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Parallel Recognition by Virtue of Differentiation between Carbonyls, Acetals and Enones

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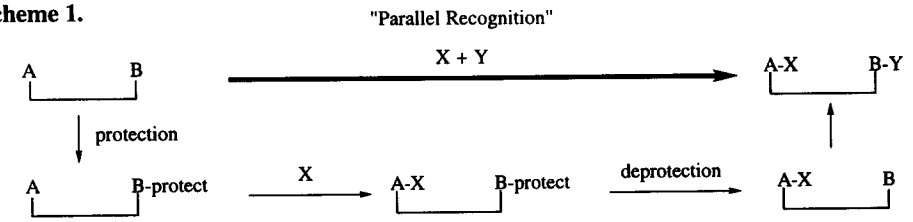
Abstract: "Parallel recognition", a new concept for compacting synthetic processes in which different transformations are performed simultaneously on separate reaction sites, has been advanced. Ketones/α,β-enones and aldehydes/acetals are able to react selectively with different silyl nucleophiles in parallel. The subtle differentiation between the substrates possessing similar reactivities has recourse to the strong preference of ketene silyl acetal for ketones/α,β-enones. © 1998 Elsevier Science Ltd. All rights reserved.

INTRODUCTION

"Parallel recognition" is a novel, versatile concept for compaction of multi-step synthetic processes. As shown in Scheme 1, when manifold transformations are required on separate reaction sites in a substrates, the protection-deprotection process is usually invoked. Namely, the initial protection of B is followed by conversion of A to A-X and, then, B-Y is generated after deprotection of B. "Parallel recognition" stemmed from the idea that if these transformations could be exercised simultaneously, a highly expeditious and convenient process is achieved to arrive at the final goal in one-pot and one-step. The protection-deprotection

Scheme 1.



steps are no more necessary and the reaction time is saved as the manifold transformations proceed in parallel. For this concept to be realized (eq. 1), unique chemoselectivities needs to be explored. A should react with X in preference to Y (eq. 2) while B should react with Y in preference to X (eq. 3) under the same reaction conditions. It is not easy to satisfy these demands because the simultaneous reaction in the same pot requires A and B to be similar in reactivities. We have already communicated the realization of such processes with recourse to the unique reactivities of ketene silyl acetals in $(C_6F_5)_2SnBr_2$-catalyzed Mukaiyama-aldol reaction.[1] In this paper, we describe a full account of this type of recognition.

$$A + B + X + Y \longrightarrow A\text{-}X + B\text{-}Y \quad (1)$$

$$A + X + Y \longrightarrow A\text{-}X \left(+ A\text{-}Y\right) \quad (2)$$

$$B + X + Y \longrightarrow B\text{-}Y \left(+ B\text{-}X\right) \quad (3)$$

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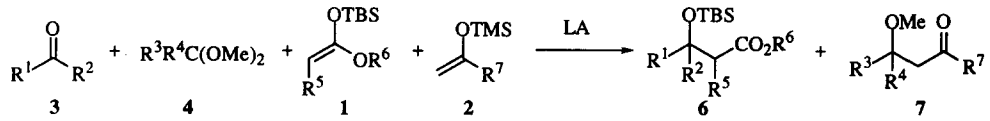
RESULTS AND DISCUSSION

Table 1 summarizes the results of "parallel recognition" between ketone **3** and acetal **4** with enol silyl ethers **1** and **2** derived from esters and ketones, respectively.[2] Besides $(C_6F_5)SnBr_3$[3] (entry 1), various Lewis acids were screened for reaction of acetophenone (**3a**) and benzaldehyde dimethylacetal (**4a**) with **1a** and **2a**. TMSOTf worked effectively as well (entry 2) while the reactions with $TiCl_4$, $SnCl_4$, and BF_3OEt_2 were not so straightforward due to the contamination by the cross aldol product derived from **1a** and **4a** (entries 3-5). $Sc(OTf)_3$ afforded an excellent yield of **6** but a poor yield of **7** (entry 6). When acetals of aliphatic aldehyde **4b** and ketone **4c** constituted the substrate array, $(C_6F_5)_2SnBr_2$ failed to afford **7ab** and **7ac** in good yields (entries 7 and 8) whereas a satisfactory outcome was obtained with TMSOTf (entry 9). Other various combinations of aromatic/aliphatic ketones and acetals gave rise to the exclusive recognition (entries 10-14). Replacement of **2a** by **2b** gave the similar results (entries 15-29). With this enol silyl ether, even **4b** and **4c** afforded satisfactory yields of **7bb** and **7bc**. When monomethyl-substituted ketene silyl acetal **1b** was subjected to the reaction, **2a** afforded a poor yield of acetal aldolate **7aa** (entry 30) while a satisfactory yield was obtained with **2b** (entry 31).

Table 1. Parallel Recognition between Ketone and Acetal with Ketene Silyl Acetal and Enol Sily Ether.[a]



