and concentrated to afford a tan solid that was recrystallized from ethanol to provide the iodobenzaldehyde **4c** (3.20 g, 85%) as a white solid: mp 100–101 °C; ^{1}H NMR δ 10.28 (s, 1 H), 7.70 (d, 1 H, J = 2.02 Hz), 7.36 (d, 1 H, J = 2.0 Hz), 3.95 (s, 3 H), 3.88 (s 3 H); IR (mull) 1670 cm^{-1}. Anal. Calcd for $C_9H_9IO_3$: C, 37.01; H, 3.11. Found: C, 37.38; H, 3.05.

Formation of 2a from 4c. The aldehyde **4c** (200 mg, 0.685 mmol) was dissolved in *tert*-butyl alcohol (5 mL), and 1.25 M dipotassium hydrogen phosphate (2.7 mL) and 1.0 M potassium permanganate (4.1 mL) were added. The reaction mixture was stirred at 20 °C (30 min) and then quenched with saturated Na_2SO_3. The resulting solution was adjusted to pH 3 with concd HCl then extracted with $CHCl_3$. The organic portion was extracted with 1 N NaOH. The aqueous basic layer was acidified to pH 3 with 1 N H_3PO_4 then extracted with $CHCl_3$. The chloroform layer was dried and filtered, and the solvent was removed under reduced pressure to yield the acid **2a** (180 mg, 86%).

(*S*)-2,3-Dimethoxy-*N*-[(1-ethyl-2-pyrrolidinyl)methyl]-5-iodobenzamide (1a, Epidepride). The benzoic acid **2a** (600 mg, 1.95 mmol) was dissolved in CH_2Cl_2 (10 mL), and to this solution was added DMF (2 drops) and oxalyl chloride (0.425 mL, 4.87 mmol). The mixture was stirred at room temperature (1 h), and the solvent was removed in vacuo affording the corresponding acid chloride as a pale yellow residue (not characterized). The residue was dissolved in CH_2Cl_2 (10 mL), and the aminopyrrolidine **3**[36] (623 mg, 4.87 mmol) in CH_2Cl_2 (5 mL) was added to this solution. The reaction mixture was allowed to stir for 1 h (20 °C), and the solvent was removed under reduced pressure. The crude product was redissolved in CH_2Cl_2 (20 mL) and washed with 1 N NaOH (20 mL), and the phases were separated. The organic portion was dried and filtered, and the solvent was removed in vacuo to afford a yellow oil that was purified by column chromatography (silica gel; 1:9 MeOH–CH_2Cl_2) to yield epidepride **1a** (810 mg, 100%) as a yellow oil: ^{1}H NMR δ 8.30 (br s, 1 H), 8.03 (d, 1 H, J = 1.62 Hz), 7.28 (d, 1 H, J = 1.62 Hz), 3.89 (s, 3 H), 3.88 (s, 3 H), 3.77 (ddd, 1 H, J = 13.6, 7.0, 3.2 Hz), 3.33 (dt, 1 H, J = 14.0, 3.8), 3.32 (br t, 1 H, J = 7.2 Hz), 2.89 (dq, 1 H, J = 11.8, 7.4 Hz), 2.62 (br m, 1 H), 2.19 (m, 1 H), 1.77–1.63 (m, 5 H), 1.15 (t, 3 H, J = 7.2 Hz); IR (neat) 3330, 1640 cm^{-1}. Anal. Calcd for $C_{16}H_{23}IN_2O_3$: C, 45.95; H, 5.45. Found: C, 46.17; H, 5.56.

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Registry No. **1a**, 107188-87-4; **2a**, 134419-42-4; **3**, 22795-99-9; **4a**, 86-51-1; **4b**, 71295-21-1; **4c**, 7396-66-9; **4d**, 148-53-8; **4e**, 7359-14-0; **4f**, 7740-05-8; **5a**, 6342-70-7; **5b**, 134419-43-5; **5c**, 134419-44-6; **5d**, 134419-45-7; **5e**, 134419-46-8; **6a**, 877-22-5; **6b**, 134419-47-9; **7a**, 79315-43-8; **7b**, 111381-04-5; **8a**, 107189-00-4; **8b**, 134528-76-0; **9**, 134419-48-0; **10**, 134419-49-1.

Unique Catalysis by Eu(dppm)$_3$: Catalytic Molecular Recognition in Aldol and Michael Reactions†

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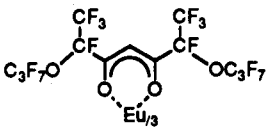
Development of efficient catalysis of C–C bond formations is the current subject of intensive activities.[1] For aldol-type reactions of carbonyl compounds with enol silyl ethers in particular, several catalysts including chiral ones have been developed.[2] It occurred to us that Eu(dppm)$_3$, tris[di(perfluoro-2-propoxypropionyl)methanato]europium(III) (**1**), originally developed by Ishikawa et al. as a chiral NMR shift reagent,[3] ought to be a superb catalyst for certain C–C bond-forming reactions[4] because of the stronger Lewis acidity due to the highly fluorinated ligand. Disclosed herein are the preliminary observations on the unique catalysis by Eu(dppm)$_3$ in the aldol and Michael reactions.



