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$P(PhCH_2NCH_2CH_2)_3N$ Catalysis of Mukaiyama Aldol Reactions of Aliphatic, Aromatic, and Heterocyclic Aldehydes and Trifluoromethyl Phenyl Ketone

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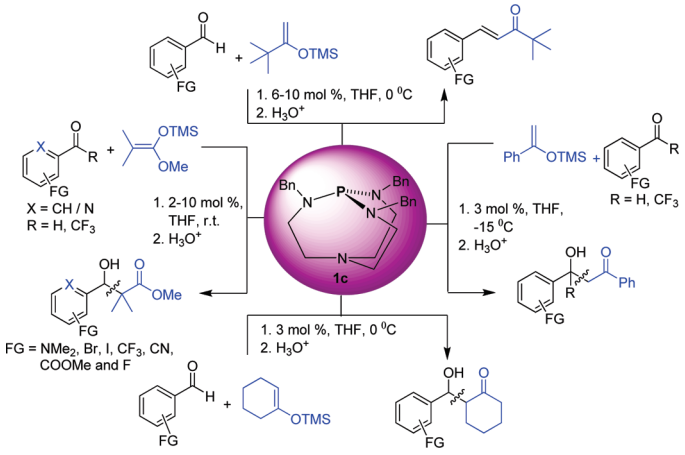

Herein we find that proazaphosphatrane **1c** is a very efficient catalyst for Mukaiyama aldol reactions of aldehydes with trimethylsilyl enolates in THF solvent. Only the activated ketone 2,2,2-trifluoroacetophenone underwent clean aldol product formation with a variety of trimethylsilyl enolates under similar conditions as the aldehydes. The reactions were carried out at room temperature using (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane, whereas the temperature was −15 °C in the case of 1-phenyl-1-(trimethylsilyloxy)ethylene. The reaction conditions are mild and operationally simple, and a variety of aryl functional groups, such as nitro, amino, ester, chloro, trifluoromethyl, bromo, iodo, cyano, and fluoro groups, are tolerated. Product yields are generally better than or comparable to those in the literature. 1-Phenyl-1-(trimethylsilyloxy)ethylene, 1-(trimethylsilyloxy)cyclohexene, and 2-(trimethylsilyloxy)furan underwent clean conversion to β-hydroxy carbonyl compounds under our reaction conditions. In the case of bulky (2,2-dimethyl-1-methylenepropoxy)trimethylsilane, only α,β-unsaturated esters were isolated. Heterocyclic aldehydes, such as pyridine-2-carboxaldehyde, benzofuran-2-carboxaldehyde, benzothiophene-2-carboxaldehyde, and 1-methyl-2-imidazolecarboxaldehyde, gave good yields of Mukaiyama products. An optimized synthesis for the catalyst **1c** is also reported herein.

Introduction

The Mukaiyama aldol reaction[1] is a versatile carbon−carbon bond-forming reaction which occurs between an enoxysilane and a carbonyl compound to form β-hydroxy carbonyl compounds. The most common application of this transformation involves complex molecule synthesis[2]

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(such as fragment coupling[3] and chiral building block construction),[4] and it has been the subject of intensive investigation for the past three decades.[2] Moreover, the Mukaiyama reaction has significant advantages over the classical aldol reaction,[5] such as mild reaction conditions, nonreversibility, good yields of aldol products, and lower production of dehydrated side products.[6] Initially, stoichiometric amounts of Lewis acids were used to promote Mukaiyama transformations, but it is now more common to employ catalytic loadings of these promoters whose role is believed to be the activation of the electrophilic carbonyl carbon substrate. Among the considerable number of such catalysts are Me_3SiOTf,[7] Me_3SiI,[8] $Me_3SiCl/SnCl_2$,[9] $Ph_3CCl/SnCl_2$,[10] Ph_3CClO_4,[11] trityl salts;[12] various rhodium complexes;[13] trivalent lanthanum,[14a] $Ln(OTf)_3$ (Ln = Yb,[14b] Gd, Lu),[14c] and scandium[14e] triflates; $Yb[C(SO_2C_8F_{17})_3]_3$ and $Sc[C(SO_2C_8F_{17})_3]_3$;[14f] iron,[15a,b] ruthenium,[15c] palladium[15c,d] and bis[(bis1,3-trimethylsilyl)cyclopentadienyl]ytterbium(III) chloride[16a] complexes; and $[Et_3Si(toluene)]B(C_6F_5)_4$,[16b] $[Cp_2Zr(O\text{-}t\text{-}Bu)THF[BPh_4]$,[16c] $BiCl_3-NaI$,[16d] $Sc(OTf)_3$–water,[16e] $(PfOBu_2SnOSnBu_2OPf)_2$,[16f] $Bi(OTf)_3$,[16g] $Bi(OTf)_3$/ionic liquids,[16h] $Cp_2Zr(OTf)_3$,[16i] complexes of Ti(IV),[6b,17a] 1,3-dihalotetraalkyldistannoxane,[17c] $[Mo_2(OAc)_4]/O_2$,[17d] Ln-Br_3,[17e] scandium trisdodecanesulfonate,[17f] B-[3,5-bis(trifluoromethyl)phenyl]oxazaborolidine,[17g] SmI_2,[18a] $MgI_2\cdot(OEt_2)_n$,[18b] polymer-supported $Sc(OTf)_3$,[18c,d] titanium silicates,[18e,f] montmorillonite K10,[18g] $SmCl_3$,[18h] $FeCl_2$,[18i] zinc triflate,[18j] $Sc(OTf)_3$ in PEG,[18k,l] a dinuclear titanium(IV) complex of *p*-*tert*-butylthiacalix[4]arene,[18m] aluminum bis(trifluoromethylsulfonyl)amides,[18n] sulfated-metal oxides,[18o] $Sc(OTf)_3$/amphiphilic calix[6]arene complex,[18p] $InCl_3$,[18q] sulfated-ZrO_2,[18r] MCM-41,[18s] diphenyltin sulfide/silver perchlorate,[18t] $BF_3\cdot OEt_2$,[18u] Sn-MCM-48,[18v] mesoporous-Mn^{2+} catalyst,[18w] $CuF\cdot 3PPh_3\cdot 2EtOH/(EtO)_3$-SiF,[18x] and tris(pentafluorophenyl)boron.[18y]

Lewis bases that have been employed to nucleophilically activate the enoxysilane substrate include 0.5 mol % of sodium phenoxide–phosphine oxides,[19] 20 mol % of tris(2,4,6-trimethoxyphenyl)phosphine,[20] 1 mol % of quaternary ammonium dendrimers containing iodide counterions,[21a] 1 mol % of SBA-15 functionalized TBD (1,5,7-triazabicyclo[4.4.0]dec-5-ene),[21b] 20 mol % of DBU,[21c] 10 mol % a polystyrene-bound phosphoramide,[21d] quaternary

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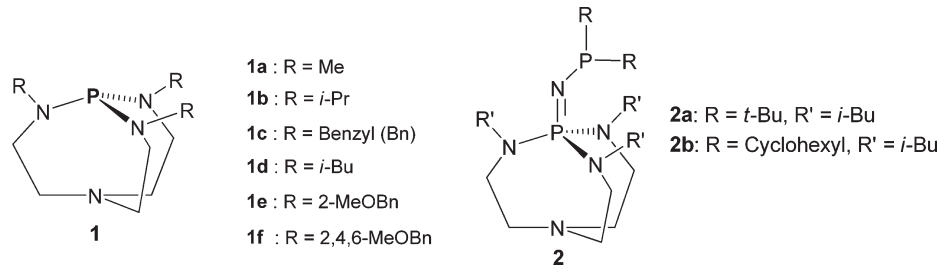

FIGURE 1. Proazaphosphatranes (**1**) and iminoproazaphosphatranes (**2**).

ammonium fluoride salts,[21e] 5−10 mol % of fluorides,[22] 10 mol % of lithium alkoxides,[23a] 10 mol % of lithium acetate,[23b,c] 10 mol % of *N*-oxides,[24] and 10 mol % of *N*-methylimidazole.[25] Mukaiyama et al. also reported such reactions employing 1 equiv of lithium amide[26] or 10 mol % of acetate catalysts[27] and recently, Song et al. reported a catalytic method with 0.5 mol % of N-heterocyclic carbenes as catalysts.[28]

It has also been reported that Mukaiyama aldol reactions can proceed without catalysts in highly polar solvents such as DMF,[29a] DMSO,[29a] water,[29b] and ionic liquids.[29c] Another catalytic system utilizes iodine whose mechanism of action is suggested to involve an electron-transfer pathway.[30]

The activation of silyl enolates in which the Lewis acidity of the silicon atom has been enhanced by a Lewis base has been studied by Denmark et al., who introduced phosphoramide Lewis bases to catalyze the aldol reaction of trichlorosilyl enolates with aldehydes.[31] Similarly, Hosomi and co-workers reported a Mukaiyama reaction using a dimethylsilyl enolate in the presence of an aldehyde or imine substrate and $CaCl_2$ in dry or aqueous DMF solvent.[32]

Previous work in our laboratories has established that bicyclic proazaphosphatranes[33] (Figure 1) bearing methyl, isobutyl, or benzyl groups on the PN_3 nitrogens are highly effective catalysts, promoters, and ligands for Pd-catalyzed cross-coupling reactions, such as Buchwald−Hartwig aminations,[34a] Stille couplings,[34b] and Suzuki reactions.[34c] Proazaphosphatranes are strongly basic, with pK_a values of their P-protonated N_{basal}→P transannulated conjugate acids in the range 32−34 in MeCN.[34d] To the extent that N_{basal}→P transannulation may be occurring during reactions catalyzed by **1**, the nucleophilicity of the phosphorus may be enhanced.[33b] Previously, we reported the activation of silicon−carbon bonds by strongly Lewis basic proazaphosphatranes in the silylation of alcohols with *tert*-butyldimethylsilyl chloride (TBDMSCl),[35] desilylation of TBDMS ethers,[36] addition of TMSCN to carbonyl compounds,[37] and nucleophilic aromatic substitution of aryl fluorides with aryl TBDMS (or TMS) ethers.[38] As part of our ongoing efforts to expand synthetic methodologies facilitated by the use of proazaphosphatranes as catalysts, we report here efficient activation of silicon in silyl enolates using **1c** as a catalyst in Mukaiyama aldol reactions (Scheme 1).

Results and Discussion

Although we reported the synthesis of **1c** previously,[39] we now describe a more convenient set of reaction conditions (Scheme 2). Both synthetic methods involve three steps, but step 1 is now better optimized, and in step 3 the more convenient base LiHMDS is employed instead of KO-*t*-Bu. Although our overall yield of 38% for **1c** is lower than that obtained via our previously reported route (48%), the present protocol provides more consistent yields in the deprotonation step.

For optimization of the Mukaiyama reaction conditions, the room-temperature aldol reaction of the electron-rich aryl aldehyde shown in the model reaction in (Table 1) was chosen. All of the proazaphosphatranes screened (**1a**−**f**) resulted in good to excellent isolated yields of aldol products which were obtained after room temperature acid hydrolysis.