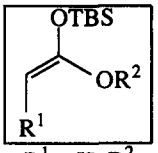
3 4 1 2 6 7

Entry	1	2	3	4	LA	Yield(%)[b] 6	7
1	**1a**	**2a**	**3a**	**4a**	$(C_6F_5)_2SnBr_2$	**6aa** 89	**7aa** 73
2	**1a**	**2a**	**3a**	**4a**	TMSOTf	**6aa** 96	**7aa** 77
3	**1a**	**2a**	**3a**	**4a**	$TiCl_4$[c]	**6aa** 55[d]	**7aa** 30[e]
4	**1a**	**2a**	**3a**	**4a**	$SnCl_4$[c]	**6aa** 62	**7aa** 72[f]
5	**1a**	**2a**	**3a**	**4a**	BF_3OEt_2[c]	**6aa** 90[g]	**7aa** 67[h]
6	**1a**	**2a**	**3a**	**4a**	$Sc(OTf)_3$	**6aa** 98	**7aa** 3
7	**1a**	**2a**	**3a**	**4b**	$(C_6F_5)_2SnBr_2$	**6aa** 85	**7ab** 24
8	**1a**	**2a**	**3a**	**4c**	$(C_6F_5)_2SnBr_2$	**6aa** 85	**7ac** 21
9	**1a**	**2a**	**3a**	**4c**	TMSOTf	**6aa** 98	**7ac** 95
10	**1a**	**2a**	**3b**	**4a**	$(C_6F_5)_2SnBr_2$	**6ab** 79	**7aa** 63
11	**1a**	**2a**	**3d**	**4a**	$(C_6F_5)_2SnBr_2$	**6ad** 75	**7aa** 77
12	**1a**	**2a**	**3e**	**4a**	$(C_6F_5)_2SnBr_2$	**6ae** 74	**7aa** 85
13	**1a**	**2a**	**3e**	**4b**	$(C_6F_5)_2SnBr_2$	**6ae** 84	**7ab** 24
14	**1a**	**2a**	**3f**	**4a**	$(C_6F_5)_2SnBr_2$	**6af** 74	**7aa** 80
15	**1a**	**2b**	**3a**	**4a**	$(C_6F_5)_2SnBr_2$	**6aa** 83	**7ba** 62
16	**1a**	**2b**	**3a**	**4b**	$(C_6F_5)_2SnBr_2$	**6aa** 83	**7bb** 83
17	**1a**	**2b**	**3a**	**4c**	$(C_6F_5)_2SnBr_2$	**6aa** 84	**7bc** 83
18	**1a**	**2b**	**3b**	**4a**	$(C_6F_5)_2SnBr_2$	**6ab** 80	**7ba** 64
19	**1a**	**2b**	**3b**	**4b**	$(C_6F_5)_2SnBr_2$	**6ab** 83	**7bb** 65
20	**1a**	**2b**	**3b**	**4c**	$(C_6F_5)_2SnBr_2$	**6ab** 76	**7bc** 75
21	**1a**	**2b**	**3d**	**4a**	$(C_6F_5)_2SnBr_2$	**6ad** 78	**7ba** 57
22	**1a**	**2b**	**3d**	**4b**	$(C_6F_5)_2SnBr_2$	**6ad** 81	**7bb** 78
23	**1a**	**2b**	**3d**	**4c**	$(C_6F_5)_2SnBr_2$	**6ad** 86	**7bc** 82

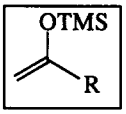
(Table 1 continued)

24	**1a**	**2b**	**3e**	**4a**	$(C_6F_5)_2SnBr_2$	**6ae** 81	**7ba** 60
25	**1a**	**2b**	**3e**	**4b**	$(C_6F_5)_2SnBr_2$	**6ae** 82	**7bb** 80
26	**1a**	**2b**	**3e**	**4c**	$(C_6F_5)_2SnBr_2$	**6ae** 83	**7bc** 83
27	**1a**	**2b**	**3f**	**4a**	$(C_6F_5)_2SnBr_2$	**6af** 82	**7ba** 64
28	**1a**	**2b**	**3f**	**4b**	$(C_6F_5)_2SnBr_2$	**6af** 83	**7bb** 83
29	**1a**	**2b**	**3f**	**4c**	$(C_6F_5)_2SnBr_2$	**6af** 86	**7bc** 78
30	**1b**	**2a**	**3a**	**4a**	$(C_6F_5)_2SnBr_2$	**6ba** 83	**7aa** 21
31	**1b**	**2b**	**3a**	**4a**	$(C_6F_5)_2SnBr_2$	**6ba** 64	**7ba** 65

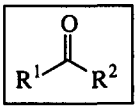
[a] Reaction Conditions: **1**:**2**:**3**:**4**:LA = 1.0:1.3:5.0:1.0:0.1; CH_2Cl_2; -78 °C, 5 h. [b] Determined by GLC. [c] LA = 1.0 equiv. to **1**. [d] A mixture of hydroxy ester (7%) and silyl ether (48%). [e] An aldolate from **1a** and **4a** was formed in 36% yield. [f] An aldolate from **1a** and **4a** was formed in 4% yield. [g] A mixture of hydroxy ester (58%) and silyl ether (32%). [h] An aldolate from **1a** and **4a** was formed in 3% yield.



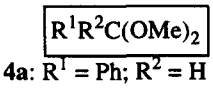
1a: R^1 = H; R^2 = Et
b: R^1 = Me; R^2 = Me



2a: R = ^{t}Bu
b: R = Ph

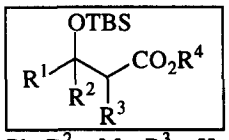


3a: R^1 = Ph; R^2 = Me
b: R^1 = 4-MeOC$_6$H$_4$; R^2 = Me
c: R^1 = 2,4-(MeO)$_2$C$_6$H$_3$; R^2 = Me
d: R^1 = *n*-C$_4$H$_9$; R^2 = Me
e: R^1 = *n*-C$_6$H$_{13}$; R^2 = Me
f: R^1; R^2 = $(CH_2)_5$

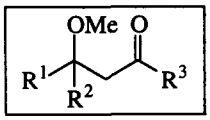


4a: R^1 = Ph; R^2 = H
b: R^1 = *n*-C$_7$H$_{15}$; R^2 = H
c: R^1 = *n*-C$_6$H$_{13}$; R^2 = Me

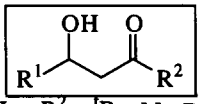
5a: R = *n*-C$_5$H$_{11}$
b: R = *n*-C$_7$H$_{15}$
c: R = Ph



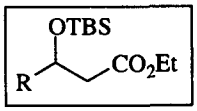
6aa: R^1 = Ph; R^2 = Me; R^3 = H; R^4 = Et
ab: R^1 = 4-MeOC$_6$H$_4$; R^2 = Me; R^3 = H; R^4 = Et
ac: R^1 = 2,4-(MeO)$_2$C$_6$H$_3$; R^2 = Me; R^3 = H; R^4 = Et
ad: R^1 = *n*-C$_4$H$_9$; R^2 = Me; R^3 = H; R^4 = Et
ae: R^1 = *n*-C$_6$H$_{13}$; R^2 = Me; R^3 = H; R^4 = Et
af: R^1, R^2 = $(CH_2)_5$; R^3 = H; R^4 = Et
ba: R^1 = Ph; R^2 = Me; R^3 = Me; R^4 =Me



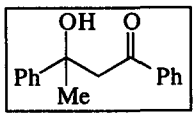
7aa: R^1 = Ph; R^2 = H; R^3 = ^{t}Bu
ab: R^1 = *n*-C$_7$H$_{15}$; R^2 = H; R^3 = ^{t}Bu
ac: R^1 = *n*-C$_6$H$_{13}$; R^2 = Me; R^3 = ^{t}Bu
ba: R^1 = Ph; R^2 = H; R^3 = Ph
bb: R^1 = *n*-C$_7$H$_{15}$; R^2 = H; R^3 = Ph
bc: R^1 = *n*-C$_6$H$_{13}$; R^2 =Me; R^3 = Ph