1

In order to define the scope of the Eu catalysis, we first attempted reactions of various carbonyl/enol silyl ether pairs in the presence of 2.5 mol % of (+)-Eu(dppm)$_3$ in the range of −78 to 25 °C. We found that the Eu(III) catalyst was effective only for the reactions of aldehydes or α,β-unsaturated ketones with ketene silyl acetals (KSA) but totally ineffective for any pairs of ketone/KSA and aldehyde/ketone-derived enol silyl ether.[5] Thus, the Eu catalysis provides remarkable levels of chemoselectivity for both carbonyl and enol silyl ether partners.[6]

In addition, the Eu catalysis shows high levels of aldehyde discrimination in the competitive aldol reactions with KSA (Table I). First, the Eu catalyst can differentiate the steric difference in aldehydes to much higher extents than those observed with a stoichiometric use of $TiCl_4$ even at lower temperature (entries 1 and 2). Second, the Eu catalyst can uniquely recognize the delicate difference in electronic effect involved in benzaldehydes. Interestingly enough, *p*-nitrobenzaldehyde ($\sigma_{p\text{-}NO_2}$ = +0.78)[7] is *less* reactive than benzaldehyde in the Eu-catalyzed process (eq 1). More significantly, the Eu catalyst shows the remarkable preference for *o*-methoxybenz-

† Presented at the 52nd Annual Meeting of the Chemical Society of Japan, Kyoto, April 1–4, 1986, Paper 3Y29,3Y30.

(1) For reviews: (a) Morrison, J. D. *Asymmetric Synthesis*; Academic Press: New York, 1984; Vol. 3B. (b) Bosnich, B. *Asymmetric Catalysis*; Martinus Nijhoff Publishers: Dordrecht, 1986. (c) Kagan, H. B. In *Comprephenisve Organometalic Chemistry*; Wilkinson, G., Ed.; Pergamon: New York, 1982; Vol. 8. (d) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods 1989*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; Vol. 5.

(2) Achiral catalyst. (a) $TrClO_4$: Mukaiyama, T.; Kobayashi, S.; Murakami, M. *Chem. Lett.* **1985**, 447. (b) (COD)Rh(DPPB)X: Sato, S.; Matuda, I.; Izumi, Y. *Tetrahedron Lett.* **1986**, *27*, 5517. (c) ZnX_2: Kita, Y.; Yasuda, H.; Tamura, O.; Ito, F.; Ke, Y. Y.; Tamura, Y. *Tetrahedron Lett.* **1985**, *26*, 5777. (d) Cray montmorillonite: Kawai, M.; Onaka, M.; Izumi, Y. *Chem. Lett.* **1986**, 1581. Chiral catalyst: (e) $Cl_2Ti(OR^*)_2$ and $ClAlL^*_2$; Reetz, M. T.; Kyung, S.-H.; Bolm, C.; Zierke, T. *Chem. Ind.* **1986**, 824. (f) RhL*: Reetz, M. T.; Vougioukas, A. E. *Tetrahedron Lett.* **1987**, *28*, 793. (g) $Sn(OTf)_2$ and a chiral diamine: Mukaiyama, T.; Kobayashi, S.; Uchiro, H.; Shiina, I. *Chem. Lett.* **1990**, 129, and references. (h) $O{=}Ti(OR^*)_2$: Mukaiyama, T.; Inubushi, A.; Suda, S.; Hara, R.; Kobayashi, S. *Chem. Lett.* **1990**, 1015.

(3) Kawa, H.; Yamaguchi, F.; Ishikawa, N. *Chem. Lett.* **1982**, 153.

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(5) Similar Eu-catalyzed reactions of diethyl ketone/KSA of methyl propionate and benzaldehyde/enol silyl ether of diethyl ketone or methoxyacetone did not provide the aldol product even after 3 days at room temperature, whereas the equimolar use of $TiCl_4$ provided the adducts in good yields even at −78 °C.

(6) For the chemoselective carbonyl addition of organotitanium reagents, see: Reetz, M. T. *Top. Curr. Chem.* **1982**, *106*, 1.

(7) Wells, P. R. *Linear Free Energy Relationships*; Academic Press: New York, 1968.

