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Erythro-Selective Aldol-Type Reaction of *N*-Sulfonylaldimines with Methyl Isocyanoacetate Catalyzed by Gold(I)

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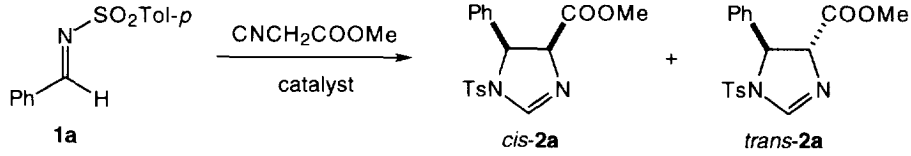
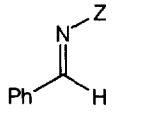
Abstract: Reaction of *N*-tosylaldimines **1** with methyl isocyanoacetate in the presence of 1 mol % of AuCl(*c*-HexNC) gave 4-methoxycarbonyl-5-alkyl-2-imidazolines **2** with high (over 89%) *cis* selectivity. The *cis*-imidazolinecarboxylates were isomerized into *trans* isomers by treatment with triethylamine. Hydrolysis of the *cis*- and *trans*-imidazolinecarboxylates gave *erythro*- and *threo*-α,β-diamino acids, respectively.

Aldol-type reaction of aldehydes with isocyanocarboxylates forming oxazolinecarboxylates is one of the useful methods for the preparation of β-hydroxy-α-amino acids.[1,2] Recently, the aldol reaction has been extended to catalytic enantioselective synthesis of β-hydroxy-α-amino acids by use of a well-designed chiral ferrocenylbisphosphine-gold(I)[3,4] or -silver(I)[5] catalyst. However, there have been very few reports on the reaction of imines with isocyanocarboxylates,[6] which would provide an efficient route to α,β-diamino acids. Here we report that the aldol reaction of sulfonylimines with methyl isocyanoacetate is catalyzed by transition metal complexes such as AuCl(*c*-HexNC)[7] to give *cis*-imidazolinecarboxylates with high diastereoselectivity.[8]

Scheme 1



1a *cis*-**2a** *trans*-**2a**



Z = Ph (**3a**)
Z = C_6H_4COOMe-*p* (**3b**)
Z = $P(O)Ph_2$ (**3c**)

Several imines of benzaldehyde were examined for the aldol reaction with methyl isocyanoacetate in refluxing dichloromethane in the presence of 5 mol % of cuprous chloride (Scheme 1), the copper(I) salt having been known to catalyze the aldol reaction with aldehydes.[2] It was found that *N*-*p*-toluenesulfonylimine **1a**[9] undergoes the copper-catalyzed aldol reaction to give 4-methoxycarbonyl-5-phenyl-1-*p*-toluenesulfonyl-2-imidazoline (**2a**) in a quantitative yield (entry 1 in Table 1). The catalytic aldol reaction is very slow or does not take place with imines containing phenyl (**3a**), *p*-carbomethoxyphenyl (**3b**), and diphenylphosphinyl (**3c**) on the nitrogen. In the absence of the catalyst, the aldol reaction of sulfonylimine **1a** does not take place at all under otherwise the same reaction conditions. Interestingly, some other transition metal salts or complexes also catalyzed the aldol reaction of sulfonylimine **1a** (entries 2-8), the diastereoselectivity in forming *cis*-**2a** or *trans*-**2a** being dependent on the catalysts used. The highest *cis* selectivity was observed with gold(I) catalyst,

Table 1. Aldol Reaction of Imines **1** with Methyl Isocyanoacetate[a]

