Table 1. Results of cyclic voltammetric studies.[a]

Cation	E_{red1}	E_{red2}
4	−0.066	−0.762
phenalenium[b]	0.5 (0.7)	−1.1 (−0.9)

[a] Tetrabutylammonium tetrafluoroborate (4 mM) as the supporting electrolyte, scan rate 50 mV s^{-1}, 25°C; potential in volts vs. Ag/Ag$^+$, measured with a 25 μm Pt working microelectrode in MeCN; reduction peak potentials are for a quasi-reversible redox reaction; the observed potentials were corrected with reference to ferrocene/ferrocenium (Fc/Fc$^+$; $E_{1/2} = +0.089$ V) as an internal standard. [b] The originally reported[9] reduction potentials for phenalenium tetrafluoroborate (listed in parentheses) were given in volts vs. SCE. For comparison these data were converted into values vs. Ag/Ag$^+$ reference electrode according to Equation (a).[10]

$$E(\mathrm{Ag/Ag^+}) = E(\mathrm{SCE}) - 0.226\ \mathrm{V} \qquad \text{(a)}$$

(−6.76 eV), the SOMO energy of the trinaphthophenalenyl radical (−4.55 eV) is lower than that of phenalenyl radical (−4.43 eV).

Received: July 21, 1997 [Z 10705 IE]
German version: *Angew. Chem.* **1998**, *110*, 95–96

Keywords: arenes · cations · hydrocarbons · phenalenes · polycycles

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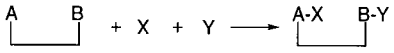
Parallel Differentiated Recognition of Ketones and Acetals**

Jian-xie Chen and Junzo Otera*

Integration of multistep chemical reactions into one-pot reactions is of great significance from both economical and ecological points of view. A number of one-pot processes, which are named tandem, cascade, domino reactions, etc., have received much attention.[1–3] In these protocols, similar or different types of reactions are performed in sequence without isolating intermediates. This strategy is particularly elegant in that the preceding reaction creates the necessary functionality for the subsequent one. Accordingly, the relevant reaction sites are inherited from one step to the next. In practical synthesis, however, we often need to carry out chemical transformations on separate reaction sites within a molecule. Conventionally, such transformations have been executed in a stepwise, not a one-pot, manner. If the manifold reactions could be performed simultaneously (that is, in parallel), the process would be efficient and expeditious [Eq. (1)]. Here we wish to advance a new concept based on



(1)

such parallel (or horizontal) treatment rather than the conventional series (or vertical) strategy.

To arrive at the ultimate goal of parallel recognition [Eq. (1)], we require a new concept of chemoselectivity in which a mixture of substrates A and B reacts with a mixture of reagents X and Y to furnish products A–X and B–Y exclusively or predominantly over other possible products [Eq. (2)]. The requirement would be satisfied if product AX could be formed predominantly over BX in the competition reaction of substrates A and B with reagent X [Eq. (3)] and

$$\mathrm{A + B + X + Y \longrightarrow A\text{–}X + B\text{–}Y} \qquad (2)$$

$$\mathrm{A + B + X \longrightarrow A\text{–}X\ (+B\text{–}X)} \qquad (3)$$

$$\mathrm{A + B + Y \longrightarrow B\text{–}Y\ (+A\text{–}Y)} \qquad (4)$$

BY in preference to AY in the reaction with reagent Y [Eq. (4)]. To our knowledge, no such treatment has been put forth intentionally, although the analogous selectivity might have incidentally resulted from unintentional performances on rare occasions.[4]

For reaction (2) to occur efficiently the substrates A and B should be similar to each other in chemical reactivity, so that reactions (3) and (4) can proceed under the identical reaction conditions. They should simultaneously undergo different reactions irrespective of the other. The reagents X and Y also

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[**] This work was supported by the Japanese Society for the Promotion of Science under the "Research for the Future" Program (JSPS-PFTF96P00303)