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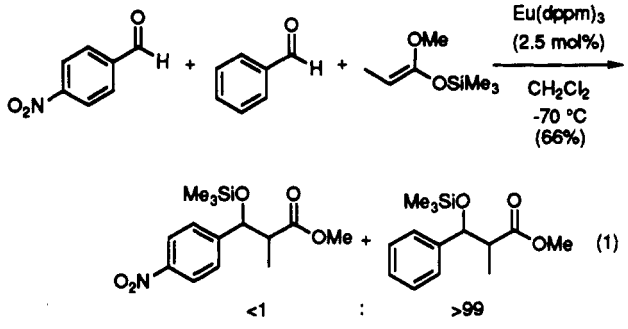
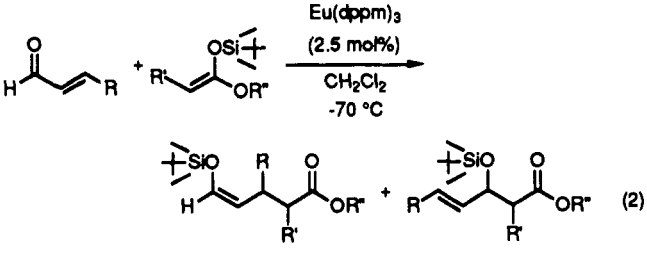
aldehyde ($\sigma_{o\text{-}OMe}$ = −0.27 to −0.67)[7] over benzaldehyde, although the former is sterically more hindered (entry 4). These results suggest that the relative reactivity of aldehydes in the Eu-catalyzed process is determined almost solely by the coordinating ability of aldehydes toward $Eu(dppm)_3$, not by the electrophilicity of aldehydes themselves. A similar argument can be extended to explain the high levels of molecular recognition between α-benzyloxy aldehyde and aldehydes devoid of benzyloxy group, where the former is preferentially complexed in the chelation way,[8] indeed giving the β,γ-syn diastereomer as the major product (entries 5 and 6).



(1)

Finally, the Eu catalyst is also sensitive to the steric parameters involved in α,β-unsaturated carbonyls in the competition of aldol vs Michael additions (eq 2). The β-unsubstituted enal (R = H) preferably affords the Michael adduct, whereas the β-substituted one (R = Me) yields both the aldol and Michael adducts, the former adduct predominating with the sterically less demanding KSA (R′ = H).[9] In contrast, similar Eu-catalyzed reactions of α,β-unsaturated ketones such as cyclopentenone give only the Michael adducts as the enol silyl ether forms.[10]



(2)

R = H	R′ = Me	R" = Me	>99	:	<1	(85%)
R = Me	R′ = Me	R" = Me	44	:	56	(65%)
R = Me	R′ = H	R" = Et	15	:	85	(85%)

In summary, $Eu(dppm)_3$ is demonstrated to effectively recognize the delicate difference in steric and/or electronic factors in both carbonyl and silyl enol ether partners.[11] Thus, the Eu catalyst is ranked at a unique position among catalysts for aldol and Michael additions. Further studies are in progress on stereochemistry of the Eu-catalyzed processes.

Experimental Section

General. (+)-$Eu(dppm)_3$ (30 w/v % CCl_2FCClF_2 solution) was purchased from Daiichi Kagaku Yakuhin Co. Dichloromethane was freshly distilled from CaH_2. ^1H NMR and ^{13}C NMR spectra were measured on a Varian EM 390 or JEOL EX-90Q spectrometer. IR spectra were recorded on a JASCO A-102 spectrometer. Liquid chromatographic analysis was conducted on a Shimazu LC-6A instrument.

General Procedure of the Eu-Complex Catalyzed Aldol Reaction: Competition with Benzaldehyde and *p*-Nitrobenzaldehyde. To a solution of benzaldehyde (102 μL, 1.0 mmol) and *p*-nitrobenzaldehyde (151 mg, 1.0 mmol) in CH_2Cl_2 (3 mL) was added a 30 w/v % $CF_2ClCFCl_2$ solution of (+)-$Eu(dppm)_3$ (172 μL, 0.025 mmol) at room temperature under an argon atmosphere. After cooling down to −78 °C, 1-methoxy-1-[(trimethylsilyl)oxy]-1-propene (160 μL, 1.0 mmol) was added to the catalyst solution. After stirring for 4 h at that temperature, the reaction mixture was poured into saturated NH_4Cl (10 mL). The resultant solution was extracted three times with EtOAc (totally 100 mL). The combined organic layer was washed with saturated $NaHCO_3$ (20 mL) and brine (30 mL). The extract was dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was desilylated without purification. To the solution of the crude aldols in THF (2 mL) was added a 1 N THF solution of TBAF (1.5 mL, 1.5 mmol) at room temperature. After being stirred for 2 h, the reaction mixture was poured into water (10 mL) and extracted three times with EtOAc (totally 100 mL). The combined organic layer was washed with water, two times (totally 50 mL), and brine (30 mL). The extract was dried over $MgSO_4$ and evaporated under reduced pressure. Silica gel chromatography provided methyl 3-hydroxy-2-methyl-3-phenylpropionate exclusively in 66% yield (128 mg, α,β-syn/anti = 53:47).