8ab: R^1 = *n*-C$_7$H$_{15}$; R^2 = ^{t}Bu **bb**: R^1 = *n*-C$_7$H$_{15}$; R^2 = Ph
ac: R^1 = Ph; R^2 = ^{t}Bu **bc**: R^1 = Ph; R^2 = Ph
ba: R^1 = *n*-C$_5$H$_{11}$; R^2 = Ph



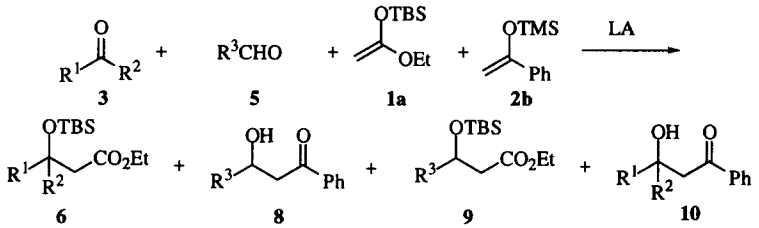
9aa: R = *n*-C$_5$H$_{11}$
ab: R = *n*-C$_7$H$_{15}$
ac: R = Ph



10ba

The direct recognition between unprotected ketone and aldehyde that is synthetically more important but difficult is achievable as shown in Table 2. Among the Lewis acids screened here, only $(C_6F_5)_2SnBr_2$ worked for the present purpose (entry 1). TMSOTf and $Sc(OTf)_3$ gave undesired cross aldol **9ab** (entries 2 and 3) while a considerable amount of **10ba** was formed with $TiCl_4$ and $SnCl_4$ (entries 4 and 5). BF_3OEt_2 failed to drive the reaction between aldehyde and enol silyl ether (entry 6). Satisfactory results were obtained with $(C_6F_5)_2SnBr_2$ for other combinations of ketone and aldehyde (entries 7-11) although slight yields of **9aa** were detected in some cases.

Table 2. Parallel Rcognition between Ketone and Aldehyde with Ketene Silyl Acetal and Enol Silyl Ether.[a)]

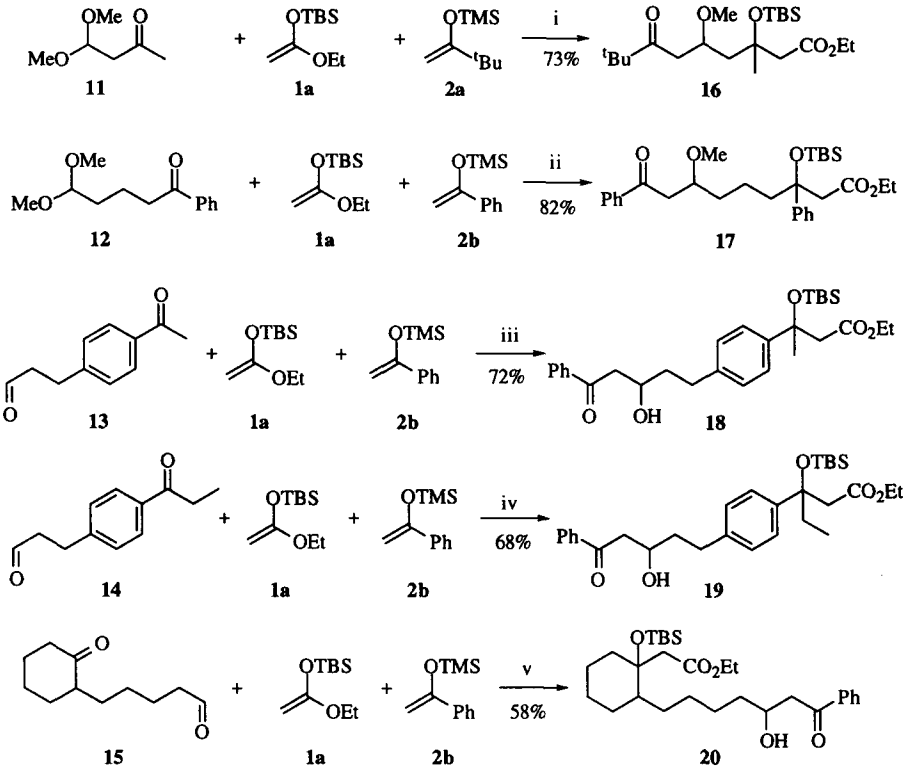


				Yield(%)[b)]			
Entry	3	5	LA	6	8	9	10
1	**3a**	**5a**	$(C_6F_5)_2SnBr_2$	**6aa** 72	**8ba** 61	0	0
2	**3a**	**5b**	TMSOTf	**6aa** 74	**8bb** 73	**9ab** 7	0
3	**3a**	**5b**	$Sc(OTf)_3$	**6aa** 66	**8bb** 37	**9ab** 7	0
4	**3a**	**5a**	$TiCl_4$[c)]	**6aa** 47[d)]	**8ba** 34	0	**10ba** 33
5	**3a**	**5a**	$SnCl_4$[c)]	**6aa** 13[e)]	**8ba** 16	0	**10ba** 25
6	**3a**	**5a**	BF_3OEt_2[c)]	**6aa** 94[f)]	**8ba** 0	0	0
7	**3b**	**5a**	$(C_6F_5)_2SnBr_2$	**6ab** 82	**8ba** 70	0	0
8	**3c**	**5a**	$(C_6F_5)_2SnBr_2$	**6ac** 73	**8ba** 74	**9aa** 1	0
9	**3d**	**5a**	$(C_6F_5)_2SnBr_2$	**6ad** 59	**8ba** 54	**9aa** 3	0
10	**3f**	**5a**	$(C_6F_5)_2SnBr_2$	**6af** 73	**8ba** 70	**9aa** 2	0

[a)] Reaction Conditions: **1**:**2**:**3**:**5**:LA = 1.0:1.3:1.0:1.0:0.1 (or 0.2 for $(C_6F_5)_2SnBr_2$); CH_2Cl_2; -78 °C, 5 h. [b)]Determined by GLC for **6** and 1H NMR (Ph_3CH as an internal standard) for **8**. [c)] LA = 1.0 equiv. relative to **1**. [d)] A mixture of hydroxy ester (35%) and silyl ether (12%). [e)] A mixture of hydroxy ester (3%) and silyl ether (10%). [f)] A mixture of hydroxy ester (89%) and silyl ether (5%).