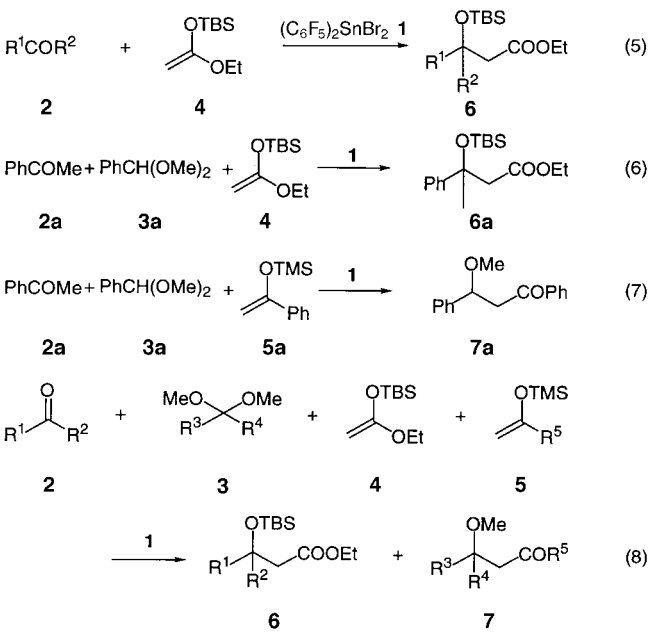
  1433-7851/98/3701-0091 $ 17.50+.50/0

Table 1. Mukaiyama–aldol reaction of ketene silyl acetal **4** with ketone **2**, catalyzed by **1**.[a]

2		Reaction time [h]	Yield of **6** [%][b]
R^1	R^2		
Ph	CH_3	2	92
Ph	C_2H_5	5	85
C_2H_5	CH_3	1	87
n-C_6H_{13}	CH_3	2	95
t-C_4H_9	CH_3	4.5	78
$(CH_2)_5$		2	93

[a] Reaction conditions: 2:4:1 = 1.0:3:0.1, CH_2Cl_2, −78°C. [b] Yield of isolated product after column chromatography.

need to work in this way. In studies on synthetic applications of organotin Lewis acids we disclosed that bis(pentafluorophenyl)tin dibromide (**1**)[5] effects the Mukaiyama–aldol reaction of ketene silyl acetal **4** with ketones **2** quite smoothly [Eq. (5), TBS = *tert*-butyldimethylsilyl; Table 1]. These are the first examples, to our knowledge, in which ketones are successfully activated by an organotin Lewis acid. In addition, no reaction occurs with acetals **3** under the same reaction conditions. As a result, the competition reaction between acetophenone (**2a**) and benzaldehyde dimethyl acetal (**3a**) towards **4** furnishes ketone adduct **6a** exclusively (Eq. 6),[6] satisfying the condition for Equation (3). On the other hand, reaction of enol silyl ether **5a** derived from acetophenone led



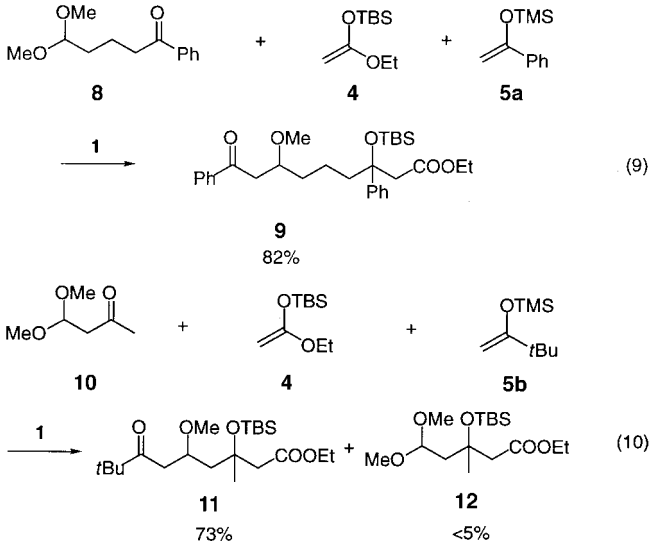
to the totally opposite outcome, giving acetal aldolate **7a** exclusively [Eq. (7), TMS = trimethylsilyl],[7] satisfying the condition for Equation (4). With these results in hand, we treated a mixture of **2** and **3** with a mixture of **4** and **5** [Eq. (8)].[8] A clean reaction took place, and the catalyst indeed fulfilled a double role. As shown in Table 2, only the doublet **6** and **7** emerged, and no products derived from other combinations were detected at all.

Table 2. Chemospecific parallel reactions (8).