***α,β-syn*-Methyl 3-hydroxy-2-methyl-3-phenylpropionate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 1.12 (d, J = 7.0 Hz, 3 H), 2.50 (bs, 1 H), 2.86 (m, 1 H), 3.65 (s, 3 H), 5.10 (d, J = 4.7 Hz, 1 H), 7.3–7.4 (m, 5 H); IR (neat) 3450, 1730, 1090, 700 cm^{-1}; HPLC (Zorbax SIL, eluent, hexane/EtOAc = 4/1, flow rate 1.0 mL/min, detection 254 nm light); t_R of syn isomer 13.1 min, t_R of anti isomer 18.8 min.

***α,β-anti*-Methyl 3-hydroxy-2-methyl-3-phenylpropionate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 1.00 (d, J = 7.5 Hz, 3 H), 2.50 (bs, 1 H), 2.83 (m, 1 H), 3.72 (s, 3 H), 4.75 (d, J = 8.6 Hz, 1 H), 7.3–7.4 (m, 5 H); IR (neat) 3450, 1730, 1090, 700 cm^{-1}; HPLC (vide supra).

***α,β-syn*-Methyl 3-hydroxy-2-methylpentanoate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 0.93 (t, J = 6.7 Hz, 3 H), 1.08 (d, J = 6.7 Hz, 3 H), 1.1–1.3 (m, 2 H), 2.52 (m, 1 H), 2.97 (bs, 1 H), 3.67 (s, 3 H), 3.78 (dt, J = 3.6, 6.5 Hz, 1 H); IR (neat) 3450, 2950, 2880, 1730, 830 cm^{-1}; HPLC (Zorbax SIL, eluent, hexane/EtOAc = 10/1, flow rate 1.0 mL/min, detection RI); t_R of syn isomer 30.1 min, t_R of anti isomer 31.0 min.

***α,β-anti*-Methyl 3-hydroxy-2-methylpentanoate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 0.93 (m, 3 H), 1.10 (d, J = 6.7 Hz, 3 H), 1.1–1.3 (m, 2 H), 2,48 (m, 1 H), 2.97 (bs, 1 H), 3.55 (dt, J = 6.9, 6.7 Hz, 1 H), 3.67 (s, 3 H); IR (neat) 3450, 1730, 830 cm^{-1}; HPLC (vide supra).

***α,β-anti*-Methyl 3-hydroxy-2,4,4-trimethylpentanoate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (s, 9 H), 1.35 (d, J = 6.7 Hz, 3 H), 2.76 (dq, J = 2.3, 6.7 Hz, 3 H), 3.18 (d, J = 2.3 Hz, 1 H), 3.53 (bs, 1 H), 3.70 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 18.5, 26.3, 30.9, 39.1, 51.9, 83.5, 178.3; IR (neat) 3450, 1730, 830 cm^{-1}; HPLC (Zorbax SIL, eluent, hexane/EtOAc = 10/1, flow rate 1.0 mL/min, detection RI); t_R of anti isomer 10.5 min.

Ethyl 3-hydroxy-3-phenylpropionate: ^1H NMR (90 MHz, $CDCl_3$) δ 1.23 (t, J = 6.7 Hz, 3 H), 2.63 (dd, J = 5.6, 11.5 Hz, 1 H), 2.65 (dd, J = 6.5, 11.5 Hz, 1 H), 2.90 (bs, 1 H), 4.16 (q, J = 6.7 Hz, 2 H), 5.13 (dd, J = 5.6, 6.5 Hz, 1 H), 7.3–7.4 (m, 5 H); IR (neat) 3450, 1730, 700 cm^{-1}.

Ethyl 3-hydroxy-4,4-dimethylpentanoate: ^1H NMR (90 MHz, $CDCl_3$) δ 0.90 (s, 9 H), 1.25 (t, J = 6.7 Hz, 3 H), 2.38 (dd, J = 9.5, 16.5 Hz, 1 H), 2.52 (dd, J = 3.0, 16.5 Hz, 1 H), 3.58 (bs, 1 H), 3.70 (dd, J = 3.0, 9.5 Hz, 2 H), 4.16 (q, J = 6.7 Hz, 2 H); IR (neat) 3450, 1730 cm^{-1}.

