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Unusual Carbonyl Differentiation in the Lewis Acid-Catalyzed Allylation of Aldehydes with Tetraallyltin. Applications to Parallel Recognition and Shotgun Process

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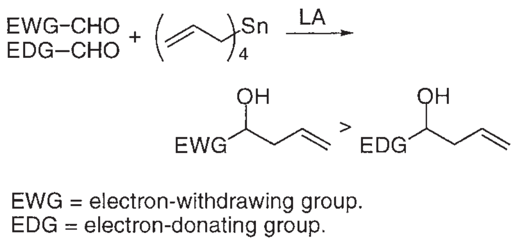
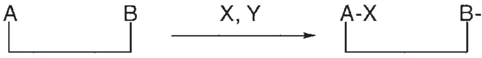
In contrast to conventional substrate selectivity in Lewis-acid promoted nucleophilic reactions wherein less electrophilic aldehydes react preferentially over the more electrophilic counterparts, addition of tetraallyltin to aldehydes occurs in a reversed sense. The substrate selectivity in Lewis acid-promoted nucleophilic addition is generally dependent on the combinations of substrates, nucleophiles, catalysts, etc. Such diversity leads to two one-pot protocols, parallel recognition and shotgun process wherein different chemical transformations take place directly on the separate reaction sites without recourse to protection–deprotection procedures. These two protocols are tunable by controlling the electronic properties of the substrates.

The differentiation between carbonyl groups is of great importance in modern synthetic chemistry.[1] It is particularly difficult to differentiate between aldehydes due to their high reactivity. Lewis acid-promoted nucleophilic addition has served considerably to this end, and it is generally accepted that less electrophilic substrates react preferentially over the more electrophilic counterparts because of the stronger coordination with a Lewis acid and, hence, more effective activation of the former.[2] Nakai et al. and we independently discovered that aldol reactions of ketene silyl acetals with various carbonyls under catalysis of europium complexes[3] or organotin Lewis acids[4] exhibited such a preference explicitly. More recently, Yamamato et al. reported that the similar tendency can be expanded in a somewhat more general manner to other Lewis acid-promoted reactions like allylation with allyltributyltin, Diels–Alder reaction between α-enones and cyclopentadiene, and reduction with tributyltin hydride.[5] In this paper, we disclose that such a general trend is not always the case and can be reversed under certain conditions. As far as we know, the only precedent example exhibiting the reversed selectivity was put forth by Mori et al. that competition between cyclohexanecarbaldehyde and benzaldehyde in a Me_2AlCl-catalyzed reaction with TMSCN (trimethylsilyl cyanide) resulted in the exclusive formation of cyanohydrin trimethylsilyl ether of the former aldehyde.[6] We have now found that the use of tetraallyltin leads to a preferential consumption of more electrophilic aldehyde irrespective of the catalysts (Scheme 1).



Scheme 1.



Scheme 2.

Recently, we advanced new concepts for one-pot process, “parallel recognition”[7] and “shotgun process”.[8] Both protocols enable to conduct different transformations directly on the separate functions without recourse to protection–deprotection manipulations giving rise to a single product (Scheme 2). In the parallel recognition, both reactions proceed simultaneously with exclusive formation of A–X and B–Y owing to a kinetic effect even if exposure of a substrate bearing A and B functions to the reagent X or Y results in the formation of a mixture, A–X/B–X or A–Y/B–Y. The shotgun process is feasible when A rapidly reacts with X in an exclusive manner. Upon quick consumption of the reagent X before the reaction of B starts, this function has no choice but to react with the remaining Y. As a result, the exclusive reaction of B with Y is realized even if the reaction of B with a mixture of X and Y is innately non-selective. We exemplify herein that the reversal of the substrate selectivity, as mentioned above, can be utilized in these new one-pot protocols. More significantly, the parallel recognition and shotgun processes are tunable depending on the reactivity of the substrates.[9]