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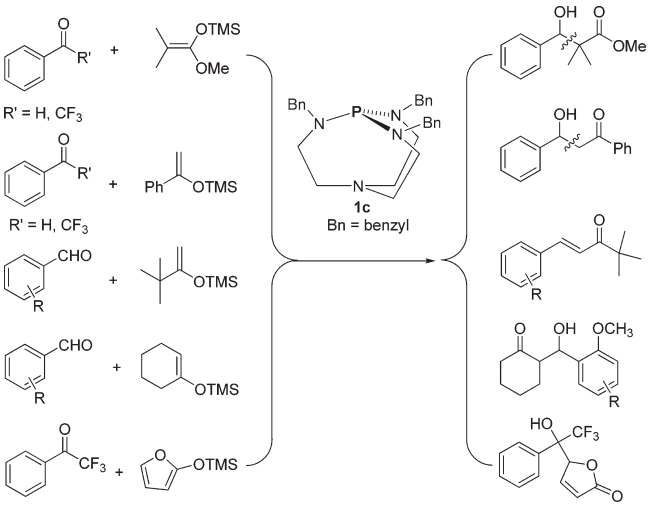
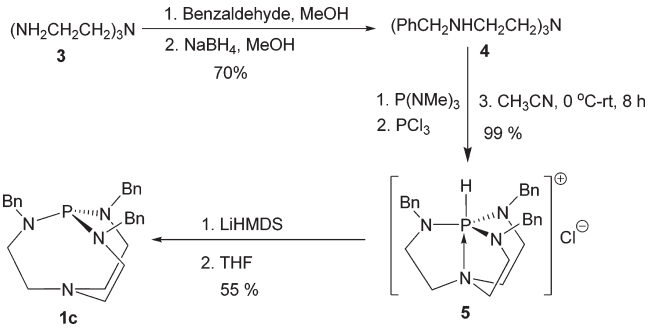
SCHEME 1. Mukaiyama Aldol Reactions of Various Silyl Enol Ethers Catalyzed by 1c



SCHEME 2. Synthesis of Catalyst 1c

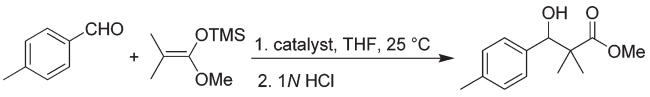


Since catalysts **1b** and **1c** produced nearly the same product yield (entries 2 and 3, respectively), we reduced the catalyst loading to 0.5 mol % which revealed the somewhat better performance of **1c** (entries 7 and 8). Although we found that the bulky catalyst **1d** showed better activity in a variety of transformations,[33] **1c** was best in the present transformation, as well as in Stille reactions on which we reported previously.[34b,39] The origin of the beneficial influence of the benzyl groups of catalyst **1c** and the *i*-Bu substituents of **1d** on different reactions is not clear.

Very recently, we reported the synthesis of **2a**[40a] and **2b**[40a] and their applications as bulky, air-stable, and electron-rich ligands in both palladium-catalyzed Suzuki[40b] and in Buchwald−Hartwig aminations.[40c] In the Mukaiyama aldol screening reaction in Table 1, both catalysts showed comparable results under the same reaction conditions (entries 9 and 10, Table 1). The control experiment shown in Table 1, entry 11, reveals the need for a catalyst to presumably activate the silicon center in the Mukaiyama aldol reaction. It is interesting that 8 out of the 12 methods found in the literature employ 5−20 mol % of catalyst (see footnote c of Table 1) to reach moderate to high product yields. On the other hand, an NHC[28] and a 1,3-dihalotetraalkyldistannoxane[17c]

(40) (a) Kingston, J. V.; Ellern, A.; Verkade, J. G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4960–4963. (b) Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2007**, *72*, 2816–2822. (c) Venkat Reddy, Ch.; Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2008**, *73*, 3047–3062.

TABLE 1. Survey of Proazaphosphatranes in a Mukaiyama Aldol Reaction Using (1-Methoxy-2-methyl-1-propenyloxy)trimethylsilane[a]



entry	catalyst	yield[b] (%)
1	**1a**	82
2	**1b**	91
3	**1c**	92 (79−99)[c]
4	**1d**	77
5	**1e**	89
6	**1f**	90
7[d]	**1b**	87
8[d]	**1c**	90
9	**2a**	90
10	**2b**	91
11	none	nr[e]

[a]Reaction conditions: catalyst (2.0 mol %), aldehyde (2.0 mmol), silyl ether (2.4 mmol), THF (4 mL), 24 h, room temperature, followed by 1 N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel column chromatography. [c]References 15c, 17c, 18c, 20, 21c, 23a, 23b, 26a, 26c, 27b, 27c, and 28. [d]Using 0.5 mol % of the catalyst **1c**. [e]nr = no reaction after 24 h.

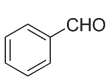
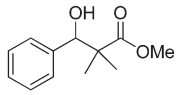
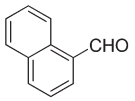
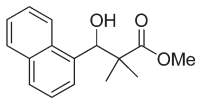
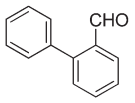
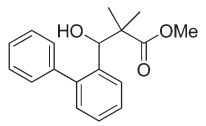
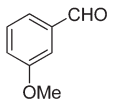
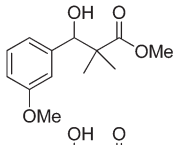
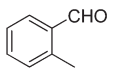
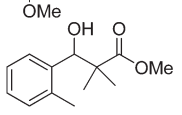
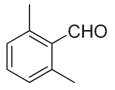
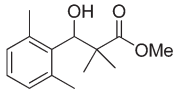
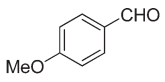
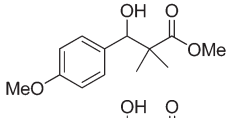
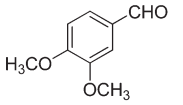
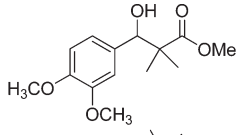
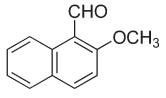
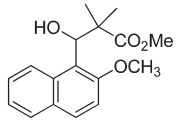
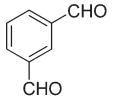
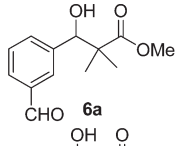
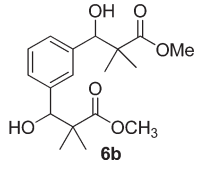
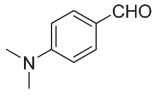
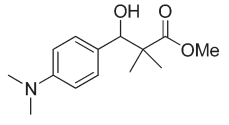
produced 83 and 99% product yields using only 0.5 and 0.025 mol % of catalyst, respectively.

A variety of aldehydes were tested (Table 2) using the optimized reaction conditions reported in footnote a of Table 1 (unless stated otherwise in Table 2). As is evident from Table 2, both electron-neutral and electron-donating aldehydes reacted with equal ease with $Me_2C{=}C(OMe)$-$OSiMe_3$, affording the desired aldols in good to excellent yields. Electron-neutral aryl aldehydes, such as benzaldehyde (Table 2, entry 1), 1-naphthaldehyde (entry 2), and *o*-phenylbenzaldehyde (entry 3), also underwent clean addition reactions with $Me_2C{=}C(OMe)OSiMe_3$ to give the expected aldol products in good to excellent yields. Aldehydes with electron-donating substituents, such as *m*-methoxybenzaldehyde (entry 4), *o*-tolualdehyde (entry 5), 2,6-dimethylbenzaldehyde (entry 6), *p*-methoxybenzaldehyde (entry 7), 3,4-dimethoxybenzaldehyde (entry 8), and 2-methoxy-1-naphthaldehyde (entry 9), resulted in moderate to excellent isolated yields of aldol products. Excellent isolated yields were obtained when sterically hindered aldehydes, such as *o*-tolualdehyde (Table 2, entry 5), 2,6-dimethylbenzaldehyde (entry 6), and *o*-phenylbenzaldehyde (entry 3), were employed under our reaction conditions. Disubstituted isophthalaldehyde also participated in this reaction by providing a 93% combined yield of mono- and disubstituted products (entry 10) when the ratio of isophthaldehyde/(1-methoxy-2-methyl-1-propenyloxy)trimethylsilane was 1:2.4.

It is interesting to note that the reaction of $Me_2C{=}C$-$(OMe)OSiMe_3$ with *p*-*N*,*N*-dimethylaminobenzaldehyde gave a poor yield of product (47%) when the neutralization workup step was carried out with saturated aqueous $NaHCO_3$. However, an excellent isolated yield (96%) was obtained when the product was isolated as the TMS-protected alcohol in a separate experiment. Using the stronger base NaOH, instead of $NaHCO_3$, gratifyingly gave an excellent isolated yield of aldol product (90%) (Table 2, entry 11).

A variety of aldehydes bearing electron-withdrawing groups were screened with $Me_2C{=}C(OMe)OSiMe_3$ under the optimized conditions mentioned in Table 1, entry 3, and

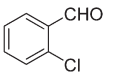
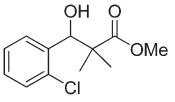
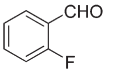
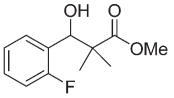
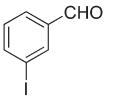
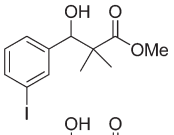
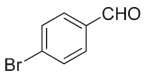
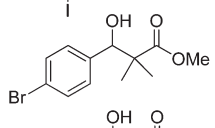
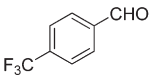
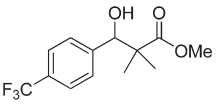
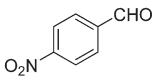
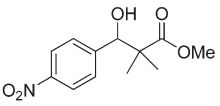
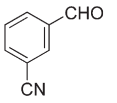
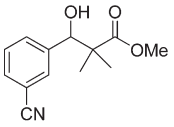
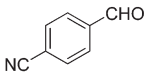
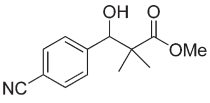
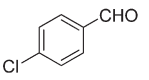
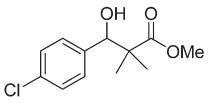
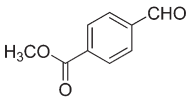
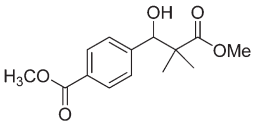
TABLE 2. Scope of the Mukaiyama Aldol Reaction of Aldehydes with $(CH_3)_2C{=}C(OCH_3)OSi(CH_3)_3$ Catalyzed by 1c[a]

Entry	Aldehyde	Product	Yield[b]	Lit. Yield (%)
1			93%	(20-100%)[c]
2			81%	(82-97)[d]
3[e]			92%	–
4			95%	–
5[e]			92%	(93%)[f]
6			86%	–
7			90%	(44-98%)[g]
8[e]			91%	–
9[e]			69%	–
10[h]		 **6a**	93%[i]	–
		 **6b**		
11[j]			47%[k] 96%[m] 90%[n]	(83%)[l]