***α,β-syn*-Methyl 3-hydroxy-2-methyl-3-(*p*-methoxyphenyl)propionate:**[12] ^1H NMR (90 MHz, $CDCl_3$) δ 1.12 (d, J = 6.9 Hz, 3 H), 2.82 (m, 1 H), 3.00 (bs, 1 H), 3.60 (s, 3 H), 3.76

(8) Review on chelation vs nonchelation control: Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556.

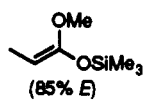
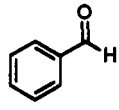
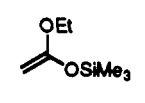
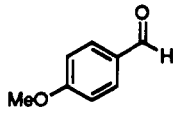
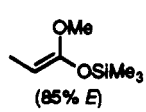
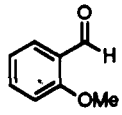
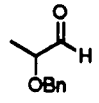
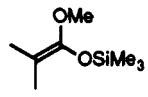
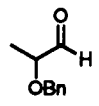
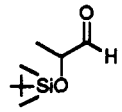
(9) For the 1,4-addition of organolithium reagents to α,β-unsaturated ketones by the complexation with a stoichiometric amount of bulky aluminum reagents (MAD and MAT), see: Maruoka, K.; Ito, T.; Sakurai, M.; Nonoshita, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 3588.

(10) Yields of the Michael adducts (−40 °C): cyclopentenone, 72% (3,1′-syn/anti = 57:43); cyclohexenone, 85% (3,1′-syn/anti = 59:41).

(11) For the discrimination of acetals with dibutyltin bis(triflate), see: Sato, T.; Otera, J.; Nozaki, H. *J. Am. Chem. Soc.* **1990**, *112*, 901.

(12) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294.

Table I. Catalytic Molecular Recognition by (+)-Eu(dppm)$_3$ in Aldol Reaction[a]

entry	aldehydes	KSA	temp (°C)	aldols ratio		% yield[a]
1		 (85% *E*)	0	>99[d] :	<1[e]	61
			[-78	77 :	23	88]^b
2			-40	>99 :	<1	57
			[-40	45 :	55	78]^b
3		 (85% *E*)	-78	87[f] :	13[g]	83
4			-78	95[h] :	5	78
			[-78	68 :	32	82]^b
5			-40	>99[i] :	<1	80
6			-40	97 :	3[j]	82

[a] The reaction was carried out by using an equimolar mixture of two different aldehydes (1.0 mmol) with 1 equiv of KSA in CH_2Cl_2 in the presence of 2.5 mol % (+)- or (−)-Eu(dppm)$_3$ at the indicated temperature for several hours. [b] Values in parentheses refer to the ratios obtained with a stoichiometric use of $TiCl_4$. [c] Combined yield after desilylation and column chromatographic purification. [d] α,β-syn/anti = 40:60. [e] α,β-syn/anti = <5:>95. [f] α,β-syn/anti = 50:50. [g] α,β-syn/anti = 53:47. [h] α,β-syn/anti = 65:35. [i] β,γ-syn/anti = 92:8. [j] β,γ-syn/anti = 29:71.

(s, 3 H) 4.97 (d, J = 5.1 Hz, 1 H), 6.87 (m, 2 H), 7.27 (m, 2 H); IR (neat) 3450, 1730, 830 cm^{-1}.

***α,β-anti*-Methyl 3-hydroxy-2-methyl-3-(*p*-methoxyphenyl)propionate:**[12] ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.93 (d, J = 6.9 Hz, 3 H), 2.77 (m, 1 H), 3.00 (bs, 1 H), 3.70 (s, 3 H), 3.76 (s, 3 H), 4.67 (d, J = 8.5 Hz, 1 H), 6.87 (m, 2 H), 7.27 (m, 2 H); IR (neat) 3450, 1730, 830 cm^{-1}.

***α,β-syn*-Methyl 3-hydroxy-2-methyl-3-(*o*-methoxyphenyl)propionate:** ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.10 (d, J = 6.9 Hz, 3 H), 2.97 (m, 1 H), 3.15 (bs, 1 H), 3.63 (s, 3 H), 3.83 (s, 3 H), 5.25 (d, J = 5.0 Hz, 1 H), 6.95 (m, 2 H), 7.36 (m, 2 H); IR (neat) 3450, 1730, 760 cm^{-1}.

***α,β-anti*-Methyl 3-hydroxy-2-methyl-3-(*o*-methoxyphenyl)propionate:** ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.04 (d, J = 6.9 Hz, 3 H), 3.02 (m, 1 H), 3.20 (bs, 1 H), 3.70 (s, 3 H), 3.84 (s, 3 H), 5.01 (d, J = 9.0 Hz, 1 H), 6.98 (m, 2 H), 7.33 (m, 2 H); IR (neat) 3450, 1730, 760 cm^{-1}.