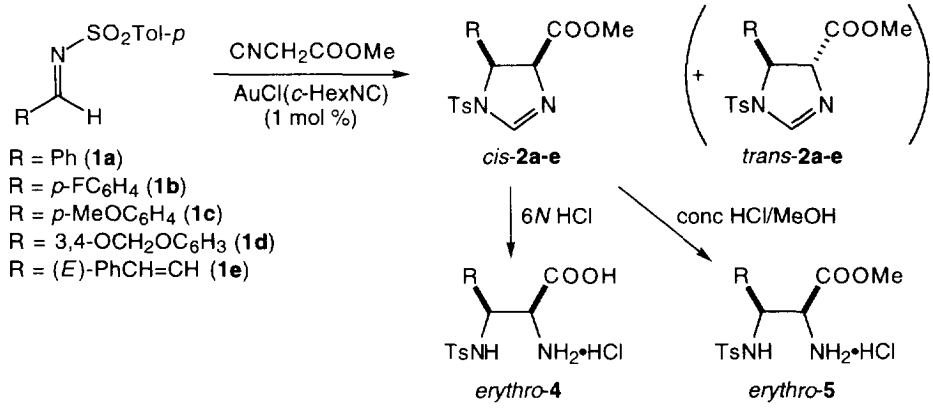
entry	imine **1**	catalyst	solvent	reaction temp (°C)	reaction time (h)	yield (%)[b] of **2**	ratio[c] of *cis/trans*
1	**1a**	CuCl (5 mol %)	CH_2Cl_2	reflux	2	>99	73/27
2	**1a**	AuCl(*c*-HexNC) (5 mol %)	CH_2Cl_2	reflux	23	>99	83/17
3	**1a**	AuCl(*c*-HexNC) (1 mol %)	MeCN	20	8	>99	89/11
4	**1a**	AgOTf (5 mol %)	CH_2Cl_2	reflux	24	90	75/25
5	**1a**	$PdCl_2(MeCN)_2$ (5 mol %)	CH_2Cl_2	reflux	24	96	54/46
6	**1a**	$NiCl_2(PPh_3)_2$ (5 mol %)	CH_2Cl_2	reflux	3	>99	38/62
7	**1a**	$[RhCl(COD)]_2$ (5 mol %)	CH_2Cl_2	20	0.2	>99	70/30
8	**1a**	$[RuCl_2(COD)]_n$ (5 mol %)	CH_2Cl_2	reflux	75	89	52/48
9	**1b**	AuCl(*c*-HexNC) (1 mol %)	MeCN	20	18	>99	90/10
10	**1c**	AuCl(*c*-HexNC) (1 mol %)	MeCN	20	40	>99	90/10
11	**1d**	AuCl(*c*-HexNC) (1 mol %)	MeCN	20	40	>99	90/10
12	**1e**	AuCl(*c*-HexNC) (5 mol %)	MeCN	35	40	95	95/5

[a] Solvent (1.0 mL), imine (0.50 mmol), methyl isocyanoacetate (0.55 mmol), and catalyst (0.025 or 0.005 mmol). [b] Isolated yield by silica gel column chromatography. [c] The ratio was determined by ^1H NMR of the products.

AuCl(*c*-HexNC), which gave *cis*-**2a** with 83% selectivity (entry 2). Silver(I), palladium(II), nickel(II), rhodium(I), and ruthenium(II) complexes gave lower *cis*-selectivity than the gold(I). The *cis* selectivity in the gold(I)-catalyzed reaction was increased to 89% by carrying out the reaction in acetonitrile at 20 °C (entry 3).[10]