The parallel recognition was highlighted by intramolecular versions (Scheme 2). Exposure of a mixture of ketene silyl acetal **1** and enol silyl ether **2** to keto acetals **11** and **12** in the presence of a catalytic amount of $(C_6F_5)_2SnBr_2$ furnished sole products **16** and **17**, respectively: **1a** was incorporated in the carbonyl function whereas **2** reacted with the acetal moiety exclusively. The clean recognition also holds for keto aldehydes **13**-**15** and a sole product emerged in each case. Particularly noteworthy is the high yields obtained with **13** and **14** in which the two carbonyls are intervened by the aromatic ring so that the intramolecular interaction between them could not take place. Thus, the possible mechanism that involves the initial attack of **1a** on the aldehyde moiety followed by the intramolecular transfer of the incorporated ester fragment to the ketone moiety is unambiguously ruled out. Apparently, **1a** and **2b** separately attack on the remote carbonyl functions in an exclusive manner.

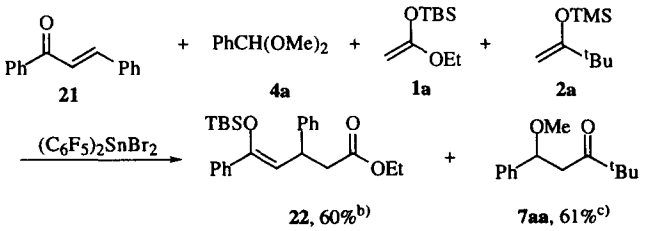
Scheme 2.



Reaction conditions: (i) **11**:**1a**:**2a**:$(C_6F_5)_2SnBr_2$ = 1.0:1.0:4.0:0.3; CH_2Cl_2; -78°C; 7 h.
(ii) **12**:**1a**:**2b**:$(C_6F_5)_2SnBr_2$ = 1.1:1.0:4.0:0.4; CH_2Cl_2; -78°C; 7 h. (iii) **13**:**1a**:**2b**:$(C_6F_5)_2SnBr_2$ = 1.0:1.3:2.0:0.2; CH_2Cl_2; -78°C; 6 h. (iv) **14**:**1a**:**2b**:$(C_6F_5)_2SnBr_2$ = 1.0:1.3:2.0:0.2; CH_2Cl_2; -78°C; 6 h.
(v) **15**:**1a**:**2b**:$(C_6F_5)_2SnBr_2$ = 1.0:1.3:3.0:0.4; CH_2Cl_2; -78°C; 6 h.

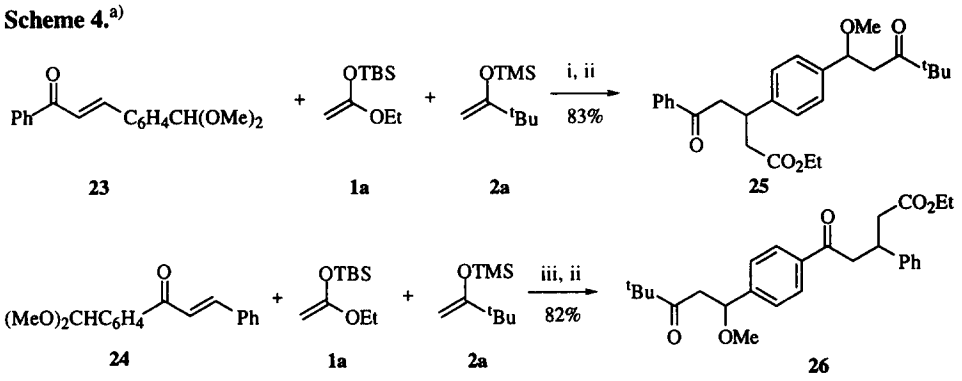
"Parallel recognition" can be applied to the competition between the Michael vs aldol reactions (Scheme 3). Under the catalysis of $(C_6F_5)_2SnBr_2$, ketene silyl acetal **1a** suffered Michael addition with **21** while enol silyl ether **2a** reacted with acetal **4a**. No crossover reactions were observed. The same recognition holds in case of intramolecular versions as well (Scheme 4). Substrates **23** and **24** that have both an α,β-unsaturated enone moiety and an acetal function exhibited the explicit recognition of **1a** and **2a** to afford single products **25** and **26**, respectively.

Scheme 3.[a)]



a) Reaction conditions: **21**:**4a**:**1a**:**2a**:$(C_6F_5)_2SnBr_2$ = 1.0:1.0:1.3:2.0:0.2; CH_2Cl_2; -78°C; 6 h.
b) Determined by ^1H NMR. c) Determined by GLC.

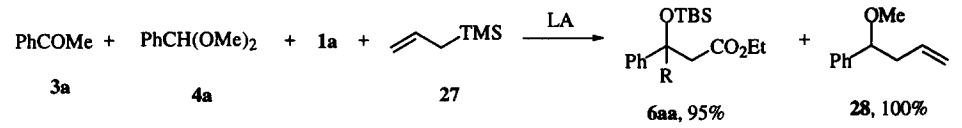
Scheme 4.[a)]



[a)] Reaction conditions: (i) **23**:**1a**:**2a**:$(C_6F_5)_2SnBr_2$ = 1.0:1.3:5.0:0.2; CH_2Cl_2; -78°C; 8 h. (ii) Bu_4NF; THF/H_2O, rt. (iii) **24**:**1a**:**2a**:$(C_6F_5)_2SnBr_2$ = 1.0:1.3:5.0:0.2; CH_2Cl_2; -78°C; 8 h.

Another type of "parallel recognition" was realized between ketene silyl acetal and allylsilane (Scheme 5). In parallel with the exclusive reaction of **1a** with acetophenone, allyltrimethylsilane (**27**) furnished a quantitative yield of allylation product **28** upon reaction with acetal **4a**.

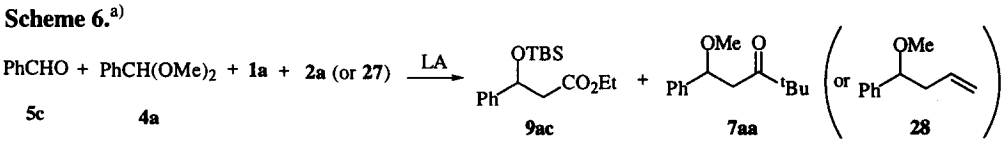
Scheme 5.[a)]



[a)] Reaction conditions: **3a**:**4a**:**1a**:**27**:TMSOTf = 1.0:1.0:1.3:2.0:0.1; CH_2Cl_2; -78 °C; 9 h.