2		**3**		**5**	Yield [%][a]	
R^1	R^2	R^3	R^4	R^5	**6**	**7**
Ph	CH_3	n-C_6H_{13}	CH_3	Ph	84[b]	83[c]
Ph	CH_3	n-C_7H_{15}	H	Ph	83	83
Ph	CH_3	Ph	H	tBu	89	73
4-$MeOC_6H_4$	CH_3	n-C_7H_{15}	H	Ph	83	65
n-C_6H_{13}	CH_3	n-C_6H_{13}	CH_3	Ph	83	83
n-C_6H_{13}	CH_3	n-C_7H_{15}	H	Ph	82	80
n-C_6H_{13}	CH_3	Ph	H	tBu	74	85
n-C_4H_9	CH_3	n-C_6H_{13}	CH_3	Ph	86	82
$(CH_2)_5$		Ph	H	tBu	74	80
$(CH_2)_5$		n-C_6H_{13}	CH_3	Ph	86	78

[a] Yields of **6** based on **4** and of **7** based on **3** were determined by gas chromatography. [b] 72% yield of isolated product. [c] 61% yield of isolated product.

This protocol was successfully applied to an intramolecular reaction. Keto acetals **8** and **10** were exposed to a mixture of enol silyl ethers **4** and **5** in the presence of **1** [Eqs. (9) and (10)].[9] As sole product **9**[10] was obtained in reaction (9), while reaction (10) provided a small amount of monoconverted product **12** in addition to major product **11**. Never-



theless, the complete parallel chemospecificity held in these cases as well.

We have already revealed the synthetic usefulness of weak Lewis acidity of organotin catalysts.[5, 11–13] It is the weak acidity of **1** that has enabled the parallel recognition. Its weak Lewis acidity is essential for detecting the subtle differences between ketone and acetal. Somewhat similar but actually different selectivity was found with a $Bu_2Sn(OTf)_2$ catalyst: Mukaiyama–aldol reaction of both **4** and **5** with acetal **3** took place smoothly but no reaction with ketone **2**.[11] Apparently, this catalyst succeeded in differentiating the substrates to some extent but failed to differentiate between reagents **4** and **5**. Moreover no preference for ketone over acetal was observed. This contrast well illuminates the unique activities of **1**.

  1433-7851/98/3701-0092 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **1998**, *37*, No. 1/2

The intramolecular version is significant from a synthetic point of view, because it has potential as a new strategy for highly expeditious chemical processes. The following advantages are apparent for the parallel treatment: 1) No special elaboration on substrates is required. 2) Reactions that are commonly encountered in organic synthesis are employable. Needless to say, the carbonyl differentiation is not the only method suitable for this concept. 3) Conceivably, the scope will be expanded to a wider range where more than two parallel transformations are performed.

Promotion of multifold reactions by a single catalyst is of great importance. In some sequential reactions, catalysts work for more than one reaction,[14–18] yet each step involves a single reaction; hence, the catalysts are not required to promote several reactions simultaneously. On the other hand, the parallel recognition demands that the catalysts effect simultaneous reactions in a exclusive manner. Many catalysts, however, are available that can activate different types of reaction, and, accordingly, the concept of parallel recognition will find a variety of applications if the reaction conditions are suitably adjusted.

Experimental Section

General intermolecular parallel recognition: To a dichloromethane solution (3 mL) of **1** (31 mg, 0.05 mmol) was added a solution of ketone **2** (2.5 mmol) and acetal **3** (0.5 mmol) in dichloromethane (2 mL) at $-78^{\circ}C$. Then, a dichloromethane solution (2 mL) of **4** (0.5 mmol) and **5** (0.65 mmol) was added. The reaction mixture was stirred at this temperature for 4 h. Water (2 mL) was added to this solution. The reaction mixture was extracted with dichloromethane, and the extract washed with water and brine. The organic layer was dried (Na_2SO_4), and the solvent removed. The crude product thus obtained was analyzed by GLC.