***β,γ-syn*-Methyl 4-(benzyloxy)-3-hydroxy-2,2-dimethylpentanoate:**[13] ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.17 (s, 3 H), 1.25 (s, 3 H), 1.26 (d, J = 6.7 Hz, 3 H), 3.28 (d, J = 2.2 Hz, 1 H), 3.35 (s, 3 H), 3.40 (bs, 1 H), 3.65 (dq, J = 2.2, 6.7 Hz, 1 H), 4.23 (d, J = 12.0 Hz, 1 H), 4.55 (d, J = 12.0 Hz, 1 H), 7.33 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 16.5, 22.5, 23.4, 45.1, 51.4, 70.7, 73.6, 80.7, 127.6, 128.0, 138.1, 177.3; IR (neat) 3450, 1740, 1100, 700 cm^{-1}; HPLC (Zorbax SIL, eluent, hexane/EtOAc = 5/1, flow rate 1.0 mL/min, detection 254 nm light); t_R of syn isomer 8.7 min, t_R of anti isomer 15.2 min.

***β,γ-anti*-Methyl 4-(benzyloxy)-3-hydroxy-2,2-dimethylpentanoate:**[13] ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.18 (s, 3 H), 1.23 (s, 3 H), 1.28 (d, J = 6.7 Hz, 3 H), 2.46 (bs, 1 H), 3.40 (s, 3 H), 3.43 (dq, J = 6.2, 6.7 Hz, 1 H), 3.78 (d, J = 6.2 Hz, 1 H), 4.30 (d, J = 12.0 Hz, 1 H), 4.52 (d, J = 12.0 Hz, 1 H), 7.33 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 16.5, 19.5, 23.7, 45.5, 51.4, 70.8, 76.2, 78.6, 127.5, 128.2, 138.3, 177.5; IR (neat) 3450, 1730, 830 cm^{-1}; HPLC (vide supra).

***β,γ-syn*-Methyl 4-[(*tert*-butyldimethylsilyl)oxy]-2,2-dimethyl-3-hydroxypentanoate:** ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.07 (s, 3 H), 0.08 (s, 3 H), 0.87 (s, 9 H), 1.07 (s, 3 H), 1.10 (d, J = 6.6 Hz, 3 H), 1.13 (s, 3 H), 3.06 (bs, 1 H), 3.58 (s, 3 H), 3.83 (dq, J = 2.5, 6.6 Hz, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ −4.5, −3.6, 18.0, 20.8, 22.6, 26.0, 46.4, 51.6, 68.2, 79.3, 177.4; IR (neat) 3450, 1730, 1260 cm^{-1}; HPLC (Zorbax SIL, eluent, hexane/EtOAc = 15/1, flow rate 1.0 mL/min, detection RI); t_R of syn isomer 9.7 min, t_R of anti isomer 20.4 min.

***β,γ-anti*-Methyl 4-[(*tert*-butyldimethylsilyl)oxy]-2,2-dimethyl-3-hydroxypentanoate:** ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.87 (s, 9 H), 1.17 (d, J = 6.6 Hz, 1 H), 1.22 (s, 3 H), 1.23 (s, 3 H), 2.57 (bs, 1 H), 3.57 (s, 3 H), 3.6–4.0 (m, 2 H);

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^{13}C NMR (22.5 MHz, $CDCl_3$) δ -4.5, -4.3, 18.1, 19.8, 21.4, 23.4, 26.0, 45.6, 51.7, 70.3, 80.0, 177.5; IR (neat) 3450, 1740, 1260 cm^{-1}; HPLC (vide supra).

General Procedure of the Eu-Complex Catalyzed Reaction with Enal: Preparation of Methyl 5-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-4-pentenoate. To a solution of acrolein (66 μL, 1.0 mmol) in CH_2Cl_2 (3 mL) was added a 30 w/v % $CF_2ClCFCl_2$ solution of (+)-Eu(dppm)$_3$ (172 μL, 0.025 mmol) at room temperature. After cooling to -70 °C, (*E*)-1-[(*tert*-butyldimethylsilyl)oxy]-1-methoxy-1-propene (304 mg, 1.5 mmol) was added to the solution. The reaction mixture was stirred for 1 h at that temperature and poured into saturated $NaHCO_3$. The resultant mixture was extracted with EtOAc, three times (totally 100 mL), and washed with brine. The extract was dried over $MgSO_4$ and evaporated under reduced pressure. The resultant crude product was purified by column chromatography to give methyl 5-[(*tert*-butyldimethylsilyl)oxy]-2-methyl-4-pentenoate in 85% yield (220 mg).