Results and Discussion

Competition towards Aldehydes. According to the conventional selectivity, aromatic aldehydes are more reactive than more electrophilic aliphatic ones in the Lewis acid-promoted nucleophilic addition reactions, and few reactions are available by which aliphatic aldehydes undergo nucleophilic addition at the synthetically employable level. The present study has its foundation on a finding of facile allylation of nonanal with tetraallytin (**1**) under catalysis of various Lewis acids like TMSOTf, Me_2AlCl, $(C_6F_5)_2SnBr_2$, and $Et_2O \cdot BF_3$ (Table 1).[10]

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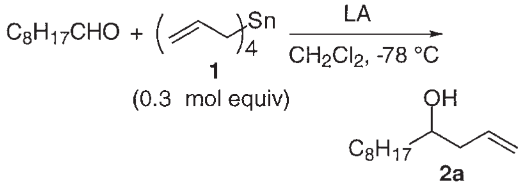
Table 1. Allylation of Nonanal with Tetraallyltin by Various Lewis Acids

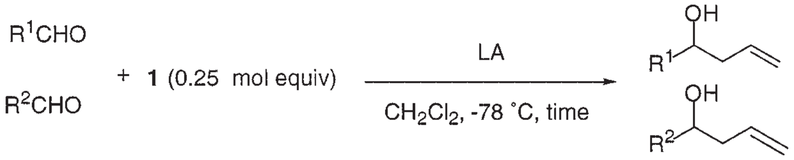


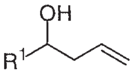
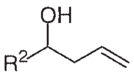
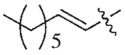
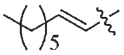
Entry	LA	Time/h	Yield/%[a)
1	TMSOTf (10 mol%)	6	91
2	Me_2AlCl (100 mol%)	2	91
3	$(C_6F_5)_2SnBr_2$ (10 mol%)	6	77
4	$Et_2O\cdot BF_3$ (100 mol%)	5	93

a) Determined by GLC.

These results imply that even highly electrophilic aldehydes are capable of undergoing allylation. Then, we conducted competitive reactions with different aldehydes. As shown in Table 2, nonanal or 4-nitrobenzaldehyde, upon treatment with a theoretical amount (0.25 mol equiv) of **1**, underwent allylation predominantly over less electrophilic benzaldehyde or 4-methoxybenzaldehyde under the catalysis of various Lewis acids (entries 1–9). On the other hand, benzaldehyde was the winner against further less electrophilic 4-methoxybenzaldehyde and 2-nonenal (entries 10 and 11) in the presence of trimethylsilyl triflate (TMSOTf) catalyst.[11] Quite naturally, the analogous preference for the more electrophilic aldehydes was attained in 4-nitrobenzaldehyde/4-methoxybenzaldehyde and nonanal/2-nonenal arrays (entries 12 and 13). The crucial role of the Lewis acids in the above reactions is evident from the fact that no reaction took place in the absence of the Lewis acid un-

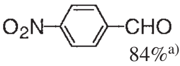
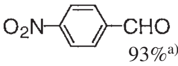
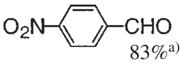
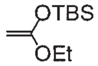
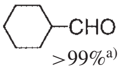
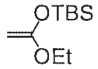
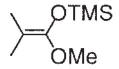
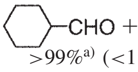
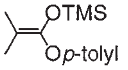
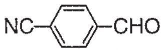
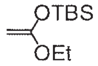
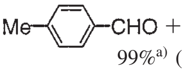
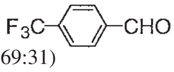
Table 2. Allylation between Two Different Aldehydes with Various Lewis Acids