Example of typical intramolecular parallel recognition: To a dichloromethane solution (5 mL) of **1** (122 mg, 0.2 mmol) and keto acetal **8** (122 mg, 0.55 mmol) was added a solution of **4** (101 mg, 0.5 mmol) and **5a** (384 mg, 2.0 mmol) in dichloromethane (2 mL) at $-78^{\circ}C$. The reaction mixture was stirred at this temperature for 7 h, after which water was added. The reaction mixture was extracted with dichloromethane, and the extract washed with water and brine. The organic layer was dried (Na_2SO_4), and the solvent removed. The residue was chromatographed on silica gel (eluent hexane/ethyl acetate 8/1) to give **9** (210 mg, 82 %). This compound was stirred in HF/CH_3CN solution at room temperature for 7 h. Usual workup and column chromatography quantitatively furnished the desilylated product (ethyl 8-benzoyl-3-hydroxy-7-methoxy-3-phenyloctanoate): ^1H NMR ($CDCl_3$): $\delta = 1.07$ (t, 3H, $J = 7.1$ Hz, CH_3), 1.42–1.82 (m, 6H, $3CH_2$), 2.77–3.24 (m, 4H, $2CH_2$), 3.25, 3.26 (1:1 mixture of diastereomers; s, 3H, OCH_3), 3.78 (m, 1H, CH), 4.00 (q, 2H, $J = 7.1$ Hz, CH_2), 4.40 (br., 1H, OH), 7.20–7.57 (m, $8H_{arom}$), 7.91 (m, $2H_{arom}$); ^{13}C NMR ($CDCl_3$): δ[19] = 13.85, 19.01 (19.07), 34.25 (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 $C_{24}H_{31}O_5$ [$(M+1)^+$] 399.2171, found 399.2188; C,H analysis calcd. for $C_{24}H_{30}O_5$: C 72.34, H 7.59; found: C 72.39, H 7.34.

11: ^1H NMR[20] ($CDCl_3$): $\delta = 0.07$ (s, 3H, CH_3), 0.08 (s, 3H, CH_3), 0.83 (s, 9H, *t*Bu), 1.12 (s, 9H, *t*Bu), 1.24 (t, 3H, $J = 7.1$ Hz, CH_3), 1.43 (s, 3H, CH_3), 1.65–1.95 (m, 2H, CH_2), 2.51 (m, 2H, CH_2), 2.54–2.86 (m, 2H, CH_2), 3.24 (s, 3H, OCH_3), 3.89–3.93 (m, 1H, CH), 4.08 (q, 2H, $J = 7.1$ Hz, CH_2); ^{13}C NMR ($CDCl_3$): $\delta = -2.08$ (−1.96),[19] 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; C,H analysis calcd. for $C_{21}H_{42}O_5Si$: C 62.64, H 10.51; found: C62.87, H 10.68.

12: ^1H NMR ($CDCl_3$): $\delta = 0.09$ (s, 6H, CH_3), 0.84 (s, 9H, *t*Bu), 1.24 (t, 3H, $J = 7.1$ Hz, CH_3), 1.40 (s, 3H, CH_3), 1.87–2.01 (m, 2H, CH_2), 2.51 (m, 2H, CH_2), 3.28 (s, 6H, OCH_3), 4.09 (q, 2H, $J = 7.1$ Hz, CH_2), 4.61 (t, 1H, $J = 5.0$ Hz, CH); C,H analysis calcd. for $C_{16}H_{34}O_4Si$: C 57.45, H 10.24; found C 57.02, H, 9.89.

Received: June 24, 1997
Revised version: September 16, 1997 [Z10595/10596IE]
German version: *Angew. Chem.* **1998**, *110*, 96–98

Keywords: aldol reactions · carbonyl differentiation · chemoselectivity · one-pot reactions · tin

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[7] Reaction conditions: **2a**:**3a**:**5a**:**1** = 1.0:1.0:1.3:0.1, CH_2Cl_2, $-78^{\circ}C$, 5 h; yield of isolated product: 63 %.
[8] Reaction conditions: **2**:**3**:**4**:**5**:**1** = 5.0:1.0:1.0:1.3:0.1, CH_2Cl_2, $-78^{\circ}C$, 5 h. It is crucial to use an excess of **2** to consume **4** as quickly as possible, otherwise the decomposition of the catalyst is inevitable during the reaction, resulting in low yields of **7**.
[9] Reaction conditions: **8**:**4**:**5**:**1** = 1.1:1.0:4.0:0.4 or **10**:**4**:**5**:**1** = 1.0:1.0:4.0:0.3; CH_2Cl_2, $-78^{\circ}C$, 7 h. Yields of isolated products were determined after column chromatography.
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  1433-7851/98/3701-0093 $ 17.50+.50/0