Supporting Information

Organocatalytic direct Michael reaction of ketones and aldehydes with β -nitrostyrene in brine

Nobuyuki Mase,[†] Kaori Watanabe,[†] Hidemi Yoda,[†] Kunihiko Takabe,^{*,†}
Fujie Tanaka,[‡] Carlos F. Barbas III[‡]

Department of Molecular Science, Faculty of Engineering, Shizuoka University, 3-5-1 Johoku, Hamamatsu 432-8561, Japan and The Skaggs Institute for Chemical Biology and the Departments of Chemistry and Molecular Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037

tcktaka@ipc.shizuoka.ac.jp

[†] Shizuoka University, [‡]The Scripps Research Institute

General. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates (Merck 60 F₂₅₄) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in ethanol followed by heating. Flash column chromatography was performed using KANTO silica gel 60N (particle size 63-210 μ m). ¹H NMR and ¹³C NMR spectra were recorded on JEOL JNM-AL spectrometer at ambient temperature. Chemical shifts are given in δ relative to tetramethylsilane (TMS), the coupling constants *J* are given in Hz. The spectra were recorded in CDCl₃ as solvent at ambient temperature. TMS served as internal standard (δ = 0 ppm) for ¹H NMR and CDCl₃ was used as internal standard (δ = 77.0) for ¹³C NMR. Infrared spectra were recorded on a SHIMADZU FTIR-8200A spectrometer. Mass spectra were recorded on a SHIMADZU GCMS-QP5050 spectrometer. HPLC was carried out using a SHIMADZU LC-10AD intelligent pump, SPD-10A UV detector, and C-R8A integrator. All Michael reactions were carried out under an atmosphere of air in a closed system.

Organic substrates cyclohexanone (**5a**, 108-94-1), cyclopentanone (**5f**, 120-92-3), tetrahydrothiopyran-4-one (**5g**, 1072-72-6), acetone (**5h**, 67-64-1), *n*-butyraldehyde (**5i**, 123-72-8), isobutyraldehyde (**5j**, 78-84-2), 2-methylbutyraldehyde (**5k**, 96-17-3), 2-methylvaleraldehyde (**5l**, 123-15-9), *trans*- β -nitrostyrene (**6a**, 5153-67-3), L-proline (**8**, 147-85-3), L-prolinol (**9**, 23356-96-9), and (*S*)-1-(2-pyrrolidinylmethyl)pyrrolidine (**10a**, 51207-66-0) were obtained from commercial sources and were used without any purification. Michael acceptors, such as (*E*)-1-methoxy-4-(2-nitrovinyl)benzene (**6b**, 5576-97-6), (*E*)-2-(2-nitrovinyl)furan (**6c**, 32782-45-9), (*E*)-2-(2-nitrovinyl)naphthalene (**6d**, 37629-37-1), and (*E*)-1-nitro-3-(2-nitrovinyl)benzene (**6e**, 34441-47-9) were prepared by the methods previously described.¹ Catalyst **10b** was prepared by the methods previously described.² Michael adducts **7** are all known compounds. Seawater was taken from Pacific Ocean at Nakatajima Dune in Hamamatsu city and used without any purification.

A representative procedure for the Michael reaction using the diamine/acid bifunctional catalyst in brine was the following procedure for the reaction of cyclohexanone (**5a**) with *trans*- β -nitrostyrene (**6a**) in brine using the diamine **10b**/TFA bifunctional catalyst: To a mixture of diamine **10b** (19.0 mg, 0.05 mmol) in brine (0.5 mL) trifluoroacetic acid (3.9 μ L, 0.05 mmol) was added at 25 °C under air in a closed system. The reaction mixture was stirred for 3 min, then cyclohexanone (**5a**, 104 μ L, 1.0 mmol) and *trans*- β -nitrostyrene (**6a**, 75.3 mg, 0.5 mmol) were added. The reaction mixture was stirred for 24 h. Brine was removed by decantation. If extraction was needed, brine phase was extracted with ethyl acetate (3 x 1 mL) and organic extracts were dried over Na₂SO₄. Diastereoselectivity and conversion were determined by ¹H NMR analysis of the crude Michael product after short column chromatography purification (SiO₂, 1 g) to remove the catalyst. Purification by flash column chromatography (silica gel, hexane/AcOEt) gave the Michael product **7a** as a colorless solid. The enantiomeric excess (ee) of **7a** was determined by chiral HPLC analysis.

References

1. Andrey, O.; Alexakis, A.; Bernardinelli, G. *Org. Lett.* **2003**, *5* (14), 2559-2561.
2. (a) Betancort, J. M.; Sakthivel, K.; Thayumanavan, R.; Tanaka, F.; Barbas, C. F., III *Synthesis* **2004**, (9), 1509-1521. (b) Betancort, J. M.; Barbas, C. F., III *Org. Lett.* **2001**, *3* (23), 3737-3740. (c) Asami, M. *Bull. Chem. Soc. Jpn.* **1990**, *63* (3), 721-727.

