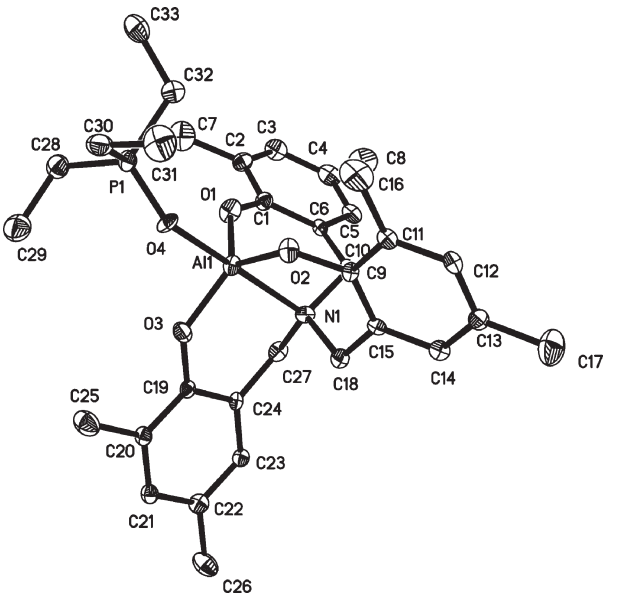
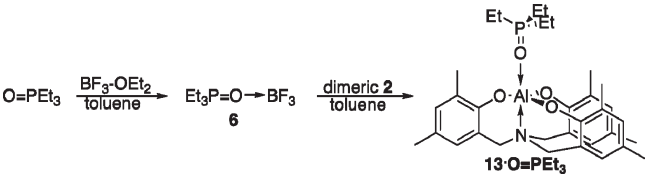


FIGURE 3. Computer drawing of the molecular structure of **13**·O=PEt_3 at the 50% probability level. Hydrogen atoms are omitted for clarity.

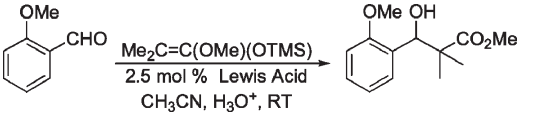
SCHEME 2. Reactions of Triethylphosphine Oxide with F_3B·OEt_2 and Alumatrane Dimer 2



supportive of our earlier calculational results indicating that **13** is more Lewis acidic than BF_3.[26] Another experiment was carried out with 2.5 mol % of alumatrane dimer **2** and 5 mol % of diethyl ether in order to demonstrate that the presence of diethyl ether does not materially affect the outcome of the reaction. Pleasingly, 92% of the desired product was obtained (entry 3). Since energy is also required to dissociate the ether moiety from BF_3·OEt_2, we carried out a reaction using 5 mol % of BF_3 obtained from a commercially available stock solution containing 15% BF_3 in acetonitrile. Only 24% of the desired product was obtained in this reaction (entry 4).

Since **13**·O=PEt_3 represents only the second example of an Al·O=PEt_3 adduct and, more particularly, the first example of an alumatrane·O=PEt_3 adduct whose molecular structures have been determined by X-ray means, it is of interest to compare some structural parameters of **13**·O=PEt_3 with analogous metrics in phosphine oxide **14** and in selected Lewis acid phosphine oxide complexes **15**–**18** (Table 7). The P=O bond in **13**·O=PEt_3 is within 3× the esds for this link in **14**–**18**. Thus, there appears to be no significant effect of the Lewis acids considered here on the P=O bond distances in their phosphine oxide adducts **15**–**18**. The LA–O bond length in **13**·O=PEt_3 is longer than that in **17**, an observation that can be rationalized by the higher coordination number of the aluminum in **13**·O=PEt_3 in which the transannular N enriches the electron density on the metal

TABLE 6. Comparison Reactions between Alumatrane Dimer 2 and F_3B·OEt_2



entry	Lewis acid	yield (%)[a,b]
1	**2**	97
2	BF_3·OEt_2	35
3	**2**[c]	92
4	BF_3[d]	24

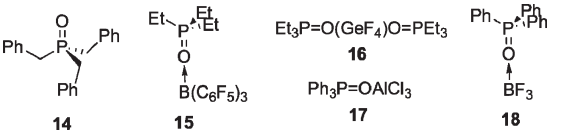
[a]Reaction conditions: 1 mmol of *o*-anisaldehyde, 1.2 mmol of methyl trimethylsilyl dimethylketene acetal, 2.5 mol % alumatrane dimer **2**, 5 mL of CH_3CN, RT, 1 h, then H_3O^+ treatment. [b]Average of two runs. [c]5 mol % of diethyl ether added to the reaction mixture. [d]5 mol % as a 15% solution in CH_3CN.