[a]Reaction conditions: aldehyde (2.0 mmol), TMS ether (2.4 mmol), **1c** (3.0 mol % unless otherwise stated), THF (4.0 mL), room temperature for 24 h, followed by 1N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel chromatography. [c]References 17d−f, 18c−g, 20, 21c, 23a, 23c, 24, 25, 26a, 28, 29a−c, and 30. [d]References 17d, 23a, 26a, and 28. [e]Using 6 mol % of **1c**. [f]Reference 18c. [g]References 15c, 17e, 18e, 20, 21b, 23a, 24, 25, 26a, 27b, 27c, 28, 29a, and 29c. [h]Using 10 mol % of **1c** and 4.8 mmol of $Me_2C{=}C(OMe)OSiMe_3$. [i]Combined isolated yield of **6a** (49%) and **6b** (44%). [j]Using 10 mol % of catalyst **1c**. [k]$NaHCO_3$ was used for neutralizing excess HCl used for the hydrolysis of the TMS ether. [l]Reference 28. [m]Isolated yield as the TMS ether. [n]NaOH was used in place of $NaHCO_3$ for neutralizing excess HCl used for the hydrolysis of the TMS ether.

the results are summarized in Table 3. 2-Chlorobenzaldehyde and 2-fluorobenzaldehyde provided excellent isolated product yields (entries 1 and 2, respectively) while 3-iodobenzaldehyde (Table 3, entry 3) and 4-bromobenzaldehyde (entry 4) both gave good yields of product. Electron-deficient 4-(trifluoromethyl)benzaldehyde gave a

TABLE 3. Scope of Mukaiyama Aldol Reaction of Functionalized Aldehydes with $(CH_3)_2C{=}C(OCH_3)OSi(CH_3)_3$ Catalyzed by 1c[a]

Entry	Aldehyde	Product	Yield[b]	Lit. Yield (%)
1			91%	(65%[c], <5%[d])
2			77%	–
3[e]			95%	–
4[f]			72%	(34-92)[g]
5[f]			84%	(33-68%)[h]
6			62%	(32-97)[i]
7[f]			58%	–
8			74%	(69-90%)[j]
9[f]			91%	(63-94)[k]
10			82%	(99%)[l]

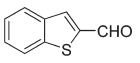
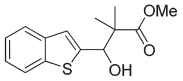
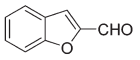
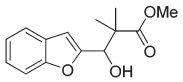
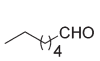
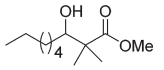
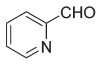
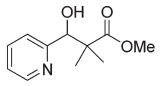
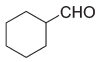
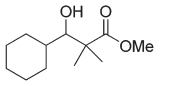
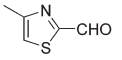
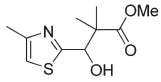
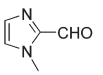
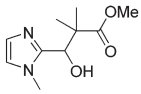
[a]Reaction conditions: aldehyde (2.0 mmol), TMS ether (2.4 mmol), **1c** (3.0 mol % unless otherwise stated), THF (4.0 mL), room temperature, 24 h, followed by 1N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel chromatography. [c]Reference 24. [d]Reference 15c. [e]Using 10 mol % of catalyst **1c**. [f]Using 6 mol % of catalyst **1c**. [g]References 15c, 17e, 23a, 26a, and 26c. [h]Reference 17d. [i]References 17e, 18f, 21b, 23a, 23b, 24, 25, 26a–c, 27b, 27c, and 28. [j]References 18f, 23a, 26a, 26c, and 28. [k]References 15c, 17e, 18c, 21c, 23a, 23b, 24, 25, 26a, 26c, 27b, 27c, 28, 29c, and 30. [l]References 23b and 27b.

moderate yield (entry 5), as did the *p*-nitro (entry 6), *m*-cyano (entry 7), and *p*-cyano (entry 8) analogues. *p*-Chloro- and ester-functionalized aldehydes underwent clean reactions giving good to excellent yields of products (entries 9 and 10, respectively).

We then turned our attention to screening various heterocyclic and aliphatic aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ (Table 4). Both 5- and 6-membered ring aldehydes bearing N, O, or S heteroatoms afforded the expected aldol product in poor to excellent isolated yields. Sulfur-containing 2-benzothiophenecarboxaldehyde afforded an excellent isolated product yield (Table 4, entry 1), 2-benzofurancarboxaldehyde gave a very good yield (Table 4, entry 2), and an enolizable aliphatic aldehyde (entry 3) also provided a good yield of the corresponding aldol product. However, 2-pyridinecarboxaldehyde and cyclohexanecarboxaldehyde gave only modest isolated product yields (entries 4 and 5, respectively). Nevertheless, the yield in entry 5 exceeded that previously reported in the literature. The two 5-membered heterocyclic aldehydes in Table 4 (entries 6 and 7) gave only low yields of the corresponding products. However, in the case of entry 6, a modest isolated yield (53%) was obtained when the product was isolated as the TMS-protected alcohol in a separate experiment.

In screening the reaction of $PhC(=CH_2)OSiMe_3$ with *o*-anisaldehyde using proazaphosphatranes **1a**–**d** (Table 5, entry 1), **1c** gave the best product yield (82%) in accord with the previous findings in the present work. We then screened several aldehydes with the same silyl enol ether. Thus, electron-rich *p*-tolualdehyde and electron-poor *p*-chlorobenzaldehyde gave a moderate and a modest yield of product, respectively (entries 2 and 3). A sterically bulky and an enolizable aliphatic acyclic aldehyde gave a modest and a good product aldol yield, respectively (entries 4 and 5), and

TABLE 4. Scope of Mukaiyama Aldol Reaction of Heterocyclic Aldehydes with $(CH_3)_2C{=}C(OCH_3)OSi(CH_3)_3$ Catalyzed by 1c[a]

Entry	Aldehyde	Product	Yield[b]	Lit. Yield (%)
1[c]			92%	–
2			89%	–
3			80%	(47-80)[d]
4			67%	(53-97%)[e]
5			67%	(35-48)[f]
6[c]			36% 53%[g]	–
7[c]			52%	–

[a]Reaction conditions: aldehyde (2.0 mmol), TMS ether (2.4 mmol), **1c** (3.0 mol % unless otherwise stated), THF (4 mL), room temperature, 24 h, followed by 1 N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel column chromatography. [c]Using 10 mol % of catalyst **1c**. [d]References 14a, 18g, and 18h. [e]References 23b, 26b, 27b, 29b, and 29c. [f]References 20 and 27b. [g]Isolated yield as the TMS ether.

$C_6H_9OSiMe_3$ with electron-deficient *p*-nitrobenzaldehyde provided an excellent isolated product yield as the *syn* isomer selectively (entry 6). Electron-neutral benzaldehyde and electron-rich *o*-anisaldehyde afforded good and excellent isolated product yields, respectively, with predominant *syn* isomer selectivity in both cases (entries 7 and 8).

The use of bulky $Me_3CC(=CH_2)(OSiMe_3)$ was then investigated as shown in Table 6. To our surprise, the unsaturated ketone **7b** was obtained rather than the desired aldol product **7a** when we carried out the reaction at 0 °C (Table 6, entry 1). An attempt to optimize the reaction to selectively produce aldol product by lowering the reaction temperature to −20 °C failed to give aldol product, and the same yield of dehydrated product (entry 2) was produced as was the case at 0 °C. Lowering the temperature to −78 °C for the same length of time did not produce any observable product, and only starting materials were recovered (entry 3). At room temperature, this reaction did not proceed to complete conversion, and only a moderate yield of α,β-unsaturated ketone **7b** (entry 4) was isolated. We then expanded the scope of this trimethylsilyl enol ether to a diverse range of aldehydes using the conditions in entry 1 of Table 6.

As seen in Table 7, catalyst **1c** gave good to excellent isolated yields of the corresponding α,β-unsaturated bulky ketones for aldehydes bearing a variety of functional groups. Our methodology is compatible with fluoro (Table 6, entry 1), iodo (Table 7, entry 1), and acid-sensitive cyano (Table 7, entry 2) substituents; the heterocyclic aldehydes benzofuran-2-carboxaldehyde (entry 3), benzothiophene-2-carboxaldehyde (entry 4), and 4-methyl-2-thiazolecarboxaldehyde (entry 5); and also electron-rich 4-methoxy-1-naphthaldehyde (entry 6) and *o*-tolualdehyde (entry 7). The bulky ortho-disubstituted aldehyde in entry 8 afforded a moderate product yield, and *trans*-cinnamaldehyde (entry 9) produced the conjugated bulky ketone shown in excellent isolated yield (95%). The latter yield exceeded that previously reported in the literature using 110 mol % CsF as catalyst at 80 °C.[41] The other products listed in Table 7 have not, to our knowledge, been reported in the literature.

Our attempts to accomplish Mukaiyama aldol addition to acetophenone, benzophenone, and 4-chloroacetophenone were unsuccessful. However, 2,2,2-trifluoroacetophenone reacted with a variety of trimethysilyl enolates to provide products **8**−**12** in moderate to excellent yields as shown in Scheme 3. The reaction of $Me_2C(=C)OMe)(OSiMe_3)$ with 2,2,2-trifluoroacetophenone afforded the corresponding Mukaiyama aldol product in 91% yield as the TMS-protected product **8**. In a separate experiment, hydrolyzed product **9** was obtained in 78% yield. Interestingly, both **8** and **9** possess two vicinal quaternary carbon centers. Not surprisingly, 2,2,2-trifluoroacetophenone was found to be an excellent substrate for this reaction with $PhC(=CH_2)(OSiMe_3)$, and product **10** was isolated in 93% yield, which is comparable to the yield reported in the literature.[28] The reaction of 2,2,2-trifluoroacetophenone with 2-(trimethylsilyloxy)furan gave a good yield of product **11** with a *syn*/*anti* ratio of 2:1. As seen in Table 7, catalyst **1c** led to good to excellent isolated yields of the corresponding α,β-unsaturated ketones for aldehydes bearing a variety of functional groups. The reaction of 2,2,2-trifluoroacetophenone with bulky $Me_3C(=CH_2)(OSiMe_3)$ provided the corresponding sterically encumbered trisubstituted α,β-unsaturated ketone **12** in good isolated yield. Compounds **8**, **11**, and **12** have not been previously reported in the literature. Attempted reaction of 1-(trimethylsilyloxy)cyclohexene with 2,2,2-trifluoroacetophenone gave a complicated reaction mixture from which we were unable to isolated the desired product.