No.	structure	CAS No.	¹ H NMR (CDCl ₃ , -CHAr, δ) ^a		HPLC ^b				
			<i>syn</i>	<i>anti</i>	column	Eluent ^c	Flow rate (mL/min)	<i>syn</i> (min)	<i>anti</i> (min)
7a		(<i>S,S</i>)-84025-87-6 (<i>R,R</i>)-154568-74-8 (<i>S,R</i>)-84025-83-2 (<i>R,S</i>)-84025-84-3 relative-(<i>S,S</i>)-51262-17-0 relative-(<i>R,S</i>)-51262-18-1 racemic-4591-64-4	3.78	4.02	AS-H	80:20	0.5	19.981 (2 <i>R</i> , 1' <i>S</i>) 28.557 (2 <i>S</i> , 1' <i>R</i>)	-
7b		(<i>S,R</i>)-233257-09-5 relative-(<i>S,S</i>)-99391-23-8 relative-(<i>R,S</i>)-67861-09-0 racemic-342819-96-9	3.71	3.91	AD-H	80:20	0.5	18.467 (2 <i>R</i> , 1' <i>S</i>) 22.583 (2 <i>S</i> , 1' <i>R</i>)	20.333 23.408
7c		(<i>S,S</i>)-256338-66-6	3.97	4.18	AD-H	95:5	0.5	30.300 (2 <i>S</i> , 1' <i>R</i>) 37.617 (2 <i>R</i> , 1' <i>S</i>)	22.183 36.150
7d		(<i>S,R</i>)-748788-76-3	3.95	4.18	AS-H	50:50	0.7	8.779 (2 <i>R</i> , 1' <i>S</i>) 14.907 (2 <i>S</i> , 1' <i>R</i>)	12.066 12.381
7e		(<i>S,R</i>)-83976-47-0	3.95	4.22	AD-H	90:10	0.5	42.650 (2 <i>R</i> , 1' <i>S</i>) 51.667 (2 <i>S</i> , 1' <i>R</i>)	48.350 62.883

7f		(<i>R,R</i>)-359876-15-6 (<i>S,R</i>)-359876-14-5 (<i>R,S</i>)-475294-96-3 relative-(<i>S,S</i>)-97954-71-7 relative-(<i>R,S</i>)-67861-25-0 racemic-4591-65-5	3.70	3.83	AS-H	80:20	0.5	21.858 (2 <i>R</i> , 1' <i>S</i>) 30.525 (2 <i>S</i> , 1' <i>R</i>)	19.575 23.492
7g		(<i>S,S</i>)-360062-52-8	3.98	4.15	AS-H	50:50	0.5	16.918 (2 <i>R</i> , 1' <i>S</i>) 20.760 (2 <i>S</i> , 1' <i>R</i>)	-
7h		(<i>S</i>)-475589-23-2 (<i>R</i>)-361204-86-6 chiral-(+)-142232-08-4 chiral-(-)-122348-55-4 racemic-1574-86-3	4.00		AS-H	80:20	0.5	27.561 (<i>R</i>) 36.247 (<i>S</i>)	

No.	structure	CAS No.	¹ H NMR (CDCl ₃ , -CHO, δ) ^a		HPLC ^b				
			<i>syn</i>	<i>anti</i>	column	Eluent ^c	Flow rate (mL/min)	<i>syn</i> (min)	<i>anti</i> (min)
7i		(<i>S,R</i>)-475294-88-3 (<i>R,S</i>)-384354-59-0 relative-(<i>R,S</i>)-697745-79-2 racemic-802552-10-9	9.69	9.46	AD-H	99:1	1.0	23.733 (2 <i>R</i> , 3 <i>R</i>) 28.233 (2 <i>S</i> , 3 <i>S</i>)	25.567 27.017
7j		(<i>R</i>)-748807-16-1 racemic-93086-29-4	9.54		AS-H	90:10	0.5	22.500 (<i>S</i>) 23.467 (<i>R</i>)	
7k		(<i>R,R</i>)-748807-19-4	9.52	9.51	AD-H	97:3	0.5	23.600 (2 <i>R</i> , 3 <i>R</i>) 26.133 (2 <i>S</i> , 3 <i>S</i>)	25.358 27.142

7l		(<i>R,R</i>)-748807-20-7	9.52	9.51	OD-H	95:5	1.0	27.850 (<i>2R</i> , <i>3R</i>) 40.942 (<i>2S</i> , <i>3S</i>)	21.650 43.517
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^a Diastereoselectivities were determined by peak integration of -CHAr for **7a-7h** and of -CHO for **7i-7l**. ^b λ = 254 nm. ^c Hexane and 2-propanol were used as an eluent.