TABLE 7. Comparison of Bond Lengths and Angles of Phosphine Oxide Lewis Acid Adducts

entry	compd	P=O	LA[a]–O	LA[a]–O–P
1	**13**·O=PEt_3	1.499(6)	1.850(6)	146.2(4)
2	**14**[b]	1.488(4)		
3	**15**[c]	1.497(17)	1.533(3)	161.04(16)
4	**16**[d]	1.522(2)	1.925(2)	142.5(1)
5	**17**[c]	1.519(4)	1.733(4)	180
6	**18**[f]	1.522(3)	1.526(6)	134.5(2)

[a]LA = Lewis Acid. [b]See ref 33. [c]See ref 34. [d]See ref 35. [e]See ref 36. [f]See ref 37.

as do the three equatorial phenoxy oxygens. On the other hand, the LA–O bond length in **13**·O=PEt_3 is shorter than that in **16** wherein the lower electronegativity/electron-withdrawing effect of Ge compared with Al and the higher coordination number of **16** lengthens the LA–O bond length. The longer LA–O bond length in **13**·O=PEt_3 than in **15** and **18** can be attributed to the smaller size and greater electronegativity of B relative to Al as well as the expanded coordination number of Al in **13**·O=PEt_3. Unlike **17** (which exhibits a 180° bond angle between the phosphorus and the Lewis acid atom) **13**·O=PEt_3 displays a bond angle of 146.2°. The origin of this difference is not readily apparent.



Conclusions

We have demonstrated the usefulness of alumatrane dimer **2** in the Mukaiyama aldol reaction. Our protocol tolerates a wide variety of aryl, heterocyclic, and alkyl aldehydes and

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has high functional group tolerance. Ketone substrates failed in our protocol, however. It should be noted that our protocol requires the presence of an electron-donating OR group on the olefin of the silyl enol ether. Other silyl enol ethers [such as 1-phenyl-1-trimethylsiloxyethylene and 1-(trimethylsiloxy)cyclohexene] in the presence of *o*-anisaldehyde produced no desired products. But when 6-(*tert*-butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran was employed in this reaction, the desired product was obtained in high yield (88%). It is reasonable to suggest that the presence of the electron-inducting OR substituent on the olefinic moiety provides the latter with sufficient nucleophilicity for attack of the Lewis acid-activated carbonyl group. Our proposed mechanism receives support from the isolation and structural characterization of intermediate **4**. Evidence supporting our postulate that monomeric **2** (i.e., **13**) is more Lewis acidic than BF_3 has also been presented. Comparisons of structural parameters obtained from single-crystal X-ray experiments for **4** and **13**·O=PEt$_3$ and for related compounds in the literature are rationalized in terms of central atom electronegativity and coordination number expansion effects. Further investigations illustrating the usefulness of dimer **2** in Lewis acid-catalyzed organic reactions are underway.

Experimental Section

General Procedure for Mukaiyama Aldol Reaction of Methyl Trimethylsilyl Dimethylketene Acetal and 2-(Trimethylsiloxy) furan. To a 10 mL vial equipped with a stir bar was added 22.15 mg (2.5 mol %) of alumatrane dimer **2** in a glovebox. Acetonitrile (5 mL) followed by 1 mmol of the corresponding aldehyde were added to the vial, and then the reaction mixture was stirred for 30 min at room temperature to form the aldehyde−alumatrane adduct. The corresponding silyl enol ether (1.2 mmol) was added under inert atmosphere and then the reaction was continued for the allotted time as recorded in the tables. Then 3 mL of 2 N hydrochloric acid solution was added and the reaction mixture was stirred 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 rotovap apparatus, and then the crude product was purified by column chromatography (EtOAc:hexanes = 1:9).