Entry	R^1	R^2	LA	Time/h	Yield/%[a)		
						(Ratio)	
1	C_8H_{17}	Ph	TMSOTf (10 mol%)	12	**2a** 71	(78:22)	**2b** 20
2			$Sc(OTf)_3$ (10 mol%)	5	**2a** 58	(71:29)	**2b** 24
3			$Et_2O\cdot BF_3$ (100 mol%)	5	**2a** 88	(91:9)	**2b** 9
4			Me_2AlCl (200 mol%)	2	**2a** 78	(82:18)	**2b** 17
5	$4\text{-}O_2NC_6H_4$	Ph	TMSOTf (10 mol%)	12	**2c** 75	(82:18)	**2b** 16
6			$Sc(OTf)_3$ (10 mol%)	6	**2c** 68	(85:15)	**2b** 12
7			$Et_2O\cdot BF_3$ (100 mol%)	2	**2c** 63	(66:34)	**2b** 32
8			Me_2AlCl (200 mol%)	2	**2c** 87	(98:2)	**2b** 2
9	C_8H_{17}	$4\text{-}MeOC_6H_4$	TMSOTf (10 mol%)	12	**2a** 82	(99:1)	**2d** 1
10	Ph	$4\text{-}MeOC_6H_4$	TMSOTf (10 mol%)	12	**2b** 84	(87:13)	**2d** 13
11	Ph		TMSOTf (10 mol%)	12	**2b** 77	(82:18)	**2e** 17
12	$4\text{-}O_2NC_6H_4$	$4\text{-}MeOC_6H_4$	TMSOTf (10 mol%)	12	**2c** 91	(96:4)	**2d** 4
13	C_8H_{17}		TMSOTf (10 mol%)	12	**2a** 86	(93:7)	**2e** 6

a) Determined by GLC.

Table 3. Summary of Nucleophilic Reaction between Two Different Aldehydes with Lewis Acid

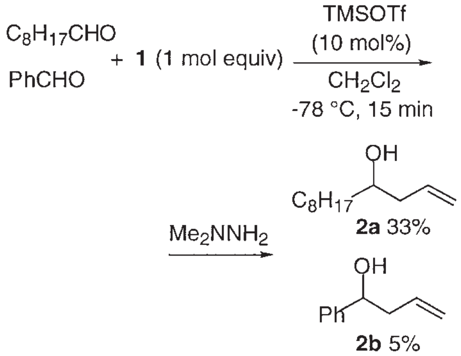
Reversed selectivity			Conventional selectivity		
Entry	Aldehyde	Reagent/Catalyst	Entry	Aldehyde	Reagent/Catalyst
R-1	$C_8H_{17}CHO + PhCHO$ 86%[a] (84:16)	TMSCN Me_2AlCl	C-1	$C_8H_{17}CHO + PhCHO$ 73%[a] (32:68)	TMSCN TMSOTf
R-2	$C_8H_{17}CHO + PhCHO$ 94%[a] (69:31)	 Me_2AlCl	C-2	 + PhCHO 84%[a] (45:55)	TMSCN Me_2AlCl
R-3	$C_8H_{17}CHO + PhCHO$ 88%[a] (63:37)	 $Et_2O{\cdot}BF_3$	C-3	 + PhCHO 93%[a] (29:71)	 $Et_2O{\cdot}BF_3$
R-4	 + PhCHO 83%[a] (73:27)	 Me_2AlCl	C-4[b]	$C_7H_{15}CHO + PhCHO$ 91%[a] (3:97)	 $(C_6F_5)_2SnBr_2$
R-5[c]	 + PhCHO >99%[a] (>99:<1)	TMSCN Me_2AlCl	C-5[d]	tBuCHO + PhCHO 57%[a] (<1:>99)	 $Eu(dppm)_3$
			C-6	$C_8H_{17}CHO + PhCHO$ 74%[a] (26:74)	 TMSOTf
			C-7[c]	 + PhCHO >99%[a] (<1:>99)	 Me_2AlCl
			C-8[e]	 + PhCHO 54%[a] (0:100)	 $Bu_2Sn(OTf)_2$
			C-9[f]	 +  99%[a] (69:31)	Bu_3SnH $Et_2O{\cdot}BF_3$

a) Total yield. b) Ref. 4c. c) Ref. 6. d) Ref. 3a. e) Ref. 4a. f) Ref. 5.

der otherwise same conditions.