Finally, employment of benzaldehyde in place of ketone should be mentioned. Since the reactivity of benzaldehyde is, in general, higher than ketones in the aldol reaction of ketene silyl acetal,[4)] it is postulated that the analogous recognition results from the benzaldehyde/acetal array. As shown in Scheme 6, TMSOTf effected perfect recognition between benzaldehyde (**5c**) and its dimethyl acetal counterpart **4a**. The reason for the lower yields in the same reaction with $(C_6F_5)_2SnBr_2$ is not apparent at the moment. Employment of allylsilane **27** in place of **2a** also induced the complete selectivity with TMSOTf.

Scheme 6.[a)]



LA = TMSOTf	96%	97%	
	97%		98%
LA = $(C_6F_5)_2SnBr_2$	59%	35%	

[a)] Reaction conditions: **5c**:**4a**:**1a**:**2a**:$(C_6F_5)SnBr_2$ = 1.0:1.0:1.3:2.0:0.1 or **5c**:**4a**:**1a**:**2a**:TMSOTf = 1.0:1.0:1.1:2.0:0.1 or **5c**:**4a**:**1a**:**27**:TMSOTf = 1.0:1.0:1.3:2.0:0.1; CH_2Cl_2; -78 °C; 8-12 h.

In summary, the unique reactivity of ketene silyl acetal has enabled us to conduct various kinds of reactions in parallel with high selectivity. The subtle differences between the substrates that are similar in

reactivity towards silyl nucleophiles can be detected by proper choice of the Lewis acids. This is primarily due to the high preference of ketene silyl acetals for ketones that are usually much less reactive than aldehydes and acetals. Particularly significant is the direct differentiation between naked ketone and aldehyde that is otherwise difficult to achieve.[5] In this process, no protection-deprotection is needed. This is advantageous for not only simplifying the process but also shortening the reaction time, which is, in particular, of economic significance in practical processes. The successful use of various silyl nucleophiles exemplifies the wide applicability of the present method. Accordingly, "parallel recognition" is of great promise for compaction of synthetic processes.[6]

EXPERIMENTAL SECTION

Parallel Recognition between Ketone and Acetal with Ketene Silyl Acetal and Enol Silyl Ether *(Typical Procedure).* To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (61 mg, 0.1 mmol) was added a CH_2Cl_2 solution (2 mL) of **3a** (610 mg, 5.0 mmol) and **4a** (152 mg, 1.0 mmol) at -78 ℃ followed by **1a** (202 mg, 1.0 mmol) and **2a** (224 mg, 1.3 mmol) in CH_2Cl_2 (2 mL). After 5 h, aqueous workup followed by evaporation afforded a crude product that was analyzed by GLC (25 m capillary column packed with CBP-5). The other reactions were carried out analogously.

6aa: ^{1}H NMR ($CDCl_3$) δ -0.11 (s, 3H), 0.08 (s, 3H), 0.93 (s, 9H), 1.09 (t, 3H, J = 7.1 Hz), 1.83 (s, 3H), 2.69, 2.82 (AB, 2H, J_{AB} = 13.4 Hz), 3.95 (q, 2H, J = 7.1 Hz), 7.23-7.34 (m, 3H), 7.44-7.49 (m, 2H). This compound was confirmed by desilylation to give the known alcohol.[7]

6ab: ^{1}H NMR ($CDCl_3$) δ -0.14 (s, 3H), 0.05 (s, 3H), 0.91 (s, 9H), 1.11 (t, 3H, J = 7.1 Hz), 1.81 (s, 3H), 2.66, 2.79 (AB, 2H, J_{AB} = 13.5 Hz), 3.80 (s, 3H), 3.98 (q, 2H, J = 7.1 Hz), 6.83 (d, 2H, J = 9.0 Hz), 7.37 (d, 2H, J = 9.0 Hz). This compound was confirmed by desilylation to give the known alcohol.[8]

6ad: ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 6H), 0.84 (s, 9H), 0.90 (t, 3H, J = 7.5 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.22-1.36 (m, 4H), 1.34 (s, 3H), 1.53-1.62 (m, 2H), 2.45 (s, 2H), 4.10 (q, 2H, J=7.1 Hz). This compound was confirmed by desilylation to give the known alcohol.[9]

6ae: ^{1}H NMR ($CDCl_3$) δ 0.07 (s, 6H), 0.84 (s, 9H), 0.88 (t, 3H, J = 6.2 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.21-1.37 (m, 8H), 1.34 (s, 3H), 1.53-1.58 (m, 2H), 2.45 (s, 2H), 4.09 (q, 2H, J = 7.1 Hz). This compound was confirmed by desilylation to give the known alcohol.[10]

6af: ^{1}H NMR ($CDCl_3$) δ 0.09 (s, 6H), 0.86 (s, 9H), 1.25 (t, 3H, J = 7.1 Hz), 1.32-1.80 (m, 10H), 2.50 (s, 2H), 4.12 (q, 2H, J = 7.1 Hz). This compound was confirmed by desilylation to give the known alcohol.[9]

6ba: ^{1}H NMR ($CDCl_3$) δ -0.34 (s, 3H), -0.05 (s, 3H), 0.85 (d, 3H, J = 7.1 Hz), 0.88 (s, 9H), 1.74 (s, 3H), 2.91 (q, 2H, J = 7.1 Hz), 3.63 (s, 3H), 7.20-7.48 (m, 5H). This compound was confirmed by desilylation to give the known alcohol.[11]

7aa[12]: ^{1}H NMR ($CDCl_3$) δ 1.07 (s, 9H), 2.61, 3.11 (ABX, 2H, J_{AB} = 16.3, J_{AX} = 4.5, J_{BX} = 8.3 Hz), 3.20 (s, 3H), 4.72 (dd, 1H, J = 4.5, 8.3 Hz), 7.26-7.38 (m, 5H).

7ab[13]: ^{1}H-NMR ($CDCl_3$) δ 0.88 (t, 3H, J = 6.7 Hz), 1.14 (s, 9H), 1.20-1.51 (m, 12H), 2.44, 2.81 (ABX, 2H, J_{AB} = 17.0, J_{AX} = 5.4, J_{BX} = 7.0 Hz), 3.31 (s, 3H), 3.70-3.75 (m, 1H, CH).