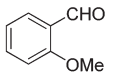
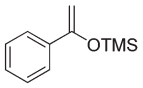
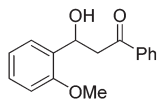
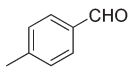
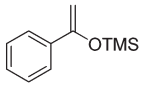
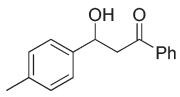
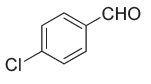
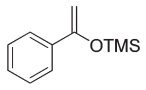
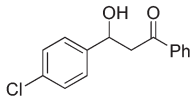
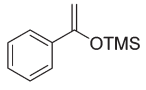
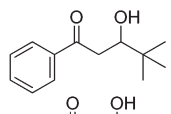
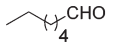
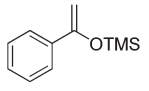
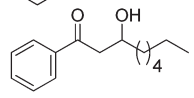
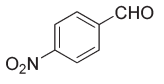
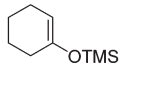
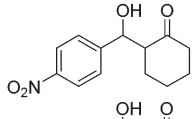
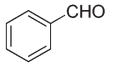
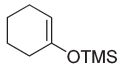
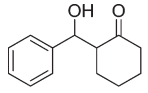
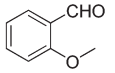
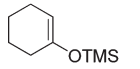
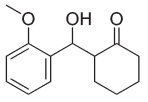
A mechanism suggested for the Mukaiyama aldol reaction of trimethylsilyl enolates with aldehydes[42] under our conditions is depicted in Scheme 4. In the literature, the Lewis base catalyzed Mukaiyama aldol reaction is proposed to proceed through the formation of a pentavalent silicon complex via Lewis base activation, which generates the naked enolate anion **C** in the presence of a large countercation.[22b,23,26a,27b,28] In path 1, **1c** initially forms a pentacoordinated silicon complex **A** in which the electron density on the silicon is enriched, consequently weakening the bonds around this atom and thus favoring ionization to species **B** and **C**. Evidence for the existence of naked anion **C** was previously presented by our group to account for the formation of both α- and γ-addition products in the reaction of crotyltrimethylsilane with aldehydes in the presence of **1a**.[43] Enolate anion **C** then nucleophilically attacks the aldehyde carbon giving the corresponding alkoxide **E** which then nucleophilically attacks cation **D** giving the TMS-protected aldol product **F**. Product **F** is subsequently hydrolyzed in a separate step to give the desired aldol product **G** with accompanying regeneration of

(41) Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *J. Organomet. Chem.* **1980**, *184*, 157–166.

(42) For useful discussions of the mechanism of Mukaiyama reactions, see: (a) Wang, L.; Wong, M. W. *Tetrahedron Lett.* **2008**, *49*, 3916–3920. (b) Denmark, S. E.; Lee, W. *Asian J. Chem.* **2008**, *3*, 327–341. (c) Patel, S. G.; Wiskur, S. L. *Tetrahedron Lett.* **2009**, *50*, 1164–1166.

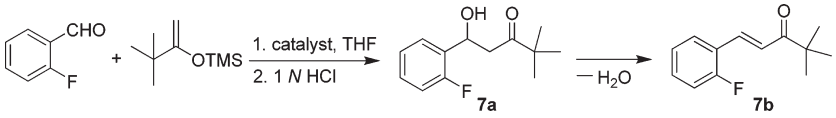
(43) Wang, Z.; Kisanga, P.; Verkade, J. G. *J. Org. Chem.* **1999**, *64*, 6459–6461.

TABLE 5. Scope of Mukaiyama Aldol Reaction of Aldehydes with $C_6H_5C(=CH_2)OSi(CH_3)_3$ and $C_6H_9OSi(CH_3)_3$ Catalyzed by 1c[a]

Entry	Aldehyde	TMS-enolate	Product	Yield (%)[b]	Lit. Yield (%)
1				82[c] 60[e] 79[f] 55[g]	(39-94)[d]
2				77	(74-89)[h]
3				69	(48-93)[i]
4				74	(88)[j]
5				80	
6				91	(66-92)[k]
7[l]				76 (94/6)[m]	(18-99)[n]
8[l]				91 (78/22)[m]	(89)[o]

[a]Reaction conditions: aldehyde (2.0 mmol), TMS ether (2.4 mmol), **1c** (3.0 mol %, otherwise stated), THF (4 mL), 0 °C, 72 h, followed by 1 N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel chromatography. [c]Using 3 mol % of **1c** [d]References 17d, 18i, and 18j. [e]Using 3 mol % of **1a**. [f]Using 3 mol % of **1b**. [g]Using 3 mol % of **1d**. [h]References 18k−m and 28. [i]References 18j−m, 25, and 28. [j]Reference 18n. [k]References 22b and 30. [l]Using 6 mol % of catalyst **1c**. [m]The syn/anti ratio was determined by using proton NMR spectroscopy. [n]References 1a, 14b, 14e, 15d, 16d, 17g, 18j, 18o−t,y, 21e, 22b, and 30. [o]Reference 18u.

TABLE 6. Scope of Mukaiyama Aldol Reaction of 2-Fluorobenzaldehyde with$(CH_3)_3CC(=CH_2)OSi(CH_3)_3$ Catalyzed by 1c[a]



entry	catalyst **1c** (mol %)	*T* (°C)	time (h)	**7a** yield[b] (%)	**7b** yield[b] (%)
1	6	0	72	0	92
2	6	−20	72	0	90
3	6	−78	72	n.r.	n.r.[c]
4	6	25	72	0	60[d]

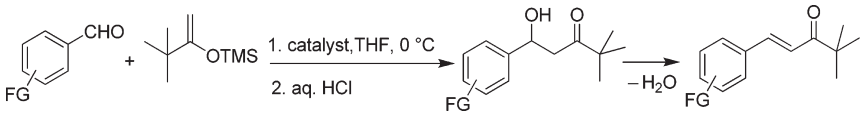
[a]Reaction conditions: aldehyde (2.0 mmol), (2,2-dimethyl-1-methylenepropoxy)trimethylsilane (2.4 mmol), THF (2.0 mL), followed by 1 N HCl (4.0 mL), 12 h. [b]Isolated yields after silica gel column chromatography. [c]No reaction. [d]^{1}H NMR spectroscopy revealed that 40% of the reaction consisted of unreacted aldehyde.

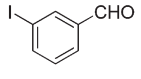
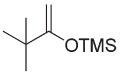
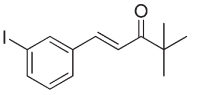
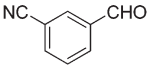
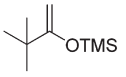
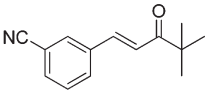
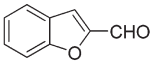
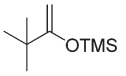
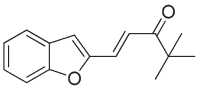
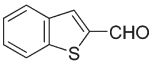
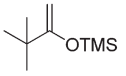
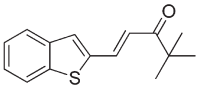
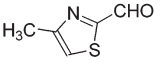
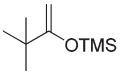
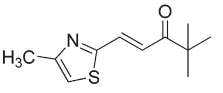
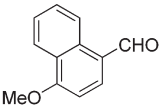
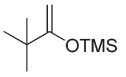
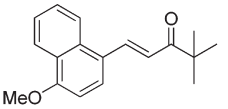
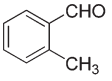
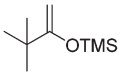
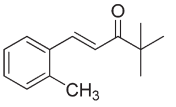
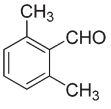
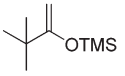
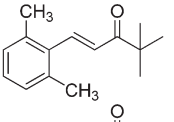
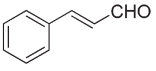
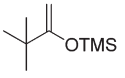
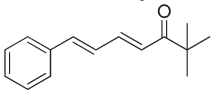
the catalyst **1c**. Another proposed route is depicted in path 2 in Scheme 4. Initially, **1c** forms a pentacoordinated silicate TMS-ketene acetal adduct **A** (as was suggested for path 1), which then coordinates with the incoming aldehyde concomitantly to form hexacoordinated cyclic intermediate **H**[20,44] in which a six-membered cyclic intermediate between the silyl enol ether and the aldehyde is formed. Subsequent steps are as discussed for path 1 to give product and regenerated catalyst **1c**.

To elucidate the nature of the active species in the mechanism in Scheme 4, we conducted ^{31}P NMR spectroscopic experiments aimed at monitoring changes in the environment of **1c**. Initially, we examined the room temperature ^{31}P NMR spectrum of **1c** in THF in the presence of equimolar amounts of $Me_2C{=}C(OMe)$-$OSiMe_3$ and *p*-tolualdehyde. A peak at 24 ppm (∼5−10% intensity) was observed which was attributed to the corresponding oxide **13**, a conclusion that was confirmed by synthesizing a

(44) Wang, Z.; Fetterly, B. M.; Verkade, J. G. *J. Organomet. Chem.* **2002**, *646*, 161–166.

TABLE 7. Synthesis of α,β-Unsaturated Bulky Ketones from Aldehydes with $(CH_3)_3CC(=CH_2)OSi(CH_3)_3$ Catalyzed by 1c[a]



entry	aldehyde	TMS-enolate	product	yield (%)[b]
1				95
2				94
3				79
4				83
5[c]				94
6				78
7[c]				90
8[c]				72
9[c]				96 (65)[d]

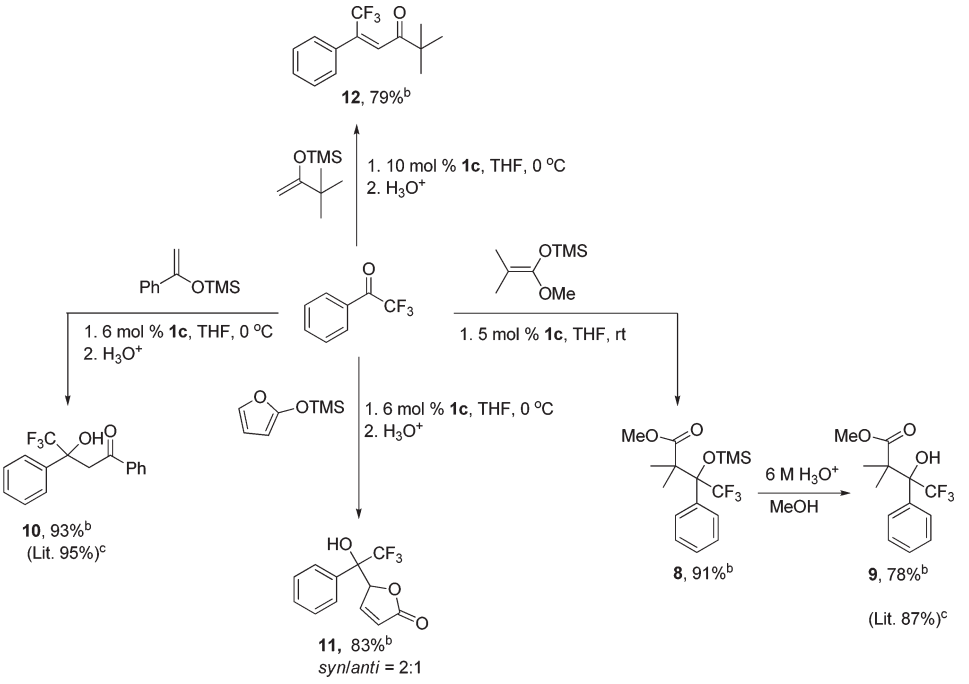
[a]Reaction conditions: aldehyde (2.0 mmol), (2,2-dimethyl-1-methylenepropoxy)trimethylsilane (2.4 mmol), **1c** (6.0 mol %), THF (4.0 mL), 0 °C, 72 h, followed by 1 N HCl (3.0 mL), 12 h. [b]Isolated yields after silica gel chromatography. [c]Using 10 mol % of **1c**. [d]Reference 41.