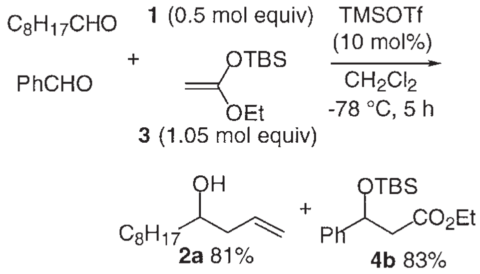
With the above results in hand, we examined other nucleophilic reactions in search of further possibilities of the selectivity reversal. It, then, has turned out that the selectivity is reversed in some limited cases. Table 3 summarizes the results obtained in this study together with reported ones. TMSCN in the presence of Me_2AlCl led to the reversal for a nonanal/benzaldehyde combination (entry R-1), yet the use of TMSOTf led to the conventional outcome (C-1). Moreover, the same sort of selectivity was also attained in the competition between benzaldehyde and 4-nitrobenzaldehyde towards TMSCN even by use of Me_2AlCl (entry C-2). Allyltributyltin is another nucleophile that gives rise to the reversal under certain conditions (entries R-2–4), while the selectivity was turned over in the presence of $Et_2O{\cdot}BF_3$ (entry C-3). No reversal of the conventional selectivity was observed with ketene silyl acetals[3,4,6] and Bu_3SnH[5] under any conditions (entries C-4–9). It is apparent from these results that less electrophilic aldehydes are not always more reactive in the acid-promoted nucleophilic reaction. The selectivity is dependent on the combinations of aldehydes, nucleophiles, and catalysts. Remarkably, however, tetraallyltin constantly exhibits the reversed preference regardless of the aldehyde arrays and catalysts.

In the reaction of tetraallyltin, the species that are involved in the allylation vary from initial $(CH_2{=}CHCH_2)_4Sn$ to transient $(CH_2{=}CHCH_2)_nSn[OCH(R)CH_2CH{=}CH_2]_{4-n}$ as the reaction proceeds, and the original tetraallyltin may not be responsible for the differentiation. In order to check this possibility, the reaction of a mixture of nonanal and benzaldehyde with an excess amount of tetraallyltin (1.0 mol equiv) was quenched with *N*,*N*-dimethylhydrazine[7d] after 15 min (Eq. 1). The high degree of preference for nonanal was observed, and, hence, the high selectivity of all relevant allyltin species was confirmed.



(1)

Parallel Recognition. The reversal of selectivity was successfully utilized for parallel recognition under the catalysis of TMSOTf (trimethylsilyl triflate). As described above, ketene silyl acetals always exhibited the normal substrate selectivity, and thus the allylation was combined with the Mukaiyama-aldol reaction of ketene silyl acetal **3** (Eq. 2).[12] Two species, a homoallyl alcohol derived from nonanal (81% yield) and an aldol adduct derived from benzaldehyde (83% yield), resulted as the sole products, while no crossover products were detected. Furthermore, a great synthetic advantage arose in this protocol that the selectivity of the respective reactions can be improved through the kinetic effect. As a matter of fact, the present TMSOTf-catalyzed competition allylation afforded a 71% yield of the homoallyl alcohol from nonanal and a 20% yield from benzaldehyde (Table 2, entry 1). Under similar conditions, the ketene silyl acetal exhibited the opposite selectivity: a 3% yield for the nonanal aldol product and an 84% yield for the benzaldehyde counterpart (Eq. 3). Integration of these two reactions in one pot gave rise to the increase in the yield of the homoallyl alcohol to the 81% from a 71% yield in the simple competition reaction. Obviously, the allylation reagents were consumed by nonanal more efficiently because of the concurrent consumption of benzaldehyde by the ketene silyl acetal.[13] That the parallel reaction actually occurred was confirmed by quenching the reaction at an early stage. The product analysis after 15 min revealed that both allylation and aldol reaction proceeded simultaneously (Eq. 4).