7ac: ^{1}H-NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 6.6 Hz), 1.16 (s, 9H), 1.27 (s, 3H), 1.25-1.75 (m, 10H), 2.72 (s, 2H), 3.18 (s, 3H); ^{13}C-NMR ($CDCl_3$) δ 14.02, 22.59, 22.68, 23.29, 26.42, 29.66, 31.84, 35.91, 43.77, 44.87, 48.43, 76.24, 213.88; HRMS: calcd for $C_{15}H_{31}O_2$ (M^++H) 243.2324, found 243.2277.

7ba[12]: ^{1}H NMR ($CDCl_3$) δ 3.24 (s, 3H), 3.08, 3.60 (ABX, 2H, J_{AB} = 16.5, J_{AX} = 4.3, J_{BX} = 8.5 Hz), 4.89 (dd, 1H, J_{AX} = 4.3, J_{BX} = 8.5 Hz), 7.26-7.59 (m, 8H), 7.93-7.98 (m, 2H).

7bb[13]: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3H, J = 6.6 Hz), 1.23-1.65 (m, 12H), 2.93, 3.29 (ABX, 2H, J_{AB} = 16.2, J_{AX} = 5.4, J_{BX} = 6.8 Hz), 3.34 (s, 3H), 3.87 (m, 1H), 7.42-7.60 (m, 3H), 7.94-8.00 (m, 2H).

7bc[14]: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3H, J = 6.6 Hz), 1.20-1.78 (m, 13H), 3.07, 3.20 (AB, 2H, J_{AB} = 14.8 Hz), 3.19 (s, 3H), 7.42-7.62 (m, 3H), 7.95-8.02 (m, 2H).

Parallel Recognition between Ketone and Aldehyde with Ketene Silyl Acetal and Enol Silyl Ether *(Typical Procedure).* To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (122 mg, 0.2 mmol) was added a CH_2Cl_2 solution (2 mL) of **3a** (120 mg, 1.0 mmol) and **5a** (100 mg, 1.0 mmol) at -78 ℃ followed by **1a** (263 mg, 1.3 mmol) and **2b** (384 mg, 2.0 mmol) in CH_2Cl_2 (2 mL). After 5 h, aqueous workup followed by

evaporation afforded a crude product that was analyzed by GLC and NMR. The other reactions were carried out analogously.

6ac: ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.19 (s, 3H), 0.96 (s, 9H), 1.04 (t, 3H, J = 7.1 Hz), 1.74 (s, 3H,), 2.83, 3.20 (AB, 2H, J_{AB} = 13.7 Hz), 3.79 (s, 6H), 3.92 (q, 2H, J=7.1 Hz), 6.43-6.49 (m, 2H), 7.52 (d, 1H, J = 8.2 Hz). This compound was confirmed by desilylation to give the alcohol: ^{1}H NMR ($CDCl_3$) δ 1.09 (t, 3H, J = 7.1 Hz), 1.60 (s, 3H), 2.82, 3.23 (AB, 2H, J_{AB} = 15.0 Hz), 3.79 (s, 3H), 3.83 (s, 3H), 3.99 (q, 2H, J = 7.1 Hz), 4.51 (s, 1H), 6.44-6.49 (m, 2H), 7.47 (d, 1H, J = 8.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 13.96, 27.63, 45.16, 55.21, 60.21, 72.29, 99.12, 103.76, 126.41, 127.32, 156.79, 159.93, 172.78; HRMS: calcd for $C_{14}H_{21}O_5$ (M^++H) 269.1389, found 269.1348; Anal.: calcd for $C_{14}H_{21}O_5$: C, 62.67; H, 7.51. found: C, 62.80; H, 7.38.

8ba[15]: ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 6.8 Hz), 1.25-1.70 (m, 8H), 3.04, 3.18 (ABX, 2H, J_{AB} = 17.7, J_{AX} = 2.5, J_{BX} = 9.0 Hz), 3.28 (br. 1H), 4.22 (m, 1H), 7.43-7.63 (m, 3H), 7.90-8.00 (m, 2H).

8bb[16]: ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz), 1.20-1.66 (m, 12H) 3.04, 3.18 (ABX, 2H, J_{AB} = 17.7, J_{AX} = 2.5, J_{BX} = 9.0 Hz), 3.28 (br. 1H), 4.21 (m, 1H), 7.42-7.63 (m, 3H), 7.92-8.00 (m, 2H).

9aa: ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 0.88 (t, 3H, J = 6.5 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.20-1.54 (m, 8H), 2.40-2.44 (m, 2H), 4.08-4.15 (m, 3H). This compound was confirmed by desilylation to give the known alcohol.[17]

9ab[18]: ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 0.88 (t, 3H, J = 6.5 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.21-1.52 (m, 12H), 2.40-2.43 (m, 2H), 4.08-4.15 (m, 3H).

10ba[19]: ^{1}H NMR ($CDCl_3$) δ 1.60 (s, 3H), 3.34, 3.80 (AB, 2H, J_{AB} = 17.5 Hz), 3.54 (s, 3H), 7.21-7.58 (m, 8H), 7.90 (m, 2H).

Reaction of Keto Acetal with Ketene Silyl Acetal and Enol Silyl Ether *(Typical Procedure).* To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (122 mg, 0.2 mmol) was added a CH_2Cl_2 solution (2 mL) of **12** (122 mg, 0.55 mmol) at -78 °C followed by **1a** (101 mg, 0.5 mmol) and **2b** (384 mg, 2.0 mmol) in CH_2Cl_2 (2 mL). After 7 h, aqueous workup followed by column chromatography on silica gel (EtOAc/hexane 1:8) to give **17** (210 mg, 82%). This compound was stirred in HF/CH_3CN solution at room temperature for 7 h. Usual work up and column chromatography on silica gel (EtOAc/hexane 1:4) quantitatively furnished the desilylation product (ethyl 8-benzoyl-3-hydroxy-7-methoxy-3-phenyloctanoate): ^{1}H-NMR ($CDCl_3$) δ 1.07 (t, 3H, J = 7.1 Hz), 1.42-1.85 (m, 6H), 2.75-3.24 (m, 4H), 3.25, 3.26 (1:1 mixture of diastereomers; s, 3H), 3.78 (m, 1H), 4.00 (q, 2H, J = 7.1 Hz), 4.40 (br. 1H), 7.20-7.57 (m, 8H), 7.89-7.94 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ 13.85, 19.01 (19.07), 34.35 (34.35), 42.99 (43.06), 45.28 (45.33), 57.11, 60.62, 74.88, 77.28, 124.92, 126.67, 128.05 (128.08), 128.47, 132.98, 137.18, 145.15, 145.19, 172.77, 198.90; HRMS: calcd for $C_{24}H_{31}O_5$ (M^++H) 399.2171, found 399.2188; Anal.: calcd for $C_{24}H_{30}O_5$: C, 72.34; H, 7.59. found: C, 72.39; H, 7.34.