Methyl 3-hydroxy-2,2-dimethyl-3-(2-benzofuran)propionate (Table 3, entry 3): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.57 (d, 1H), 7.45−7.47 (d, 1H), 7.22−7.30 (m, 2H), 6.67 (s, 1H), 4.96 (s, 1H), 3.77 (s, 3H), 3.73 (br, 1H), and 1.30−1.31 (d, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 156.8, 154.7, 128.1, 124.3, 123.0, 121.2, 111.4, 104.9, 73.9, 52.5, 47.3, 23.0, and 20.4 ppm; HRMS *m*/*z* calcd for $C_{14}H_{16}O_4$ (M^+) 248.10485, found 248.10512.

Methyl 3-hydroxy-2,2-dimethyl-3-(3-thianaphthene)propionate (Table 3, entry 5): yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84−7.90 (dd, 2H), 7.31−7.39 (m, 3H), 5.38 (s, 1H), 3.71 (s, 3H), 3.42 (br, 1H), 1.28 (s, 3H), and 1.16 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.3, 140.2, 138.7, 136.1, 124.7, 124.3, 124.1, 123.0, 122.8, 73.7, 52.4, 48.5, 23.5, and 19.6 ppm; HRMS *m*/*z* calcd for $C_{14}H_{16}O_3S$ (M^+) 264.08202, found 264.08256.

5-(Hydroxy(2-fluorophenyl)methyl)furan-2(5*H*)-one (Table 4, entry 4): clear, colorless oil (*syn*/*anti* 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.56 (m, 2H), 7.26−730 (m, 4H), 7.16−7.19 (t, 2H, *J*=7.6 Hz), 7.02−7.06 (t, 2H, *J*=8.4 Hz), 6.10−6.14 (t, 2H, *J*=7.6 Hz), 5.40−5.41 (d, 1H, *J*=4 Hz), 5.28−5.29 (d, 1H, *J* = 4 Hz), 5.19−5.20 (d, 1H, *J* = 4 Hz), 5.07−5.08 (d, 1H, *J*=4 Hz), and 3.82 (br, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 173.2, 160.9, 160.8, 158.5, 158.4, 153.5, 153.0, 130.4 (d, *J* = 8.3 Hz), 130.1 (d, *J* = 8.2 Hz), 128.6 (d, *J* = 3.6 Hz), 128.1 (d, *J* = 3.8 Hz), 125.7 (d, *J* = 13 Hz), 125.5 (d, *J* = 13.2 Hz), 124.8, 123.5 (d, *J* = 5 Hz), 123.1 (d, *J* = 4.9 Hz), 115.7 (d, *J* = 15.9 Hz), 115.4 (d, *J* = 15.7 Hz), 86.7, 85.6, 68.8, and 67.3 ppm; ^{19}F NMR (376 MHz, $CDCl_3$) δ −118.07 and −118.41 ppm; HRMS *m*/*z* calcd for $C_{11}H_9FO_3$ (M^+) 208.05357, found 208.05393.

Synthesis of 5-(Trimethylsiloxy(2-(6-methylpyridine))methyl) furan-2(5*H*)-one (Table 4, entry 6). To a 10 mL vial equipped with a stir bar was added 22.15 mg (2.5 mol %) of alumatrane dimer **2** in a glovebox. Acetonitrile (5 mL) was added to the vial, followed by 1 mmol of 6-methylpyridine-2-carboxaldehyde. The reaction mixture was stirred for 30 min at room temperature to form the aldehyde−alumatrane adduct and then 2-(trimethylsiloxy)furan (1.2 mmol) was added under inert atmosphere. The reaction was allowed to proceed for 1 h at room temperature and then the solid alumatrane dimer was filtered. The reaction mixture was concentrated on a rotovap and the crude product was purified by column chromatography (EtOAc:hexanes = 1:9). Clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61−7.65 (t, 1H, *J* = 7.6 Hz), 7.25−7.27 (d, 1H, *J* = 8 Hz), 7.08−7.13 (m, 2H), 6.10−6.11 (d, 1H, *J* = 5.6 Hz), 5.58−5.59 (d, 1H, *J* = 1.2 Hz), 5.1−5.19 (d, 1H, *J* = 2.8 Hz), 2.55 (s, 3H), and 0.11 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 158.7, 158.1, 152.8, 137.4, 123.2, 122.7, 117.7, 86.4, 74.7, 24.6, and 0.1 ppm; HRMS *m*/*z* calcd for $C_{14}H_{19}NO_3Si$ (M^+) 277.11341, found 277.11402.