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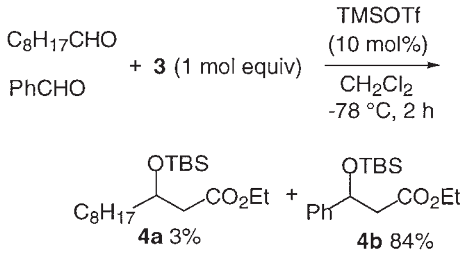

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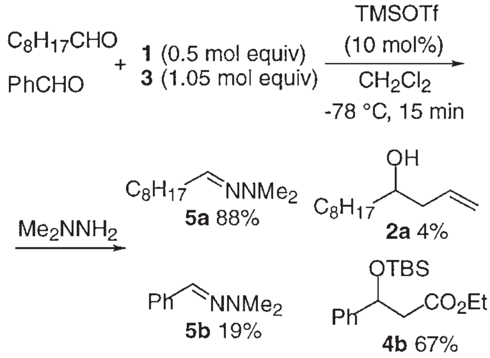
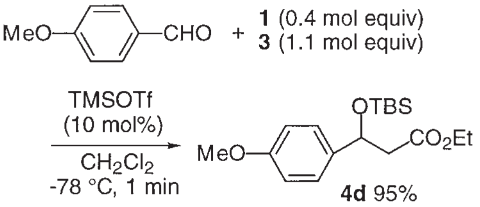


(4)

Shotgun Process. In the competition reaction towards **1**, 4-methoxybenzaldehyde exhibited much lower reactivity than benzaldehyde (compare entries 1 and 9 in Table 2). In contrast, 4-methoxybenzaldehyde towards ketene silyl acetal is expected to be more reactive than benzaldehyde on the basis of the conventional substrate selectivity. In fact, the competition reaction of the former substrate with a mixture of ketene silyl acetal and tetraallyltin led to exclusive formation of an aldol product (Eq. 5). Thus, the shotgun process composed of the allylation and Mukaiyama-aldol reactions with an equimolar mixture of nonanal and 4-methoxybenzaldehyde substrates was addressed (Eq. 6). By virtue of optimizing the amounts of **1** and **3**, the desired homoallyl alcohol and aldol adduct were exclusively accessible in high yields without formation of crossover coupling products in the presence of the TMSOTf catalyst. When the reaction had been quenched by Me_2NNH_2[7d] after 1 min even by use of only 1 mol% of TMSOTf, the aldolate was already formed quantitatively, whereas nonanal remained intact (Eq. 7), delivering an explicit evidence that the shotgun process indeed occurred. Exposure of **3** to an equimolar mixture of the two substrates provided the aldol adduct of 4-methoxybenzaldehyde quantitatively, while no aldol reaction took place with nonanal which instead underwent trimerization to a considerable extent (Eq. 8). These events consistently confirm that the instant disappearance of the aromatic aldehyde substrate by rapid and selective Mukaiyama-aldol reaction plays a key role to accomplish the shotgun process.