sample of **13** as depicted in Scheme 5. The formation of **13** could arise from the formation of an epoxide due to the putative self-condensation of *p*-toluadehyde as was observed previously in the presence of **1a**.[45] We then carried out a ^{29}Si NMR experiment at −40 °C on a THF solution of $Me_2C{=}C(OMe)OSiMe_3$ (δ ^{29}Si 19.56, THF) in the presence of an equimolar amount of **1c**. No change was observed in the ^{29}Si NMR chemical shift. Similarly, TMSOPh (δ ^{29}Si 18.21 ppm in THF) under the same conditions using **1c** as a catalyst also produced no change in the ^{29}Si NMR chemical shift. However, when we used the less bulky **1a**, a new peak at δ ^{29}Si 6.98 ppm was observed after 2 h and 10 min, which we attribute to the tetracoordinate silicon species **B** in which the anionic species **C** has been displaced. This chemical shift is in the same region as a peak we reported previously for a 1:1 mixture of TMSCN and **1a** in C_6D_6 (δ ^{29}Si 7.5 ppm) in which CN^- had been displaced. If the anion had not been displaced in both cases, an upfield rather than a downfield shift from the parent TMSX molecule would have been observed since the silicon would have become 5-coordinate.[37a] We used similar reasoning to account for the formation of both α- and γ-addition products in the reaction of crotyltrimethylsilane with aldehydes in the presence of **1a**.[43] After transient **A** forms **B** and **C** in Scheme 4, an aldehyde molecule reacts with **C** to form the alkoxide **E**, which after trimethylsilylation is acid-hydrolyzed to give the corresponding species **G** as the final product, plus the regenerated catalyst **1c**. Although we have ^{29}Si NMR evidence consistent with the formation of **B**, we have no convincing ^{31}P NMR evidence for this species. ^{31}P chemical shifts for PR_4^+ cations are generally in the range of 90−140 ppm.[46] The ^{31}P NMR chemical shift for **B** is 128 ppm at −40 °C in THF, which is virtually unchanged from the value of **1a** under the same

(45) Liu, X.; Verkade, J. G. *J. Org. Chem.* **2000**, *65*, 4560–4564.

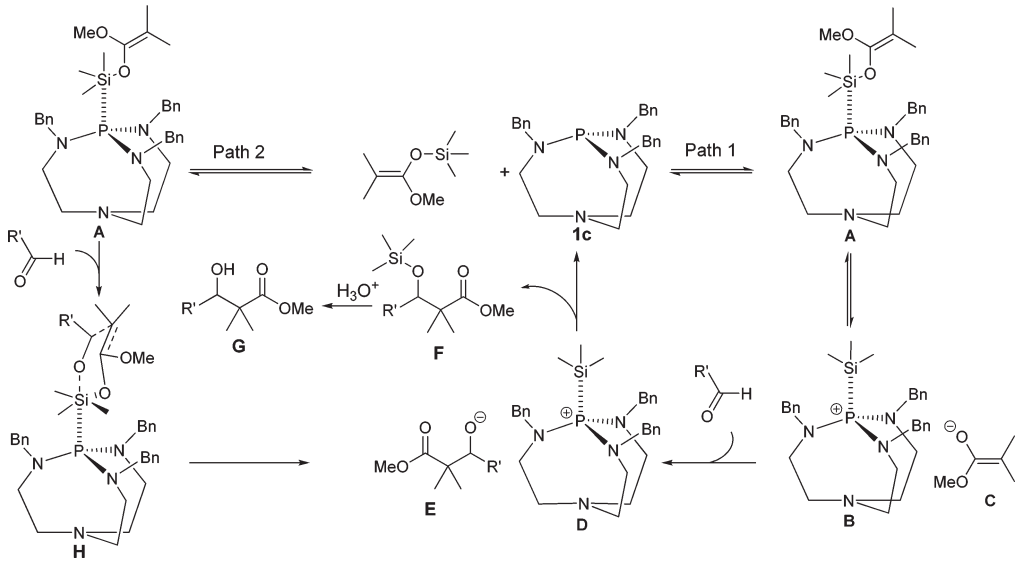
(46) *Handbook of Phosphorus Nuclear Magnetic Resonance Data*; Tebby, J. C., Ed.; CRC Press Inc.: Boca Raton, 1991.

SCHEME 3. Mukaiyama Aldol Reaction of a Trifluoromethyl Phenyl Ketone with a Variety of TMS Ethers Catalyzed by 1c[a]



[a]Reaction conditions: aldehyde (2 mmol), TMS ether (2.4 mmol), **1c** (5 mol % for **8**, 6 mol % for **9**−**11**, 10 mol % for **12**), room temperature, followed by 1 N HCl (4.0 mL), 12 h.[b]Isolated yields after silica gel chromatography.[c]Reference 28.

SCHEME 4. Proposed Reaction Pathway for the Mukaiyama Aldol Reaction of Aldehydes with $Me_2C{=}C(OMe)OSiMe_3$ Catalyzed by 1c



conditions. This result perhaps suggests a minimal perturbation of the phosphorus shielding environment as a result of a relatively weak Si−P interaction.

In summary, we have demonstrated that proazaphosphatrane **1c** is an active catalyst for the C−C bond-forming Mukaiyama aldol transformation, furnishing aldol products in generally high yields. Our methodology is compatible with electron-donating and -withdrawing aryl aldehyde functional groups (e.g., methoxy, nitro, trifluoromethyl, amino, cyano, bromo, ester, fluoro, and chloro), aliphatic and heterocyclic aldehydes which also function well in these reactions. Moreover, a variety of silyl enol ethers are compatible with our reaction conditions. Our methodology using **1c** represents an advantageous catalytic alternative to arylphosphines (wherein 20 mol % of catalyst is routinely employed). α,β-Unsaturated bulky ketone products were isolated in good to excellent yields under our reaction conditions.

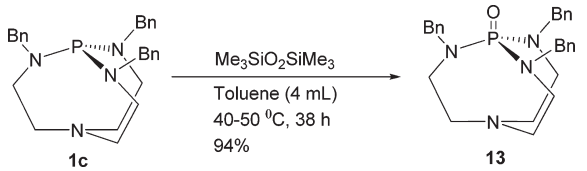
From Table 8, it is seen that of the total of 26 known Mukaiyama aldol products we found in the literature, we observed in this work higher yields for 5, comparable yields for 6, and lower yields for 15 of them. While the latter

TABLE 8. Comparison of the Efficiency of Our Catalytic Protocol with Literature Protocols

Our Product Yields Compared with Maximum Literature Yields and Our Catalyst Loadings Compared with the Lowest found in the Literature			
table	no. of our products with higher yields and (our catalyst loadings compared with lit.)	no. of our products with comparable[a] yields and (our catalyst loadings compared with lit.)	no. of our products with lower yields and (our catalyst loadings compared with lit.)
Table 1			1 (higher)
Table 2	1 (higher)	1 (higher)	3 (lower)
Table 3	2 (lower)	1 (lower)	4 (lower for 3; higher for 1)
Table 4	1 (lower)	1 (lower)	1 (lower)
Table 5		2 (lower)	5 (lower for 4; higher for 1)
Table 6	1 (lower)		
Scheme 7		1 (higher)	1 (higher)
	5 (3 lower)	6 (3 lower)	15 (11 lower)

[a]Taken here to be within ± 5%.

SCHEME 5. Synthesis of the Phosphine Oxide of Catalyst 1c



number might be considered somewhat disappointing, it is also to be noted from this table that our catalyst loadings were lower than the minimum catalyst loading (associated with the maximum yield) found in the literature in well over half (68%) of all of the cases. It should also be mentioned that our protocol resulted in the synthesis of 24 new compounds of which 12 were obtained in excellent yields, 4 in good yields, 4 in moderate yields, only 1 in a modest yield, and 3 in poor yields. The facile synthesis of catalyst **1c**, the broad range of amenable silyl enol ethers and aldehydes which can be utilized, the relatively low catalyst loading and the environmentally desirable lack of metal usage in the syntheses reported here renders our methodology attractive.

Experimental Section

General Considerations. All reactions were performed under an atmosphere of argon in oven-dried glassware. Toluene, pentane, and tetrahydrofuran (THF) were freshly distilled over sodium/benzophenone and stored over 4 Å molecular sieves under an argon atmosphere. ^{1}H (300 or 400 Hz) and ^{13}C (100.6 MHz) NMR spectra were recorded in $CDCl_3$ (unless otherwise stated); the chemical shifts are referenced to the residual peaks of $CHCl_3$ in $CDCl_3$. ^{31}P NMR spectra were recorded at ambient temperature on a 400 MHz spectrometer using standard procedures. Thin-layer chromatography (TLC) was performed using commercially prepared 60 mesh silica gel plates visualized with short-wavelength UV light (254 nm). Column chromatography was performed on silica gel (40−140 mesh) for purification of product. Electron-impact ionization experiments were performed on a triple quadrupole mass spectrometer fitted with a EI/CI ion source. Accurate mass measurements were performed using a double-focusing MS-50 mass spectrometer. All commercially available reagents were used as received. All products described in Tables 1−7 and Schemes 2 and 3 are known in the literature (unless indicated otherwise) and were characterized by comparing their ^{1}H and ^{13}C NMR spectra to the previously reported data. In all cases, the comparisons were very favorable. New compounds were characterized by ^{1}H, ^{13}C, mass (EI) spectra, and HRMS analysis.

Preparation of P(PhCH$_2$NCH$_2$CH$_2$)$_3$N (1c). Synthesis of Tribenzyl-tren (4). To 14.6 g (0.100 mol, 1.0 equiv) of freshly distilled [tris(2-aminoethyl)amine] in 75 mL of MeOH was added 30.48 mL (0.320 mol, 3.2 equiv) of benzaldehyde. The mixture was allowed to stir at room temperature over 8 h. To this mixture was added 100 mL of MeOH, and then the reaction mixture was cooled to 0−5 °C using an ice bath. $NaBH_4$ (5.67 g, 0.150 mol, 1.5 equiv) was added slowly to the mixture portionwise over a period of 1 h. Excess solvent was removed completely using a rotary evaporator, followed by dissolving the resultant slurry in 200 mL of water and extracted with CH_2Cl_2 (3 × 100 mL). The organic extracts were combined and dried over anhydrous Na_2SO_4 and filtered to remove Na_2SO_4. Excess solvent was removed under reduced pressure using a rotary evaporator. The crude light yellow oil was purified using silica gel chromatography (eluent: 10% MeOH/CH_2Cl_2) to afford 29.12 g (70%) of yellow oil.