Methyl 5-[(*tert*-butyldimethylsilyl)oxy]-2-methyl-4-pentenoate: ^1H NMR (90 MHz, $CDCl_3$) δ 0.09 (s, 6 H), 0.95 (s, 9 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 1.88 (m, 2 H), 3.27 (s, 3 H), 4.73 (m, 1 H), 6.15 (dt, *J* = 6.5, 2.0 Hz, 1 H); IR (neat) 1740, 1660, 1470, 1250, 1100, 840 cm^{-1}.

Methyl 5-[(*tert*-butyldimethylsilyl)oxy]-2,3-dimethyl-4-pentenoate (1:1 diastereomeric mixture): ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.09 (s, 6 H), 0.90 (s, 9 H) × 2, 1.05 (d, *J* = 6.7 Hz, 3 H), 1.13 (d, *J* = 6.7 Hz, 3 H), 1.26 (d, *J* = 6.7 Hz, 3 H), 1.38 (d, *J* = 6.7 Hz, 3 H), 2.3–2.7 (m, 1 H) × 2, 3.73 (s, 3 H) × 2, 5.00 (dd, *J* = 9.0, 11.5 Hz, 1 H), 5.30 (dd, *J* = 8.5, 11.5 Hz, 1 H), 6.40 (d, *J* = 11.5 Hz, 1 H), 6.41 (d, *J* = 11.5 Hz, 1 H); IR (neat) 1740, 1660, 1250, 1090 cm^{-1}.

(*E*)-Methyl 3-[(*tert*-butyldimethylsilyl)oxy]-2-methyl-4-hexenoate (1:1 diastereomeric mixture): ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 6 H), 0.09 (s, 6 H), 0.83 (s, 9 H), 0.87 (s, 9 H), 1.00 (d, *J* = 6.7 Hz, 3 H), 1.13 (d, *J* = 6.7 Hz, 3 H), 1.65 (d, *J* = 6.0 Hz, 3 H), 1.67 (d, *J* = 6.0 Hz, 3 H), 2.5–2.8 (m, 1 H) × 2, 3.63 (s, 3 H), 3.67 (s, 3 H), 4.17 (dd, *J* = 6.0, 9.0 Hz, 1 H), 4.30 (dd, *J* = 6.0, 8.5 Hz, 1 H), 5.2–5.7 (m, 2 H) × 2; IR (neat), 1740, 1250, 840 cm^{-1}.

Ethyl 5-[(*tert*-butyldimethylsilyl)oxy]-3-methyl-4-pentenoate: ^1H NMR (90 MHz, $CDCl_3$) δ 0.09 (s, 6 H), 0.95 (s, 9 H), 1.02 (d, *J* = 6.7 Hz, 3 H), 1.25 (t, *J* = 6.7 Hz, 3 H), 1.96 (m, 1 H), 2.4 (m, 1 H), 4.15 (q, *J* = 6.7 Hz, 2 H), 4.92 (dd, *J* = 8.5, 11.5 Hz, 1 H), 6.30 (d, *J* = 11.5 Hz, 1 H); IR (neat) 1730, 1660, 1250, 1080 cm^{-1}.

(*E*)-Ethyl 3-[(*tert*-butyldimethylsilyl)oxy]-4-hexenoate: ^1H NMR (90 MHz, $CDCl_3$) δ 0.09 (s, 6 H), 0.90 (s, 9 H), 1.25 (t *J* = 6.7 Hz, 3 H), 1.65 (d, *J* = 6.0 Hz, 3 H), 2.38 (dd, *J* = 6.7, 15.0 Hz, 1 H), 2.53 (dd, *J* = 7.5 Hz, 15.0 Hz, 1 H), 4.15 (q, *J* = 6.7 Hz, 2 H), 4.53 (m, 1 H), 5.53 (m, 2 H); IR (neat) 1740, 1250, 1060, 880, 840, 750 cm^{-1}.

3,1′-*syn*-3-[1′-(Carbomethoxy)ethyl]-1-[(trimethylsilyl)oxy]-1-cyclopentene:[14] ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 1.10 (d, *J* = 6.7 Hz, 3 H), 1.5–2.5 (m, 5 H), 2.90 (m, 1 H), 3.67 (s, 3 H), 4.48 (m, 1 H); IR (neat) 1730, 1680, 1250 cm^{-1}.

3,1′-*anti*-3-[1′-(Carbomethoxy)ethyl]-1-[(trimethylsilyl)oxy]-1-cyclopentene:[14] ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 1.10 (d, *J* = 6.7 Hz, 3 H), 1.5–2.5 (m, 5 H), 2.90 (m, 1 H), 3.67 (s, 3 H), 4.60 (m, 1 H); IR (neat) 1730, 1680, 1250 cm^{-1}.

3,1′-*syn*-3-[1′-(Carbomethoxy)ethyl]-1-cyclopentanone:[15] ^1H NMR (90 MHz, $CDCl_3$) δ 1.23 (d, *J* = 6.7 Hz, 3 H), 1.4–2.6 (m, 8 H), 3.67 (s, 3 H); IR (neat) 1750, 1730, 1470, 1080 cm^{-1}.