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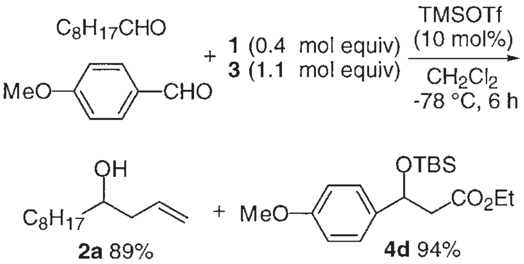

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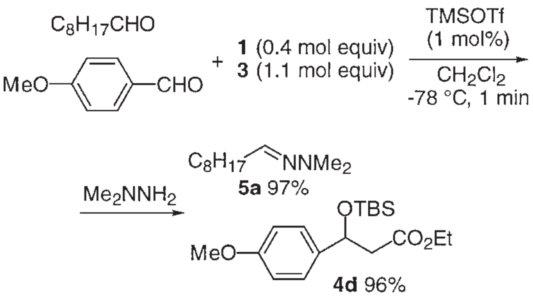

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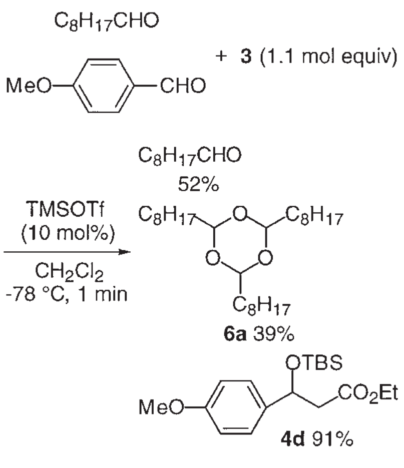
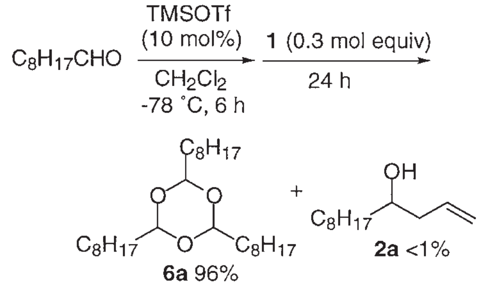


(8)

Another advantage induced by integration of reactions is apparent from Eq. 8, in which a trioxane was formed. In sharp contrast to smooth reaction of TMSOTf-promoted allylation of nonanal in the presence of **1**, the trioxane was formed quantitatively in the absence of **1**, and addition of this reagent to this mixture after 6 h furnished no homoallyl alcohol as shown in Eq. 9. It follows, therefore, that **1** serves to suppress the formation of the trioxane. Consequently, a stepwise process consisting of initial addition of **3** followed by **1** resulted in contamination of trioxane in the product mixture (Eq. 10). Of course, the reversed order of addition caused undesired allylation of 4-methoxybenzaldehyde as is evident from entry 9 in Table 2. As a whole, it is apparent that addition of the necessary reagents in one shot is much superior to the stepwise process, giving rise to not only the simplification of the experimental procedure but also the improved recognition. It should be noted that the shotgun processes on the basis of differentiation between aliphatic and aromatic aldehydes were successfully invoked already for the first synthesis of ferluic acid 3-oxohexyl ether.[9]



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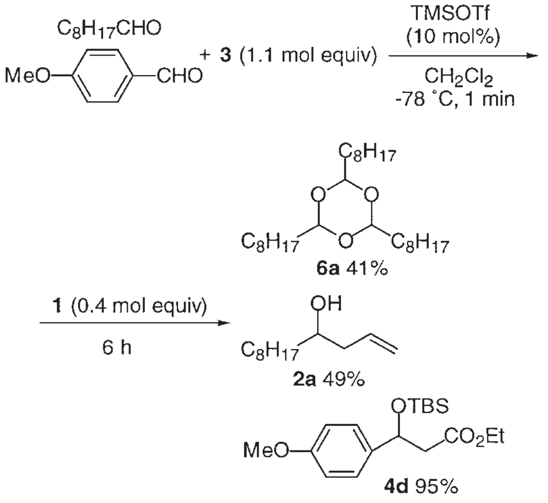

(10)