Synthesis of [HP(PhCH$_2$NCH$_2$CH$_2$)$_3$N]Cl (5). Anhydrous acetonitrile (50 mL) was charged to a single-neck round-bottom flask. The flask was cooled to 0−5 °C in an ice bath. Hexamethylphosphorous triamide (HMPT, 4.72 mL, 26.7 mmol, 2.0 equiv) was added to the flask under argon, and the mixture was stirred for 5 min. PCl_3 (1.13 mL, 13.33 mmol, 1.0 equiv) was then slowly added to the mixture via syringe. After the mixture was stirred at 0−5 °C for 15 min, benzyl-tren (**4**) (16.6 g, 40.05 mmol, 3.0 equiv) dissolved in 50 mL of anhydrous acetonitrile was added slowly through a cannula under a positive flow of argon to remove the liberated byproduct dimethylamine formed during the reaction. The reaction was continued under constant stirring overnight at room temperature. The excess solvent was then removed under reduced pressure using a rotary evaporator, 300 mL of ether and 5.0 mL of THF were added, and the reaction mixture was stirred at room temperature for 1 h. The crystalline white solid obtained was filtered and washed with ethyl ether (200 mL) to remove any organic impurities. The product was further dried under reduced pressure to obtain a free-flowing white solid (19.05 g, 99%).

Synthesis of P(PhCH$_2$NCH$_2$CH$_2$)$_3$N (1c). To a 500 mL round-bottom Schlenk flask were added [HP(PhCH$_2$NCH$_2$CH$_2$)$_3$N]Cl (**5**) (7.684 g, 16.0 mmol) and lithium bis(trimethylsilyl)amide (6.21 g, 37.12 mmol) in an argon-filled glovebox. The flask was then evacuated under reduced pressure after which ca. 50 mL of anhydrous THF was added to the heterogeneous reaction mixture under a flow of argon. The resulting light yellow solution was stirred for about 12 h at room temperature to complete the deprotonation process (with monitoring by ^{31}P NMR spectroscopy). The reaction flask was then connected to a vacuum line and kept under reduced pressure for removal of volatiles, after which 200 mL of anhydrous pentane was added with further stirring for an additional 10 h at room temperature. The resulting solution was filtered through a frit

under an argon atmosphere, and volatiles were removed under reduced pressure on a vacuum line. The solid remaining (6.12 g) was recrystallized from anhydrous pentane three times (3 × 100 mL). The colorless crystalline solid **1c** was dried under vacuum for 3 h to give 3.89 g (55% yield) of product. ^{31}P NMR (162.8 MHz, C_6D_6) 127.97 ppm.[33b]

General Reaction Procedure for the (1-Methoxy-2-methyl-1-propenyloxy)trimethylsilane. In a nitrogen-filled glovebox, a 10 mL flat-bottom flask equipped with a magnetic stir bar was charged with proazaphosphatrane catalyst **1** (2 mol % unless otherwise stated). The flask was sealed with a rubber septum, (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (2.4 mmol) was added followed by the aldehyde [(2 mmol) (if solid, dissolved in 2 mL of anhydrous THF under argon atmosphere)], and freshly distilled THF (2 mL) was then syringed into the solution. The reaction was magnetically stirred for a specified length of time (see Tables 1−4), and the progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, 5 mL of 2 N HCl was added, and after being stirred for 12 h at room temperature, the reaction mixture was transferred into a 250 mL round-bottom flask. The reaction vessel was washed with ethyl acetate (3 × 10 mL), and then all organic solvents were removed under reduced pressure using a rotary evaporator. To the flask was added 30 mL of dichloromethane, and then its contents were transferred to a separatory funnel. The reaction mixture was neutralized with satd aq $NaHCO_3$ solution, and the product was extracted with dichloromethane (3 × 30 mL). The combined organics were dried over anhydrous $MgSO_4$ (2.0 g), and then the solvent was removed under reduced pressure. The crude product was purified by using short-path silica gel (140 mesh) chromatography with ethyl acetate/hexanes as eluents in all cases.

General Reaction Procedure for the Silyl Enol Ethers 1-Phenyl-1-(trimethylsilyloxy)ethylene and 1-(Trimethylsilyloxy)-cyclohexene. To a solution of proazaphosphatrane **1** (3 mol %) in 4 mL of anhydrous tetrahydrofuran (THF) at −20 °C was added the silyl enol ether [1-phenyl-1-trimethylsiloxyethylene or 1-(trimethylsilyloxy)cyclohexene (2.4 mmol)], and then the mixture was stirred at the same temperature for 30 min. The aldehyde (2.0 mmol) was then added, the reaction mixture was brought to −5 °C, and stirring was continued for 72 h. Addition of 1 N HCl solution (3 mL) to this mixture and further stirring for 3 h at −5 °C was followed by bringing the reaction mixture to room temperature. The reaction mixture was neutralized with satd aq $NaHCO_3$ solution, and then it was extracted with ethyl acetate (3 × 30 mL). The organic layers were collected and dried over anhydrous Na_2SO_4 followed by solvent removal under reduced pressure using a rotary evaporator. The crude product was purified by flash chromatography (hexane/ethyl acetate = 90:10) on silica gel (140 mesh) to give the desired aldol product.

Methyl 3-Hydroxy-3-(2-biphenyl)-2,2-dimethylpropionate (Table 2, Entry 3). The general procedure was followed using 2-biphenylcarboxaldehyde (0.323 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (56.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 20% ethyl acetate/hexanes) to afford 0.527 g (92%) of the desired product as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (d, 1H, J = 8.0 Hz), 7.42−7.30 (m, 7H), 7.20 (d, 1H, J = 7.6 Hz), 5.27 (s, 1H), 3.75 (bs, 1H), 3.64 (s, 3H), 1.02 (s, 3H), 0.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.8, 142.5, 141.9, 137.7, 130.5, 129.9, 128.5, 127.7, 127.7, 127.4, 127.1, 74.1, 52.4, 48.4, 24.2, 19.5; HRMS m/z calcd for $C_{18}H_{20}O_3$ 284.14124, found 284.14179.

Methyl 3-Hydroxy-3-(3-methoxyphenyl)-2,2-dimethylpropionate (Table 2, Entry 4). The general procedure was followed using 3-methoxybenzaldehyde (0.272 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.00 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 15% ethyl acetate/hexanes) to afford 0.453 g (95%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26−7.21 (m, 1H), 6.88−6.82 (m, 3H), 4.86 (d, 1H, J = 4.4 Hz), 3.79 (s, 3H), 3.72 (s, 3H), 3.05 (d, 1H, J = 4.0 Hz), 1.15 (s, 3H), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.3, 159.3, 141.9, 128.9, 120.3, 113.6, 113.3, 78.8, 55.4, 52.3, 47.9, 23.2, 19.4; HRMS m/z calcd for $C_{13}H_{18}O_4$ 238.12050, found 238.12115.

Methyl 3-Hydroxy-3-(2,6-dimethylphenyl)-2,2-dimethylpropionate (Table 2, Entry 6). The general procedure was followed using 2,6-dimethylbenzaldehyde (0.268 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (18.32 mg, 2 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 8% ethyl acetate/hexanes) to afford 0.407 g (86%) of the desired product as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.06−6.99 (m, 3H), 5.59 (s, 1H), 3.73 (s, 3H), 2.95 (s, 1H), 2.56 (s, 3H), 2.38 (s, 3H), 1.26 (s, 3H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.8, 138.6, 137.5, 135.5, 131.3, 128.6, 127.4, 76.1, 52.5, 50.3, 24.2, 22.6, 20.9; HRMS m/z calcd for $C_{14}H_{20}O_3$ 236.14124, found 236.14177.

Methyl 3-Hydroxy-3-(3,4-dimethoxylphenyl)-2,2-dimethylpropionate (Table 2, Entry 8). The general procedure was followed using 3,4-dimethylbenzaldehyde (0.332 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (56.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 8% ethyl acetate/hexanes) to afford 0.489 g (91%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.86−6.83 (m, 2H), 6.75 (s, 1H), 5.25 (s, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.66 (s, 3H), 1.29 (s, 3H), 1.07 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.8, 149.2, 148.4, 129.9, 121.6, 112.2, 110.3, 68.8, 56.1, 56.1, 52.4, 49.9, 23.3, 20.3; HRMS m/z calcd for $C_{14}H_{20}O_5$ 268.13107, found 268.13179.

Methyl 3-Hydroxy-3-(2-methoxynaphthalen-1-yl)-2,2-dimethylpropanoate (Table 2, Entry 9). The general procedure was followed using 2-methoxy-1-naphthaldehyde (0.372 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 8% ethyl acetate/hexanes) to afford 0.397 g (69%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (bs, 1H), 7.81−7.74 (m, 2H), 7.46 (t, 1H, J = 8.0 Hz), 7.32 (t, 1H, J = 8.0 Hz), 7.27−7.23 (m, 1H), 5.90 (d, 1H, J = 8.0 Hz), 4.90 (bs, 1H), 3.94 (s, 3H), 3.67 (s, 3H), 1.20 (s, 3H), 1.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.5, 155.5, 133.1, 130.2, 129.3, 128.6, 126.6, 123.6, 119.9, 112.8, 75.2, 55.9, 52.0, 50.3, 24.1, 20.7; HRMS m/z calcd for $C_{17}H_{20}O_4$ 288.13615, found 288.13656.

Methyl 3-(3-Formylphenyl)-3-hydroxy-2,2-dimethylpropanoate (Table 2, Entry 10, 6a). The general procedure was followed using isophthalaldehyde (0.268 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.972 mL, 4.8 mmol), **1c** (88.8 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 20% ethyl acetate/hexanes) to afford 0.221 g (49%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.95 (s, 1H), 7.76−7.73 (m, 2H), 7.54−7.52 (m, 1H), 7.44 (t, 1H, J = 8.0 Hz), 4.93 (s, 1H), 3.67 (s, 3H), 3.48 (bs, 1H), 1.01 (s, 3H), 1.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 192.4, 177.9, 141.2, 135.9, 133.8, 129.2, 128.9, 128.5, 76.8, 52.3, 47.7, 22.7, 19.1; HRMS m/z calcd for $C_{13}H_{16}O_4$ 236.10485, found 236.10533.

Dimethyl 3,3′-(1,3-Phenylene)bis(3-hydroxy-2,2-dimethylpropanoate) (Table 2, Entry 10, 6b). The general procedure was followed using isophthalaldehyde (0.268 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.972 mL, 4.8

mmol), **1c** (88.8 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 20% ethyl acetate/hexanes) to afford 0.301 g (44%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.15−7.14 (m, 4H), 4.79 (d, 1H, J = 4.4 Hz), 3.64 (s, 6H), 3.48 (bs, 1H), 1.05 (s, 3H), 1.04 (s, 3H), 1.02 (s, 3H), 1.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.2, 139.7, 139.6, 127.2, 127.2, 127.1, 126.9, 78.5, 78.4, 52.2, 47.8, 47.8, 23.1, 22.8, 19.2, 19.1; HRMS m/z calcd for $C_{18}H_{26}O_6$ 338.17293, found 338.17906.