16: ^{1}H-NMR ($CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.83 (s, 9H), 1.12 (s, 9H), 1.24 (t, 3H, J = 7.1 Hz), 1.43 (s, 3H), 1.68, 1.91 (ABX, 2H, J_{AB} = 14.3, J_{AX} = 4.1, J_{BX} = 7.4 Hz), 2.49, 2.55 (AB, 2H, J_{AB} = 14.0 Hz), 2.56, 2.82 (ABX, 2H, J_{AB} = 17.0, J_{AX} = 5.9, J_{BX} = 6.3 Hz), 3.24 (s, 3H), 3.89-3.93 (m, 1H), 4.08 (q, 2H, J = 7.1 Hz); ^{13}C-NMR ($CDCl_3$) δ -2.08, (-1.96), 14.16, 18.05, 25.75, 26.08, 27.40, 42.34, 44.30, 47.10, 48.57, 56.58, 60.08, 73.99, 74.46, 170.94, 214.16; HRMS: calcd for $C_{20}H_{39}O_5Si$ (M^+-CH_3) 387.2567, found 387.2558; Anal.: calcd for $C_{21}H_{42}O_5Si$: C, 62.64; H, 10.51. found: C, 62.87; H, 10.68.

Reaction of Keto Aldehyde with Ketene Silyl Acetal and Enol Silyl Ether *(Typical Procedure).* To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (61 mg, 0.1 mmol) was added a CH_2Cl_2 solution (2 mL) of **13** (88 mg, 0.5 mmol) at -78 °C followed by **1a** (131 mg, 0.65 mmol) and **2b** (192 mg, 1.0 mmol) in CH_2Cl_2 (2 mL). After 6 h, aqueous workup followed by column chromatography on silica gel (EtOAc/hexane:1/4) to give **18** (179 mg, 72%): ^{1}H-NMR ($CDCl_3$) δ -0.05 (s, 3H), 0.13 (s, 3H), 0.99 (s, 9H), 1.15 (t, 3H, J = 7.1 Hz,), 1.87 (s, 3H), 1.86-2.04 (m, 2H), 2.73, 2.86 (AB, 2H, J_{AB} = 13.4 Hz), 2.74-3.00 (m, 2H), 3.12, 3.23 (ABX, 2H, J_{AB} = 17.7, J_{AX} = 3.4, J_{BX} = 8.5 Hz), 3.49 (br. 1H), 4.03 (q, 2H, J = 7.1 Hz), 4.25-4.35 (m, 1H), 7.21-7.68 (m, 7H), 7.99-8.02 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ -2.55, -2.05, 14.00, 18.33, 25.94, 28.34, 31.34, 38.03, 45.00, 51.11, 60.01, 67.10, 75.51, 125.40, 127.84, 128.04, 128.67, 133.55, 136.69, 140.31, 145.02, 170.35, 200.84; HRMS: calcd for $C_{28}H_{39}O_5Si$ (M^+-CH_3) 483.2567, found 483.2578; Anal.: calcd for $C_{21}H_{34}O_4Si$: C, 69.84; H, 8.49. found: C, 69.78; H, 8.47. The other reactions were carried out analogously.

19: ^{1}H-NMR ($CDCl_3$) δ 0.02 (s, 3H), 0.09 (s, 3H), 0.79 (t, 3H, J = 7.2 Hz), 0.94 (s, 9H), 1.03 (t, 3H, J = 7.1 Hz), 1.74-2.19 (m, 4H), 2.68-2.91 (m, 2H), 2.81, 2.92 (AB, 2H, J_{AB} = 14.3 Hz), 3.05, 3.17 (ABX, 2H, J_{AB} = 17.8, J_{AX} = 3.0, J_{BX} = 8.7 Hz), 3.34 (br. 1H), 3.91 (q, 2H, J = 7.1 Hz), 4.21-4.29 (m, 1H), 7.15-7.62

(m, 7H), 7.91-7.98 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ -2.42, -2.25, 8.51, 13.82, 18.58, 26.00, 31.25, 34.03, 37.98, 44.96, 47.50, 59.87, 67.10, 78.62, 125.88, 127.65, 127.97, 128.32, 128.56, 133.43, 136.62, 139.92, 142.61, 170.05, 200.71; HRMS: calcd for $C_{29}H_{41}O_5Si$ (M^+-CH_3) 497.2723, found 497.2724; Anal.: calcd for $C_{21}H_{34}O_4Si$: C, 70.27; H, 8.65. found: C, 70.03; H, 8.51.

20: ^{1}H NMR ($CDCl_3$) δ 0.08 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.25 (t, 3H, J = 7.1 Hz), 1.10-1.78 (m, 17H), 2.35, 2.87 (AB, 2H, J_{AB} = 12.9 Hz), 3.04, 3.18 (ABX, 2H, J_{AB} = 17.8, J_{AX} = 2.6, J_{BX} = 8.9 Hz), 3.25 (br. 1H), 4.09 (q, 2H, J = 7.1 Hz), 4.17-4.26 (m, 1H), 7.44-7.60 (m, 3H), 7.92-7.99 (m, 2H); ^{13}C-NMR ($CDCl_3$) δ -2.14, -1.73, 14.22, 18.76, 21.75, 25.74, 26.05, 26.79, 27.41, 27.47, 29.48, 29.52, 36.59, 38.04, 43.76, 44.97, 46.29, 60.22, 67.78, 76.72, 128.05, 128.63, 133.45, 136.81, 170.86, 201.00; HRMS: calcd for $C_{29}H_{49}O_5Si$ (M^++H), 505.3349, found 505.3398; calcd for $C_{28}H_{45}O_5Si$ (M^+-CH_3) 489.3036, found 489.3016; Anal.: calcd for $C_{29}H_{48}O_5Si$: C, 69.00; H, 9.58. found: C, 69.10; H, 9.47.