Experimental

General Information. All reactions were carried out under an atmosphere of argon with freshly distilled solvents, unless otherwise noted. CH_2Cl_2 was distilled from CaH_2. Silica gel (Daiso gel IR-60) was used for column chromatography. NMR spectra were recorded at 20 °C on JEOL Lambda 300 and 500 instruments and calibrated with tetramethylsilane (TMS) as an internal reference. The following abbreviations are used to indicate multiplicities: s singlet; d doublet; t triplet; q quartet; m multiplet. Mass spectra were recorded on a JEOL MStation JMS-700 spectrometer. Tetraallyltin **1** was commercially available. The following homoallyl alcohols were reported: **2a**,[14] **2b**,[15] **2c**,[15] and **2d**.[16] Aldol products, **4b**[17] and **4d**,[17] hydrazone, **5a**[18] and **5b**,[19] and trioxane **6a**[20] were reported.

Spectral Data for New Compounds. **2e**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, $J = 6.7$ Hz, 3H), 1.26–1.39 (m, 8H), 1.74 (br, 1H), 2.03 (q, $J = 6.7$ Hz, 2H), 2.22–2.37 (m, 2H), 4.12 (q, $J = 6.4$ Hz, 1H), 5.10–5.17 (m, 2H), 5.43–5.52 (m, 1H), 5.62–5.88 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0, 22.6, 28.8, 29.1, 31.7, 32.1, 42.0, 71.8, 117.9, 131.9, 132.3, 134.4; HRMS (EI) found m/z 182.1670 $[M]^+$, $C_{12}H_{22}O$ requires 182.1671.

4a: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.86–0.90 (m, 12H), 1.24–1.28 (m, 15H), 1.44–1.49 (m, 2H), 2.41 (d, $J = 0.9$ Hz, 1H), 2.43 (d, $J = 1.8$ Hz, 1H), 4.08–4.16 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ −4.8, −4.5, 14.1, 14.2, 18.0, 22.6, 24.9, 25.8, 29.2, 29.5, 29.6, 31.8, 37.6, 42.7, 60.2, 69.5, 171.9; HRMS (FAB) found m/z 345.2818 $[M + H]^+$, $C_{19}H_{41}O_3Si$ requires 345.2825.

Allylation of Nonanal (Table 1, Entry 1 as Representative Procedure). To a solution of nonanal (142 mg, 1.00 mmol) and **1** (0.07 mL, 0.30 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 6 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (91% yield).

Competition of Aldehydes (Table 2, Entry 1 as Representative Procedure). To a solution of nonanal (142 mg, 1.00 mmol), benzaldehyde (106 mg, 1.00 mmol), and **1** (60 µL, 0.25 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 12 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (71% yield) and **2b** (20% yield).

Competitive Allylation Quenched with Me_2NNH_2 after 15 min (Eq. 1). To a solution of nonanal (142 mg, 1.00 mmol), benzaldehyde (106 mg, 1.00 mmol), and **1** (0.24 mL, 1.00 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 15 min, Me_2NNH_2 (0.38 mL, 5.00 mmol) was added. The mixture was stirred for 1 h at room temperature, and then $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. GC and ^{1}H NMR analyses of the crude mixture showed the formation of **2a** (33% yield) and **2b** (5% yield), respectively.

Parallel Recognition (Eq. 2). To a solution of nonanal (142 mg, 1.00 mmol), benzaldehyde (106 mg, 1.00 mmol), **1** (0.12 mL, 0.50 mmol), and **3** (212 mg, 1.05 mmol) in CH_2Cl_2 (7 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C, and the mixture was stirred for 5 h at this temperature. After the workup described above, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (81% yield) and **4b** (83% yield), respectively.

Competitive Reaction of Ketene Silyl Acetal (Eq. 3). To a solution of nonanal (142 mg, 1.00 mmol), benzaldehyde (106 mg, 1.00 mmol), and **3** (202 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 2 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **4a** (3% yield) and **4b** (84% yield).