General Procedure for Mukaiyama Aldol Reaction of 6-(*tert*-Butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran and 1-(*tert*-Butyldimethylsilyloxy)-1-methoxyethene. To a 10 mL vial equipped with a stir bar was added 22.15 mg (2.5 mol %) of alumatrane dimer **2** in a glovebox. Acetonitrile (5 mL) was added to the vial followed by 1 mmol of the corresponding aldehyde, and then the reaction mixture was stirred for 30 min at room temperature to form the aldehyde−alumatrane adduct. The reaction mixture was then cooled to 0 °C and 1.2 mmol of the corresponding silyl enol ether was added under inert atmosphere. The reaction was allowed to proceed for the allotted time as specified in the tables and then a 0 °C solution of 3 mmol of a 1 M TBAF/THF solution was added. The mixture was stirred at 0 °C for 1 h after which 3 mL of water was added with stirring for an additional hour at 0 °C. The reaction mixture was extracted with methylene chloride (2 × 100 mL portions) and dried over Na_2SO_4. The solution was filtered and dried on a rotovap followed by purification of the crude product via column chromatography (EtOAc:hexanes = 1:9). Because the products synthesized from 6-(*tert*-butyldimethylsilyloxy)-3,4-dihydro-2*H*-pyran were new compounds and attempts to separate them failed, we were unable to determine which peaks in the ^{1}H and ^{13}C NMR spectra corresponded to the *syn* and *anti* isomers.

3-(Hydroxy(2-methoxyphenyl)methyl)tetrahydro-2*H*-pyran-2-one (Table 4, entry 7): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45−7.51 (dd, 2H, *J*=18 Hz, *J*=7.6 Hz), 7.23−7.29 (q, 2H, *J*=7.6 Hz), 6.96−7.01 (m, 2H), 6.84−6.88 (t, 2H, *J* = 8.4 Hz), 5.73 (s, 1H), 5.28−5.30 (d, 1H, *J* = 8.4 Hz), 4.49−4.50 (d, 1H, *J* = 2 Hz), 4.26−4.31 (m, 4H), 3.82 (s, 6H), 3.12−3.13 (d, 1H, *J*=3.6 Hz), 3.00−3.05 (dt, 1H, *J*=7.6 Hz, *J*=2.4 Hz), 2.79−2.84 (q, 1H, *J*=9.2 Hz), 1.75−1.88 (m, 5H), 1.53−1.58 (m, 2H), and 1.44−1.46 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 174.9, 156.8, 155.5, 129.1, 129.1, 128.8, 128.3, 127.8, 127.3, 121.2, 120.6, 110.7, 110.0, 68.9, 68.6, 68.5, 67.1, 55.6, 55.4, 46.6, 44.2, 22.3, 21.9, 21.0, and 17.9 ppm; HRMS *m*/*z* calcd for $C_{13}H_{16}O_4$ (M^+) 236.10486, found 236.10533.

3(*tert*-Butyldimethylsiloxy(methyl 4-benzoate)methyl)tetrahydro-2*H*-pyran-2-one (Table 4, entry 8): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.98 (m, 4H), 7.38−7.43 (m, 4H), 5.63 (s, 1H), 5.53−5.54 (d, 1H, *J* = 4 Hz), 4.31−4.34 (m, 1H), 4.16−4.26 (m, 2H), 3.86 (s, 6H), 2.91−2.94 (m, 1H),

2.61−2.65 (t, 1H, J = 9.2 Hz), 1.83−1.99 (m, 3H), 1.66−1.70 (m, 2H), 1.38−1.59 (m, 3H), 0.86−0.88 (d, 18H, J = 8 Hz), 0.03−0.06 (d, 6H, J = 7.6 Hz), −0.11 (s, 3H), and −0.18 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 171.1, 167.0, 166.9, 147.8, 146.7, 129.6, 129.4, 127.1, 126.1, 74.0, 73.5, 70.0, 69.3, 52.2, 52.2, 49.5, 49.1, 26.0, 25.0, 22.8, 22.3, 19.8, 18.8, 18.3, 18.3, −4.5, −4.8, −5.0, and −5.2 ppm; ESI$^+$ m/z calcd for $C_{20}H_{30}O_5Si$ (M^+) 378.19, found 379.