3,1′-*anti*-3-[1′-(Carbomethoxy)ethyl]-1-cyclopentanone:[15] ^1H NMR (90 MHz, $CDCl_3$) δ 1.20 (d, *J* = 6.7 Hz, 3 H), 1.4–2.6 (m, 5 H), 3.70 (s, 3 H); IR (neat) 1750, 1730, 1470, 1080 cm^{-1}.

3,1′-*syn*-3-[1′-(Carbomethoxy)ethyl]-1-[(trimethylsilyl)oxy]-1-cyclohexene:[14] ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 1.10 (d, *J* = 6.7 Hz, 3 H), 1.3–2.6 (m, 8 H), 3.67 (s, 3 H), 4.68 (m, 1 H); IR (neat) 1730, 1680, 1250, cm^{-1}.

3,1′-*anti*-3-[1′-(Carbomethoxy)ethyl]-1-[(trimethylsilyl)oxy]-1-cyclohexene:[14] ^1H NMR (90 MHz, $CDCl_3$) δ 0.08 (s, 9 H), 1.13 (d, *J* = 6.7 Hz, 3 H), 1.3–2.6 (m, 8 H), 3.67 (s, 3 H), 4.83 (m, 1 H); IR (neat) 1730, 1680, 1250 cm^{-1}.

3,1′-*syn*-3-[1′-(Carbomethoxy)ethyl]-1-cyclohexanone:[15] ^1H NMR (90 MHz, $CDCl_3$) δ 1.22 (d, *J* = 6.7 Hz, 3 H), 1.3–2.7 (m, 10 H), 3.67 (s, 3 H); IR (neat) 1730, 1460, 1080, cm^{-1}.

3,1′-*anti*-3-[1′-(Carbomethoxy)ethyl]-1cyclohexanone:[15] ^1H NMR (90 MHz, $CDCl_3$) δ 1.20 (d, *J* = 6.7 Hz, 3 H), 1.3–2.7 (m, 10 H), 3.70 (s, 3 H), 4.83 (m, 1 H); IR (neat) 1730, 1460, 1080 cm^{-1}.

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Synthesis of 2-Benzylidenebenzocyclobutenones via an Intramolecular Stille Coupling Reaction

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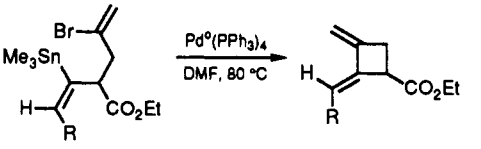
The coupling of vinylstannanes with vinyl or aryl bromides mediated by Pd^0 complexes was first by Stille[1] and has since found many applications. Particularly intriguing to us was the report by Piers and Lu who showed that an intramolecular version of this coupling reaction could be utilized to generate 2-alkylidene-3-methylenecyclobutanecarboxylates[2] (eq 1).



(1)

As part of our continuing interest in developing new routes to precursors of a variety of *o*-quinodimethanes,[3] we would like to report that the $Pd(PPh_3)_4$-catalyzed intramolecular coupling of compounds bearing both vinylstannane and aryl bromide moieties serves as a facile route to 2-benzylidenebenzocyclobutenones.

Very few examples of this arrangement of functional groups have been reported.[4] For example, 2-methylenebenzocyclobutene has been prepared in low yield by Trahanovsky[4a] via flash vacuum pyrolysis of 3-[(benzoyloxy)methyl]benzofuran and 2-(carbethoxyethylidene)-benzocyclobutenone was obtained by Cava[4b] from the dione and (carbethoxymethylene)triphenylphosphorane; the Wittig reaction did not yield the simple alkylidene analogues. The method described in this paper promises to be synthetically useful for the preparation of a variety of members of this class of compounds.

Reaction of the acetylenic ketone **1a**, prepared by coupling of 6-bromo-3,4-(methylenedioxy)benzoyl chloride with phenylacetylene in the presence of catalytic amounts of $PdCl_2(PPh_3)_2/CuI$,[5] 1.2 equiv of Bu_3SnH in toluene containing 2–3 mol % $PdCl_2(PPh_3)_2$, and PPh_3 (5.8 mol %) at room temperature for 5 min followed by a 2-h reflux, resulted in the formation of the isomeric 2-benzylidenebenzocyclobutenones **2a** and **3a** in a 1.1:1 ratio in 58% combined yield (70% based on recovered starting material). The initial exposure of **1** to these reaction conditions presumably afforded a mixture of stereoisomeric vinylstannanes **4a**,[6] which upon heating coupled with retention of configuration to give **2a** and **3a** (Scheme I).

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