Methyl 3-Hydroxy-3-(2-chlorophenyl)-2,2-dimethylpropionate (Table 3, Entry 1). The general procedure was followed using 2-chlorobenzaldehyde (0.224 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.440 g (91%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46−7.44 (m, 1H), 7.27−7.14 (m, 3H), 5.45 (s, 1H), 3.66 (s, 3H), 3.54 (bs, 1H), 1.12 (s, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.3, 137.9, 133.5, 129.6, 129.3, 128.8, 126.5, 73.4, 52.3, 48.6, 23.1, 18.7; HRMS m/z calcd for $C_{12}H_{15}ClO_3$ 242.07097, found 242.07153.

Methyl 3-Hydroxy-3-(2-fluorophenyl)-2,2-dimethylpropionate (Table 3, Entry 2). The general procedure was followed using 2-fluorobenzaldehyde (0.210 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.350 g (77%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47−7.43 (m, 1H), 7.27−7.23 (m, 1H), 7.16−7.12 (m, 1H), 7.03−6.98 (m, 1H), 5.28 (d, 1H, J = 4.4 Hz), 3.73 (s, 3H), 3.37 (d, 1H, J = 5.7 Hz), 1.15 (s, 3H), 1.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.4, 160.1 (d, J = 260 Hz), 129.4, 129.3 (d, J = 4.2 Hz), 127.4 (d, J = 12.9 Hz), 124.0 (d, J = 3.3 Hz), 115.2 (d, J = 22.8 Hz), 71.7, 52.4, 48.2, 23.1, 18.8; HRMS m/z calcd for $C_{12}H_{15}FO_3$ 226.10052, found 226.10078.

Methyl 3-Hydroxy-3-(3-iodophenyl)-2,2-dimethylpropionate (Table 3, Entry 3). The general procedure was followed using 3-iodobenzaldehyde (0.464 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (88.8 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.637 g (95%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63−7.58 (m, 2H), 7.23 (d, 1H, J = 8.0 Hz), 7.02 (t, 1H, J = 8.0 Hz), 4.79 (d, 1H), 3.70 (s, 3H), 3.13 (bs, 1H), 1.10 (s, 3H), 1.08 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): 178.1, 142.4, 136.8, 136.6, 129.5, 127.0, 93.9, 76.8, 52.3, 47.7, 22.9, 19.2 ppm; HRMS m/z calcd for $C_{12}H_{15}IO_3$ 334.00659, found 334.00734.

Methyl 3-Hydroxy-2,2-dimethyl-3-(4-(trifluoromethyl)phenyl)-propanoate (Table 3, Entry 5). The general procedure was followed using 4-(trifluoromethyl)benzaldehyde (0.272 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.463 g (84%) of the desired product as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52 (d, 2H, J = 8.0 Hz), 7.36(d, 2H, J = 8.0 Hz), 4.87 (d, 2H, J = 2.8 Hz), 3.66 (s, 3H), 3.50 (d, 2H, J = 4.0 Hz),1.08 (s, 3H), 1.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.9, 144.1, 129.9 (q, J = 32.2 Hz), 128.0, 124.2 (q, J = 270.4 Hz), 124.6 (q, J = 3.7 Hz), 77.9, 52.2, 47.6, 22.7, 19.0; HRMS m/z calcd for $C_{13}H_{15}F_3O_3$ 276.09732, found 276.09812.

Methyl 3-Hydroxy-3-(3-cyanophenyl)-2,2-dimethylpropionate (Table 3, Entry 7). The general procedure was followed using 3-cyanobenzaldehyde (0.262 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 20% ethyl acetate/hexanes) to afford 0.271 g (58%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.58 (s, 1H), 7.55−7.50 (m, 2H), 7.40 (t, 1H, J = 7.6 Hz), 4.89 (d, 1H, J = 3.6 Hz), 3.69 (s, 3H), 3.53 (d, 1H, J = 3.6 Hz), 1.09 (s, 3H), 1.06 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): 177.9, 141.8, 132.4, 131.6, 131.5, 128.8, 119.0, 112.1, 77.7, 52.6, 47.9, 22.8, 19.3 ppm; HRMS m/z calcd for $C_{13}H_{15}NO_3$ 233.10519, found 233.10548.

Methyl 3-(Benzo[*b*]thiophene-2-yl)-3-hydroxy-2,2-dimethyl-propanoate (Table 4, Entry 1). The general procedure was followed using 2-benzothiophenecarboxaldehyde (0.324 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (88.8 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.488 g (92%) of the desired product as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, 1H, J = 7.6 Hz), 7.72 (d, 1H, J = 8.0 Hz), 7.36−7.29 (m, 2H), 7.18 (s, 1H), 5.15 (d, 1H, J = 4.0 Hz), 3.76 (s, 3H), 3.51 (d, 1H, J = 4.8 Hz), 1.28 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.1, 145.1, 139.7, 139.4, 124.5, 124.4, 123.7, 122.5, 122.4, 76.1, 52.6, 48.1, 23.0, 20.5; HRMS m/z calcd for $C_{14}H_{16}O_3S$: 264.08202, found 264.08256.

Methyl 3-(Benzofuran-2-yl)-3-hydroxy-2,2-dimethylpropanoate (Table 4, Entry 2). The general procedure was followed using 2-benzofurancarboxaldehyde (0.242 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.442 g (89%) of the desired product as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, 1H, J = 7.6 Hz), 7.44 (d, 1H, J = 8.4 Hz), 7.28−7.20 (m, 2H), 6.64 (s, 1H), 4.94 (s, 1H), 3.75 (s, 3H), 3.71 (bs, 1H), 1.28 (s, 3H), 1.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.8, 156.9, 154.8, 128.1, 124.4, 123.1, 121.2, 111.5, 105.0, 74.0, 52.5, 47.4, 23.1, 20.5; HRMS m/z calcd for $C_{14}H_{16}O_4$ 248.10486, found 248.10539.

Methyl 3-Hydroxynonanoate (Table 4, Entry 3). The general procedure was followed using heptaldehyde (0.280 mL, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.345 g (80%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.67 (s, 3H), 3.57 (d, 1H, J = 4.0 Hz), 1.26−1.14 (m, 16H), 0.87−0.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.3, 76.7, 51.9, 47.2, 31.8, 31.7, 29.3, 26.7, 22.7, 22.3, 20.4, 14.1; HRMS m/z calcd for $C_{12}H_{24}O_3$ 216.17254, found 216.17291.

Methyl 3-Hydroxy-2,2-dimethyl-3-(4-methylthiazol-2-yl)propanoate (Table 4, Entry 6). The general procedure was followed using 4-methyl-2-thiazolecarboxaldehyde (0.254 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (56.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.153 g (36%) of the desired product as a pale yellow solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81 (s, 1H), 5.08 (d, 1H, J = 4.0 Hz), 4.22 (d, 1H, J = 8.0 Hz), 3.71 (s, 3H), 2.38 (s, 3H), 1.21 (s, 3H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.5, 170.3, 152.1, 114.0, 76.4, 52.4, 48.1, 21.6, 20.9, 17.2; HRMS m/z calcd for $C_{10}H_{15}NO_3S$ 264.08202, found 264.08256.

Methyl 2,2-Dimethyl-3-(4-methylthiazol-2-yl)-3-(trimethylsilyloxy)propanoate (Table 4, Entry 6). The general procedure was followed using 4-methyl-2-thiazolecarboxaldehyde (0.254 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (88.8 mg, 10 mol %), and THF

(4.0 mL). No acid hydrolysis step was performed in this case. The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.318 g (53%) of the desired product as a colorless liquid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.75 (s, 1H), 5.24 (s, 1H), 3.66 (d, 3H, J = 2.0 Hz), 2.36 (s, 3H), 1.14 (s, 3H), 1.07 (s, 3H), 0.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.3, 172.5, 152.2, 113.4, 76.8, 51.9, 48.9, 20.7, 20.4, 17.2, 0.00; HRMS m/z calcd for $C_{13}H_{23}NO_3SSi$ 301.11678, found 301.11755.

Methyl 3-Hydroxy-2,2-dimethyl-3-(1-methyl-1*H*-imidazol-2-yl)propanoate (Table 4, Entry 7). The general procedure was followed using 1-methyl-2-imidazolecarboxaldehyde (0.220 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (28 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: methanol) to afford 0.221 g (52%) of the desired product as a colorless solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (d, 1H, J = 1.2 Hz), 6.72 (d, 1H, J = 0.8 Hz), 4.73 (s, 1H), 4.50 (bs, 1H), 3.66 (s, 3H), 3.65 (s, 3H), 1.23 (s, 3H), 1.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 177.9, 147.0, 127.2, 121.5, 71.7, 52.3, 47.5, 33.5, 23.1, 21.3; HRMS m/z calcd for $C_{10}H_{16}N_2O_3$ 212.11609, found 212.11649.

3-Hydroxy-1-phenyl-1-nonanone (Table 5, Entry 5). The general procedure was followed using heptaldehyde (0.280 mL, 2.0 mmol), 1-phenyl-1-trimethylsiloxyethylene (0.486 mL, 2.4 mmol), **1c** (28.0 mg, 3 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.374 g (80%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.97−7.94 (m, 2H), 7.60−7.44 (m, 3H), 4.21 (bs, 1H), 3.26−2.98 (m, 3H), 1.63−1.29 (m, 10H), 0.89−0.86 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 201.3, 131.9, 133.8, 128.9, 128.3, 68.0, 45.2, 36.7, 32.0, 29.5, 25.7, 22.8, 14.3; HRMS m/z calcd for $C_{10}H_{16}N_2O_3$ 212.11609, found 212.11649.

(*E*)-1-(2-Fluorophenyl)-4,4-dimethylpent-1-en-3-one (Table 6, Entry 1, 7b). The general procedure was followed using 2-fluorobenzaldehyde (0.248 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.380 g (92%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, 1H, J = 16 Hz), 7.54 (t, 1H, J = 8 Hz), 7.34−7.29 (m, 1H), 7.22 (d, 1H, J = 16.0 Hz), 7.13 (t, 1H, 8.0 Hz), 7.07 (t, 1H, J = 8.0 Hz), 1.21 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.3, 161.8 (d, J = 250 Hz), 135.8 (d, J = 2.0 Hz), 131.6 (d, J = 9 Hz), 129.9 (d, J = 3.0 Hz), 124.6 (d, J = 3.0 Hz), 123.5 (d, J = 7 Hz), 123.2 (d, J = 12.0 Hz), 116.4 (d, 22.0 Hz), 43.4, 26.4; HRMS m/z calcd for $C_{13}H_{15}FO$ 206.11069, found 206.11108.

(*E*)-1-(3-Iodophenyl)-4,4-dimethylpent-1-en-3-one (Table 7, Entry 1). The general procedure was followed using 3-iodobenzaldehyde (0.348 g, 1.5 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.432 mL, 2.0 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.443 g (95%) of the desired product as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (s, 1H), 7.65 (d, 1H, J = 8.0 Hz), 7.51 (d, 1H, J = 16.0 Hz), 7.47 (d, 1H, J = 8.0 Hz), 7.10−7.05 (m, 2H), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.0, 141.3, 139.0, 137.3, 136.8, 130.7, 128.0, 122.0, 95.0, 43.5, 26.5; HRMS m/z calcd for $C_{13}H_{15}OI$ 314.0176, found 314.0168.