3-((Methyl 4-benzoate)2-methylene)trihydro-2*H*-pyran-2-one (Table 4, entry 9): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05−8.07 (d, 2H, J=8 Hz), 7.91 (s, 1H), 7.47−7.49 (d, 2H, J = 8 Hz), 4.40−4.42 (t, 2H, J=5.2 Hz), 3.92 (s, 3H), 2.86−2.89 (t, 2H, J = 6.4 Hz), and 1.96−2.01 (sep, 2H, J = 6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 166.6, 140.4, 139.5, 130.5, 130.1, 129.9, 128.1, 69.0, 52.5, 26.2, and 23.2 ppm; HRMS m/z calcd for $C_{14}H_{14}O_4$ (M^+) 246.0892, found 246.0892.

3-(Hydroxy(4-methylphenyl)methyl)tetrahydro-2*H*-pyran-2-one (Table 4, entry 10): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22−7.25 (m, 4H), 7.15−7.16 (m, 4H), 5.46 (s, 1H), 4.77−4.79 (d, 1H, J=8.8 Hz), 4.61 (br, 1H), 4.24−4.30 (m, 4H), 3.30 (br, 1H), 2.68−2.80 (m, 2H), 2.34 (s, 6H), 1.75−1.85 (m, 5H), 1.55−1.60 (m, 2H), and 1.49−1.53 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 174.2, 138.1, 138.0, 137.2, 137.0, 129.3, 129.1, 127.0, 125.8, 75.0, 71.8, 69.2, 68.7, 47.4, 46.6, 22.3, 21.8, 21.7, 21.3, 21.2, and 18.1 ppm; HRMS m/z calcd for $C_{13}H_{16}O_3$ (M^+) 220.10994, found 220.11016.

3-(Hydroxy(3-iodophenyl)methyl)tetrahydro-2*H*-pyran-2-one (Table 4, entry 11): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 2H, J = 1 Hz), 7.57−7.64 (dd, 2H, J=18 Hz, J=8 Hz), 7.28−7.30 (d, 2H, J = 7.2 Hz), 7.05−7.09 (dt, 2H, J = 7.6 Hz, J = 2.4 Hz), 5.45 (s, 1H), 4.73−4.75 (d, 1H, J = 8.8 Hz), 4.67 (br, 1H), 4.26−4.31 (m, 4H), 3.44 (br, 1H), 2.72−2.77 (m, 1H), 2.65−2.70 (m, 1H), 1.75−1.87 (m, 5H), 1.45−1.53 (m, 2H), and 1.34−1.43 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 173.9, 143.6, 142.6, 137.4, 136.5, 136.0, 134.9, 130.4, 130.2, 126.6, 125.1, 94.7, 94.6, 74.3, 71.0, 69.3, 68.7, 47.3, 46.5, 22.3, 21.7, 21.6, and 17.8 ppm; HRMS m/z calcd for $C_{12}H_{13}IO_3$ (M^+) 331.99095, found 331.99164.

Methyl 3-hydroxy-3-(3,5-dimethoxyphenyl)propionate (Table 5, entry 2): yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (s, 2H), 6.35, (s, 1H), 5.02−5.06 (dd, 1H, J=9.2 Hz, J=4 Hz), 3.70−3.76 (d, 6H, J = 72.8 Hz), 3.70 (s, 1H), 3.67 (br, 1H), and 2.64−2.76 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 161.0, 145.3, 103.6, 99.8, 70.4, 55.4, 52.0, and 43.4 ppm; HRMS m/z calcd for $C_{12}H_{16}O_5$ (M^+) 240.09977, found 240.10006.

Methyl 3-hydroxy-3-(3-cyanophenyl)propionate (Table 5, entry 3): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.54−7.60 (m, 2H), 7.42−7.46 (m, 1H), 5.12−5.16 (t, 1H, J = 6.4 Hz), 3.78 (br, 1H), 3.70 (s, 3H), and 2.69−2.70 (d, 2H, J = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 144.3, 131.5, 130.4, 129.5, 129.5, 118.8, 112.6, 69.3, 52.3, and 43.1 ppm; HRMS m/z calcd for $C_{11}H_{11}NO_3$ (M^+) 205.07389, found 205.07416.

Methyl 3-hydroxy-3-(4-acetylphenyl)propionate (Table 5, entry 4): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.90 (d, 2H, J = 8.4 Hz), 7.43−7.45 (d, 2H, J = 8 Hz), 5.15−5.18 (t, 1H, J = 5.2 Hz), 3.68 (s, 4H), 2.67−2.76 (m, 2H), and 2.55 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.1, 172.6, 148.1, 136.6, 128.8, 126.0, 70.0, 52.2, 43.2, and 26.8 ppm; HRMS m/z calcd for $C_{12}H_{14}O_4$ (M^+) 222.08921, found 222.08954.