Parallel Recognition Quenched with Me_2NNH_2 after 15 min (Eq. 4). To a solution of nonanal (142 mg, 1.00 mmol), benzaldehyde (106 mg, 1.00 mmol), **1** (0.12 mL, 0.50 mmol), and **3** (212 mg, 1.05 mmol) in CH_2Cl_2 (7 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 15 min, Me_2NNH_2 (0.38 mL, 5.00 mmol) was added. After the mixture had been stirred for 1 h at room temperature, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC and ^{1}H NMR analyses of the crude mixture showed the formation of **5a** (88% yield), **2a** (4% yield), **5b** (19% yield), and **4b** (67% yield).

Competition Reaction between Tetraallyltin and Ketene Silyl Acetal towards 4-Methoxybenzaldehyde (Eq. 5). To a solution of 4-methoxybenzaldehyde (136 mg, 1.00 mmol), **1** (0.10 mL, 0.40 mmol), and **3** (223 mg, 1.10 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 1 min, $NaHCO_3$ aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **4d** (95% yield).

Shotgun Process (Eq. 6). To a solution of nonanal (142 mg, 1.00 mmol), 4-methoxybenzaldehyde (136 mg, 1.00 mmol), **1** (0.10 mL, 0.40 mmol), and **3** (223 mg, 1.10 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 6 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (89% yield) and **4d** (94% yield).

Shotgun Process Quenched with Me_2NNH_2 after 1 min (Eq. 7). To a solution of nonanal (142 mg, 1.00 mmol), 4-methoxybenzaldehyde (136 mg, 1.00 mmol), **1** (0.10 mL, 0.40 mmol), and **3** (223 mg, 1.10 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.1 M, 0.10 mL, 0.01 mmol) at −78 °C. After the mixture had been stirred for 1 min, Me_2NNH_2 (0.38 mL, 5.00 mmol) was added. After the mixture had been stirred for 1 h at room temperature, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC and ^{1}H NMR analyses of the crude mixture showed the formation of **5a** (97% yield) and **4d** (96% yield).

Treatment of Ketene Silyl Acetal with Nonanal and 4-Methoxybenzaldehyde (Eq. 8). To a solution of nonanal (142 mg, 1.00 mmol), 4-methoxybenzaldehyde (136 mg, 1.00 mmol), and **3** (223 mg, 1.10 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 1 min, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC and ^{1}H NMR analyses of the crude mixture showed nonanal (52% recovery), **6a** (39% yield) and **4d** (91% yield).

Addition of Tetraallyltin after Mixing of Nonanal and TMSOTf (Eq. 9). To a solution of nonanal (142 mg, 1.00 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 6 h, **1** (0.07 mL, 0.30 mmol) was added. After the mixture had been stirred for 24 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (<1% yield). Then, the crude mixture was subjected to column chromatography on silica gel to afford **6a** (19:1 hexane/Et_2O, 136 mg, 96% yield).

Sequential Treatment of Ketene Silyl Acetal and Tetraallyltin (Eq. 10). To a solution of nonanal (142 mg, 1.00 mmol), 4-methoxybenzaldehyde (136 mg, 1.00 mmol), and **3** (223 mg, 1.10 mmol) in CH_2Cl_2 (5 mL) was added a CH_2Cl_2 solution of TMSOTf (0.5 M, 0.20 mL, 0.10 mmol) at −78 °C. After the mixture had been stirred for 1 min, **1** (0.10 mL, 0.40 mmol) was added. After the mixture had been stirred for 6 h, $NaHCO_3$aq (10 mL) was added. After usual workup (AcOEt/water), the organic layer was washed with 1 M HClaq, $NaHCO_3$aq, and brine. After drying over $MgSO_4$ and filtration, the organic layer was concentrated under reduced pressure. GC analysis of the crude mixture showed the formation of **2a** (49% yield) and **4d** (95% yield). Then, the crude mixture was subjected to column chromatography on silica gel to afford **6a** (19:1 hexane/Et_2O, 58 mg, 41% yield).

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