(*E*)-3-(4,4-Dimethyl-3-oxopent-1-enyl)benzonitrile (Table 7, Entry 2). The general procedure was followed using 3-cyanobenzaldehyde (0.262 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.402 g (94%) of the desired product as a colorless oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (s, 1H), 7.74 (d, 1H, J = 8.0 Hz), 7.62−7.60 (m, 1H), 7.58 (d, 1H, J = 16.0 Hz), 7.48 (t, 1H, J = 8.0 Hz), 7.15 (d, 1H, J = 16.0 Hz), 1.21 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.8, 140.2, 136.3, 133.2, 132.6, 131.4, 129.9, 123.2, 118.4, 113.4, 43.6, 26.3; HRMS m/z calcd for $C_{14}H_{15}NO$ 213.11536, found 213.11582.

(*E*)-1-(Benzofuran-2-yl)-4,4-dimethylpent-1-en-3-one (Table 7, Entry 3). The general procedure was followed using 2-benzofurancarboxaldehyde (0.292 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.362 g (79%) of the desired product as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (d, 1H, J = 16.0 Hz), 7.53 (bs, 1H), 7.47 (d, 1H, J = 8.0 Hz), 7.31 (dt, 1H, J = 8.0 Hz, J = 1.2 Hz), 7.24 (d, 1H, J = 16.0 Hz), 7.20 (d, 1H, J = 8.0 Hz), 6.90 (s, 1H), 1.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.0, 155.6, 153.2, 129.5, 128.7, 126.6, 123.5, 121.9, 121.3, 112.0, 111.5, 43.5, 26.5; HRMS m/z calcd for $C_{15}H_{16}O_2$ 228.11503, found 228.11549.

(*E*)-1-(Benzo[*b*]thiophene-2-yl)-4,4-dimethylpent-1-en-3-one (Table 7, Entry 4). The general procedure was followed using 2-benzothiophenecarboxaldehyde (0.326 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.404 g (83%) of the desired product as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, 1H, J = 16.0 Hz), 7.79−7.74 (m, 2H), 7.49 (s, 1H), 7.39−7.33 (m, 2H), 6.95 (d, 1H, J = 16.0 Hz), 1.24 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.9, 140.4, 140.1, 139.8, 136.1, 129.5, 126.4, 125.0, 124.6, 122.6, 122.2, 43.4, 26.5; HRMS m/z calcd for $C_{15}H_{16}OS$ 244.09219, found 244.09266.

(*E*)-4,4-Dimethyl-1-(4-methylthiazol-2-yl)pent-1-en-3-one (Table 7, Entry 5). The general procedure was followed using 4-methyl-2-thiazolecarboxaldehyde (0.254 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (90.0 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.391 g (94%) of the desired product as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (d, 1H, J = 16.0 Hz), 7.35 (d, 1H, J = 16.0 Hz), 6.96 (s, 1H), 2.45 (s, 3H), 1.18 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 203.8, 163.2, 155.3, 133.8, 124.2, 116.7, 43.6, 26.3, 17.4; HRMS m/z calcd for $C_{11}H_{15}NOS$ 209.08743, found 209.08770.

(*E*)-1-(4-Methoxynaphthalen-1-yl)-4,4-dimethylpent-1-en-3-one (Table 7, Entry 6). The general procedure was followed using 4-methoxy-1-naphthaldehyde (0.372 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.421 g (78%) of the desired product as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.49 (d, 1H, J = 15.6 Hz), 8.31 (d, 1H, J = 8.0 Hz), 8.20 (d, 1H, J = 8.0 Hz), 7.79 (d, 1H, J = 8.0 Hz), 7.61−7.50 (m, 2H), 7.14 (d, 1H, J = 16.0 Hz), 6.83 (d, 1H, J = 8.0 Hz), 4.04 (s, 3H), 1.27 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.4, 157.6, 140.0, 133.0, 125.8, 124.9, 123.5, 122.8, 121.3, 103.8, 55.9, 43.4, 26.7; HRMS m/z calcd for $C_{18}H_{20}O_2$ 268.14632, found 268.14673.

(*E*)-4,4-Dimethyl-1-*o*-tolylpent-1-en-3-one (Table 7, Entry 7). The general procedure was followed using *o*-tolualdehyde (0.240 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (90.0 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.364 g (90%) of the desired product as a white solid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, 1H, J = 16.0 Hz), 7.60 (d, 1H, J = 8.0 Hz), 7.27−7.19 (m, 3H), 7.05 (d, 1H, J = 16.0 Hz), 2.44 (s, 3H), 1.24

(s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.5, 140.7, 138.4, 134.2, 131.1, 130.1, 126.5, 126.4, 122.1, 43.5, 26.6, 20.1; HRMS *m*/*z* calcd for $C_{14}H_{18}O$ 202.13576, found 202.13610.

(*E*)-1-(2,6-Dimethylphenyl)-4,4-dimethylpent-1-en-3-one (Table 7, Entry 8). The general procedure was followed using 2,6-dimethylbenzaldehyde (0.268 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (88.8 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.310 g (72%) of the desired product as a white solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, 1H, J = 16.0 Hz), 7.12−7.06 (m, 3H), 6.74 (dd, 1H, J = 16.0 Hz, J = 1.2 Hz), 2.34 (s, 6H), 1.21 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.4, 141.4, 136.9, 135.1, 128.4, 128.3, 127.1, 43.4, 26.3, 21.3; HRMS *m*/*z* calcd for $C_{15}H_{20}O$ 216.15141, found 216.15173.

(4*E*,6*E*)-2,2-Dimethyl-7-phenylhepta-4,6-dien-3-one (Table 7, Entry 9). The general procedure was followed using *trans*-cinnamaldehyde (0.264 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (90.0 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.412 g (96%) of the desired product as a yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.46 (m, 3H), 7.37−7.30 (m, 3H), 6.94−6.92 (m, 2H), 6.69 (d, 1H, J = 12.0 Hz), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 204.6, 143.1, 141.3, 136.4, 129.2, 129.0, 127.3, 127.1, 124.5, 43.3, 26.6; HRMS *m*/*z* calcd for $C_{15}H_{18}O$ 214.13576, found 214.13625.

Methyl 4,4,4-Trifluoro-2,2-dimethyl-3-phenyl-3-(trimethylsilyloxy)butanoate (Scheme 3, Product 8). The general procedure was followed using 2,2,2-trifluoroacetophenone (0.348 g, 2.0 mmol), (1-methoxy-2-methyl-1-propenyloxy)trimethylsilane (0.486 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by flash column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford 0.633 g (91%) of the desired product as yellow oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.48−7.45 (m, 2H), 7.35−7.33 (m, 3H), 3.60 (s, 3H), 1.22 (s, 3H), 1.19 (s, 3H), 0.14 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 174.8, 136.5, 128.5, 127.8, 127.3, 126.1 (q, J = 288 Hz) 84.6 (q, J = 26.9 Hz), 51.9, 50.9, 26.8, 22.7, 1.8; HRMS *m*/*z* calcd for $C_{16}H_{17}F_3O$ 348.13686, found 348.13754.

5-(2,2,2-Trifluoro-1-hydroxy-1-phenylethyl)furan-2(5*H*)-one (Scheme 3, Product 11). The general procedure was followed using 2,2,2-trifluoroacetophenone (0.348 g, 2.0 mmol), 2-(trimethylsiloxy)furan (0.403 mL, 2.4 mmol), **1c** (54.0 mg, 6 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford a combined isolated yield of 0.404 g (83%). *Syn* isomer (white solid): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61−7.60 (m, 2H), 7.49−7.45 (m, 3H), 6.84−6.82 (m, 1H), 6.18−6.16 (m, 1H), 5.71 (t, 1H, J = 4.0 Hz), 4.1 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.0, 152.5, 133.4, 129.8, 129.2, 125.6, 124.5 (q, J = 280 Hz), 124.0, 83.6, 76.6 (q, J = 29 Hz); HRMS *m*/*z* calcd for $C_{12}H_9F_3O_3$ 258.05038, found 258.05075. *Anti* isomer (yellow oil): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.56−7.54 (m, 3H), 7.42−7.39 (m, 3H), 6.04−6.02 (m, 1H), 5.58 (s, 1H), 3.66 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.2, 152.5, 133.3, 129.8, 128.9, 126.4, 124.5 (q, J = 280 Hz), 124.0, 83.2, 77.9 (q, J = 20 Hz); HRMS *m*/*z* calcd for $C_{12}H_9F_3O_3$ 258.05038, found 258.05076.

(Z)-6,6,6-Trifluoro-2,2-dimethyl-5-phenylhex-4-en-3-one (Scheme 3, Product 12). The general procedure was followed using 2,2,2-trifluoroacetophenone (0.348 g, 2.0 mmol), 3,3-dimethyl-2-trimethylsiloxy-1-butene (0.518 mL, 2.4 mmol), **1c** (88.0 mg, 10 mol %), and THF (4.0 mL). The reaction mixture was purified by column chromatography on silica gel (eluent: 10% ethyl acetate/hexanes) to afford a combined isolated yield of 0.404 g (79%): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39−7.37 (m, 3H), 7.27−7.26 (m, 2H), 7.08 (bs, 1H), 1.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 205.8, 139.1 (q, J = 30.0 Hz), 131.0, 129.3, 129.1, 129.0, 128.4, 122.9 (q, J = 278 Hz), 44.5, 26.2; ^{19}F NMR ($CDCl_3$, 376 MHz) δ 68.6; HRMS *m*/*z* calcd for $C_{14}H_{15}F_3O$ 256.10749, found 256.10802.

2,8,9-Trimethyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]-undecane 1-Oxide (Scheme 5, Compound 13). To a solution of **1c** (0.133 g, 0.30 mmol) in 4.0 mL of toluene was added excess $Me_3SiOOSiMe_3$ (0.320 g, 1.80 mmol). The resulting clear solution was stirred at 40−50 °C. After 38 h, all the volatiles were removed under vacuum giving an off-white residue which upon recrystallization from anhydrous pentane yielded **13** as a colorless solid (0.130 g, 94%): ^{31}P NMR ($CDCl_3$, 162 MHz) 24.24; ^{1}H NMR ($CDCl_3$, 400 MHz) 7.61−7.59 (m, 6H), 7.37−7.26 (m, 9H), 4.25 (d, 6H, J = 8.0 Hz), 2.88−2.79 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) 139.9 (d, J = 2.3 Hz), 128.9, 128.5, 127.4, 50.9 (d, J = 5.0 Hz), 50.0, 47.4 (d, J = 3.3 Hz); HRMS *m*/*z* calcd for $C_{27}H_{33}N_4OP$ 460.23919, found 460.24045.

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Supporting Information Available: References to the known compounds, copies of ^{1}H and ^{13}C NMR spectra for all aldol products, catalyst **1c** synthesized, and HRMS reports for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.