Methyl 3-hydroxy-3-(3-methylphenyl)propionate (Table 5, entry 5): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23−7.27 (m, 1H), 7.20 (s, 1H), 7.15−7.17 (d, 1H, J = 7.2 Hz), 7.10−7.12 (d, 1H, J=7.2 Hz), 5.08−5.12 (m, 1H, J=9.2 Hz, J=3.6 Hz), 3.72 (s, 3H), 3.40 (br, 1H), 2.67−2.80 (m, 2H), and 2.37 (s, 3H) ppm; ^{13}C NMR (110 MHz, $CDCl_3$) δ 172.9, 142.6, 138.3, 128.6, 128.5, 126.4, 122.8, 70.4, 52.0, 43.4, and 21.6 ppm; HMRS m/z calcd for $C_{11}H_{14}O_3$ (M^+) 194.09429, found 194.09467.

Methyl 3-hydroxy-3-(2-fluorene)propionate (Table 5, entry 6): white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74−7.79 (m, 2H), 7.54−7.58 (m, 2H), 7.30−7.41 (m, 3H), 5.20−5.24 (dd, 1H, J=9.2 Hz, J = 3.6 Hz), 3.88 (s, 2H), 3.75 (s, 3H), 3.38 (br, 1H), and 2.74−2.88 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 143.8, 143.6, 141.7, 141.5, 141.3, 127.0, 125.2, 124.6, 122.6, 120.1, 120.1, 70.8, 52.2, 43.7, and 37.1 ppm; HMRS m/z calcd for $C_{17}H_{16}O_3$ (M^+) 268.10994, found 268.11063.

Methyl 3-Hydroxy-3-(2-biphenyl)propionate (Table 5, entry 7): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.70 (d, 1H, J = 7.6 Hz), 7.41−7.48 (m, 4H), 7.27−7.39 (m, 3H), 7.24−7.25 (d, 1H, J = 1.2 Hz), 5.28−5.31 (d, 1H, J = 9.6 Hz, J = 2.8 Hz), 3.65 (s, 3H), 3.48 (br, 1H), and 2.70−2.60 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 140.7, 140.6, 139.8, 130.2, 129.3, 128.5, 128.1, 127.7, 127.4, 126.0, 66.7, 51.9, and 42.5 ppm; HRMS m/z calcd for $C_{16}H_{16}O_3$ (M^+) 256.10994, found 256.11029.

Methyl 3-hydroxy-3-(4-methyl-2-thiazole)propionate (Table 5, entry 10): clear, colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83 (s, 1H), 5.32−5.35 (dd, 1H, J=8.4 Hz, J=3.2 Hz), 4.48 (br, 1H), 3.71 (s, 3H), 2.85−3.09 (m, 2H), and 2.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 172.5, 152.8, 114.0, 68.6, 52.2, 41.6, 17.3 ppm; HRMS m/z calcd for $C_8H_{11}NO_3S$ (M^+) 201.14596, found 201.04619.

Synthesis of Alumatrane−Aldehyde Adduct 4. To a suspension of dimer **2** (0.5 mmol) in 20 mL of toluene was added 2 mmol of *o*-anisaldehyde. The reaction was stirred at room temperature for 1 h to generate a yellowish solution that was concentrated under reduced pressure to form a yellow solid. The yellow solid was dissolved in 5 mL of toluene followed by the addition of 20 mL of pentane. The solution was placed in a freezer for 2 days to form yellow crystals that were suitable for X-ray analysis. ^{1}H NMR (400 MHz, C_6D_6) δ 10.95 (s, 1H), 8.19−8.21 (d, 1H, J = 7.6 Hz), 7.00−7.16 (m, 4H), 6.56−6.58 (m, 4H), 6.11−6.13 (d, 1H, J=8.4 Hz), 4.45 (br, 3H), 3.00 (s, 3H), 2.60 (br, 3H), 2.42 (s, 9H), and 2.28 (s, 9H) ppm; ^{13}C NMR (100 MHz, C_6D_6) δ 196.8, 164.5, 155.7, 139.6, 132.0, 131.9, 130.5, 128.2, 128.1, 127.7, 126.1, 121.6, 121.5, 112.3, 59.5, 55.5, 21.2, and 17.3 ppm.