Parallel Recognition between Enone and Acetal with Ketene Silyl Acetal and Enol Silyl Ether. To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (122 mg, 0.2 mmol) was added a CH_2Cl_2 solution (2 mL) of **21** (208 mg, 1,0 mmol) and **4a** (152 mg, 1.0 mmol) at -78 °C followed by **1a** (263 mg, 1.3 mmol) and silyl enol ether **2a** (344 mg, 2.0 mmol) in CH_2Cl_2 (2 mL). After 6 h, aqueous workup followed by evaporation afforded a crude product that was analyzed by GLC and NMR. **22**: ^{1}H NMR ($CDCl_3$) δ -0.17 (S, 3H), -0.13 (s, 3H), 0.94 (s, 9H), 1.08 (t, 3H, J = 7.1 Hz), 2.64 (d, 2H, J = 7.7 Hz), 3.96 (q, 2H, J = 7.1 Hz), 4.33 (m, 1H), 5.21 (d, 1H, J = 9.9 Hz), 7.10-7.40 (m, 10H). This compound was confirmed by desilylation to give the known alcohol.[20]

Parallel Recognition of Enone Acetal with Ketene Silyl Acetal and Enol Silyl Ether *(Typical Procedure).* To a CH_2Cl_2 solution (1 mL) of $(C_6F_5)_2SnBr_2$ (61 mg, 0.1 mmol) was added a CH_2Cl_2 solution (2 mL) of **23** (141 mg, 0.5 mmol) at -78 °C followed by **1a** (131 mg, 0.65 mmol) and **2a** (430 mg, 2.5 mmol) in CH_2Cl_2 (2 mL). After 8 h, aqueous workup followed by evaporation afforded a crude product that was treated with Bu_4NF in THF/H_2O at room temperature for 8 h. Usual work up and column chromatography (EtOAc/Hexane:1/4) to give **25** (181 mg, 83%): ^{1}H NMR ($CDCl_3$) δ 1.02, 1.03 (1:1mixture of diastereomers; s, 9H), 1.12 (t, 3H, J = 7.1 Hz), 2.55, 3.03 (ABX, 2H, J_{AB} = 16.8, J_{AX} = 8.2, J_{BX} = 4.7 Hz), 2.64, 2.79 (ABX, 2H, J_{AB} = 15.4, J_{AX} = 7.9, J_{BX} = 7.0 Hz), 3.15 (s, 3H), 3.28-3.41 (m, 2H), 3.81-3.91 (m, 1H), 4.02 (q, 2H, J = 7.1 Hz), 4.62-4.68 (m, 1H), 7.21-7.24 (m, 4H), 7.38-7.44 (m, 2H), 7.50-7.55 (m, 1H), 7.88 (d, 2H, J = 7.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.0, 25.8, 37.2, 40.7, 40.8, 44.1, 44.5, 45.2, 56.8, 60.3, 79.0, 126.7, 127.5, 128.0, 133.0, 136.8, 140.0, 142.7, 171.7, 198.1, 213.0; FAB-MS: 439 (M^++1); Anal.: calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. found: C, 73.76; H, 7.79.

26: ^{1}H NMR ($CDCl_3$) δ 1.02 (s, 9H), 1.10 (t, 3H, J = 7.1 Hz), 2.55, 3.02 (ABX, 2H, J_{AB} = 16.9, J_{AX} = 8.1, J_{BX} = 4.9 Hz), 2.63, 2.76 (ABX, 2H, J_{AB} = 15.3, J_{AX} = 7.9, J_{BX} = 7.0 Hz), 3.16 (s, 3H), 3.26-3.33 (m, 2H), 3.79-3.89 (m, 1H), 3.99 (q, 2H, J = 7.1 Hz), 4.73 (dd, 1H, J = 8.0, 3.1 Hz), 7.11-7.19 (m, 1H), 7.20-7.25 (m, 4H), 7.37 (d, 2H, J = 8.2 Hz), 7.88 (d, 2H, J = 8.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.0, 25.8, 37.5, 40.7, 44.1, 44.5, 45.0, 57.0, 60.3, 78.9, 126.7, 127.3, 128.3, 128.5, 136.3, 143.2, 147.2, 171.8, 197.7, 212.5; FAB-MS: 439 (M^++1); Anal.: calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. found: C, 74.16; H, 7.91.

Parallel Recognition of Ketone and Acetal with Ketene Silyl Acetal and Allylsilane. To a CH_2Cl_2 solution (1 mL) of TMSOTf (11 mg, 0.05 mmol) was added a CH_2Cl_2 solution (2 mL) of **3a** (60 mg, 0.5 mmol) and **4a** (76 mg, 0.5 mmol) at -78 °C followed by **1a** (131 mg, 0.65 mmol) and **27** (114 mg, 1.0 mmol) in CH_2Cl_2 (2 mL). After 9 h, aqueous workup followed by evaporation afforded a crude product that was analyzed by GLC. **28**[21]: ^{1}H NMR ($CDCl_3$) δ 2.34-2.45 (m, 1H), 2.52-2.62 (m, 1H), 3.22 (s, 3H), 4.17 (dd, 1H, J = 5.8, 7.5 Hz), 5.00-5.09 (m, 2H), 5.70-5.84 (m, 1H, CH), 7.28-7.35 (m, 5H).

Parallel Recognition of Aldehyde and Acetal with Ketene Silyl Acetal and Enol Silyl Ether*(Typical procedure).* To a CH_2Cl_2 solution (1 mL) of TMSOTf (11 mg, 0.05 mmol) was added a CH_2Cl_2 solution (2 mL) of **5c** (53 mg, 0.5 mmol) and **4a** (76 mg, 0.5 mmol) at -78°C followed by **1a** (111 mg, 0.55 mmol) and **2a** (114 mg, 1.0 mmol) in CH_2Cl_2 (2 mL). After 12 h, aqueous workup followed by evaporation afforded a crude product that was analyzed by GLC

Parallel Recognition of Aldehyde and Acetal with Ketene Silyl Acetal and Allylsilane.

To a CH_2Cl_2 solution (1 mL) of TMSOTf (11 mg, 0.05 mmol) was added a CH_2Cl_2 solution (2 mL) of **5c** (53 mg, 0.5 mmol) and **4a** (76 mg, 0.5 mmol) at -78 °C followed by **1a** (131 mg, 0.65 mmol) and **27** (172 mg, 1.0 mmol) in CH_2Cl_2 (2 mL). After 12 h, aqueous workup followed by evaporation afforded a crude product that was analyzed by GLC.

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2. Upon exposure to ketone, **1** reacted smoothly to give **6** whereas no reaction occurred between **1** and **4**. By contrast, **2** reacted with **4** quantitatively while ketone never reacted with **2**.
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