Lewis Acidity Test of Alumatrane Dimer 2. To an argon-filled 100 mL flask was added 1 mmol (134.16 mg) of triethyl phosphine oxide in 5 mL of toluene. To this solution was added 1.2 equiv of $BF_3\cdot OEt_2$ (1.2 mmol, 170.32 mg) and then the mixture was stirred for 2 h. Two layers (toluene and ether) formed during this period. After drying under reduced pressure, a ^{31}P NMR spectrum of the solid residue in C_6D_6 revealed a phosphorus shift at +78 ppm corresponding to the $BF_3\cdot O{=}PEt_3$. The solid was taken into a glovebox and weighed to determine the yield of $BF_3\cdot O{=}PEt_3$ (97% based on the triethyl phosphine oxide). To this solid was added half an equivalent of alumatrane dimer **2** (0.48 mmol, 430.20 mg). After addition of 5 mL of toluene to the reaction mixture, the suspension was stirred for 2 h after which a ^{31}P NMR spectrum revealed that all of the $F_3B\cdot O{=}PEt_3$ compound disappeared. Thus only **13**$\cdot O{=}PEt_3$ remained and no insoluble dimer **2** was observed in the solution.

Synthesis of the Boron Trifluoride Triethyl Phosphine Oxide Adduct $F_3B\cdot O{=}PEt_3$. To a 50 mL round-bottomed flask in a glovebox was charged 150 mg (1.12 mmol) of triethyl phosphine oxide. The reaction flask was removed from the glovebox, 5 mL of toluene was added, and then 190.2 mg (1.2 equiv, 1.34 mmol) of boron trifluoride diethyl ether was added under inert atmosphere. After 2 h of stirring, the solution was dried under reduced pressure to produce analytically pure desired product in 98% isolated yield. White solid; ^{1}H NMR (400 MHz, C_6D_6) δ 1.52−1.60 (dq, 6H, J=12 Hz, J=7.6 Hz) and 0.81−0.89 (dt, 9H, J=18 Hz, J=15.6 Hz) ppm; ^{13}C NMR (100 MHz, C_6D_6) δ 17.2 (d, J=65 Hz) and 5.2 (d, J=5.1 Hz) ppm; ^{31}P NMR (168 MHz, C_6D_6) δ 78.855 ppm; ^{11}B NMR (128 MHz, C_6D_6) δ −0.42 ppm; ^{19}F NMR (376 MHz, C_6D_6) δ −146.43 ppm.

Synthesis of Triethylphosphine Oxide Alumatrane Adduct 13·O=PEt$_3$. To a 100 mL round-bottomed flask in a glovebox was added 150 mg (1 equiv, 0.17 mmol) of alumatrane dimer **2** and 54.45 mg (2.4 equiv, 0.41 mmol) of triethyl phosphine oxide. The reaction flask was removed from the glovebox and 10 mL of toluene was added. After being stirred for 30 min, the solution became clear and colorless. During stirring for an additional 4 h, a white precipitate formed. The solids were filtered under inert atmosphere providing 75 mg of the desired product in 78% yield. Crystals suitable for X-ray analysis were obtained by placing the toluene extract in a freezer for 2 days. White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (s, 3H), 6.67 (s, 3H), 4.32−4.36 (d, 3H, J = 13.6 Hz), 2.81−2.85 (d, 3H, J = 13.6 Hz), 2.28 (s, 18H), 2.20−2.11 (dq, 6H, J = 12 Hz, J = 7.6 Hz), and 1.45−1.37 (dt, 9H, J = 17.2 Hz, J = 16.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.5, 130.8, 130.7, 129.3, 128.4, 127.1, 127.0, 126.6, 125.5, 124.9, 121.6, 59.2, 20.6, 18.6 (d, J = 68.2 Hz), 17.4, and 5.9 (d, J = 4.6 Hz) ppm; ^{31}P NMR (168 MHz, $CDCl_3$) δ 63.166 ppm; $APCI^+$ found 580 (calcd for $C_{35}H_{38}AlNO_5$, 579.26).

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Supporting Information Available: Tables of detailed structural and refinement data, CIF files, references to known compounds, and ^{1}H and ^{13}C NMR spectra for coupled products. This material is available free of charge via the Internet at http://pubs.acs.org.