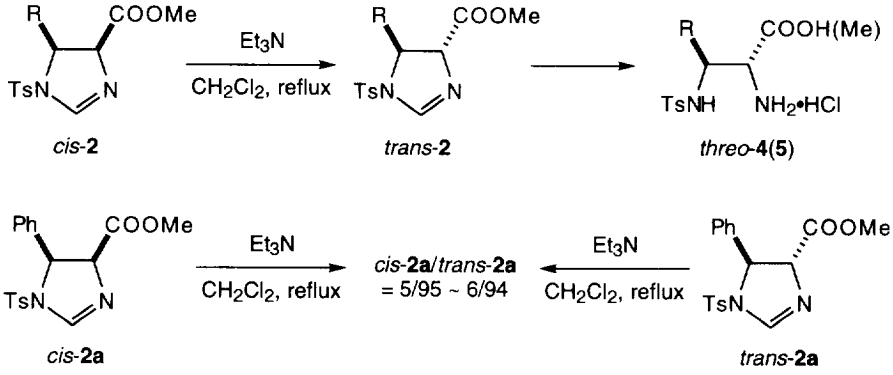
The high *cis* selectivity was also observed in the gold(I)-catalyzed reaction of *N*-sulfonylimines of *p*-fluorobenzaldehyde (**1b**), *p*-methoxybenzaldehyde (**1c**), 3,4-methylenedioxybenzaldehyde (**1d**), and cinnamaldehyde (**1e**) (Scheme 2), which gave the corresponding *cis*-imidazolinecarboxylates **2**[11] with over 90% *cis* selectivity (entries 9-12). It is interesting that the present aldol reaction of *N*-sulfonylimines proceeds with high *cis* selectivity while that of aldehydes usually gives *trans*-oxazolinecarboxylates preferentially.[2-5,10] The *cis*-imidazolines **2** were readily converted into *erythro*-α,β-diamino acids **4** or their methyl esters **5**[12] without epimerization, by treatment with 6*N* hydrochloric acid or conc HCl in methanol, respectively.

Scheme 2



The *cis*-imidazolines *cis*-**2** were isomerized into thermodynamically more stable *trans* isomers[13] by treatment with triethylamine[14] in refluxing dichloromethane for 24 h (Scheme 3). The equilibrium ratio of *cis/trans* isomers in the base-catalyzed isomerization is 5/95 ~ 6/94 for **2a**. The isomerization starting with isomerically pure *cis*-**2a** or *trans*-**2a** resulted in a mixture of the same composition of the isomers shown above after the equilibrium is reached. Acidic hydrolysis or methanolysis of *trans*-**2** in the same manner as above gave *threo* isomers of α,β-diamino acids **4** or their methyl esters **5**.[12]

Scheme 3



To summarize, we have succeeded in the catalytic aldol reaction of imines with isocyanoacetate by use of *N*-sulfonylimines and AuCl(*c*-HexNC) as a catalyst giving *cis*-imidazolines selectively, which provides an efficient route to *erythro*-α,β-diamino acids. *Threo* isomers were also accessible by the base-catalyzed isomerization of *cis*-imidazolines into *trans*-imidazolines.

Acknowledgment:

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REFERENCES AND NOTES:

1. For reviews on the aldol reaction of isocyanocarboxylates: (a) Hoppe, D. *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 789-804. (b) Matsumoto, K.; Moriya, T.; Suzuki, M. *J. Synth. Org. Chem., Jpn.* **1985**, *43*, 764-776.
2. (a) Ito, Y.; Matsuura, T.; Saegusa, T. *Tetrahedron Lett.* **1985**, *26*, 5781-5784. (b) Saegusa, T.; Ito, Y.; Kinoshita, H.; Tomita, S. *J. Org. Chem.* **1971**, *36*, 3316-3323.
3. (a) Soloshonok, V. A.; Kacharov, A. D.; Hayashi, T. *Tetrahedron* **1996**, *52*, 245-254. (b) Hayashi, T.; Sawamura, M.; Ito, Y. *Tetrahedron* **1992**, *48*, 1999-2012. (c) Ito, Y.; Sawamura, M.; Hamashima, H.; Emura, T.; Hayashi, T. *Tetrahedron Lett.* **1989**, *30*, 4681-4684. (d) Sawamura, M.; Ito, Y.; Hayashi, T. *Tetrahedron Lett.* **1989**, *30*, 2247-2250. (e) Ito, Y.; Sawamura, M.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 239-240. (f) Ito, Y.; Sawamura, M.; Kobayashi, M.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 6321-6324. (g) Ito, Y.; Sawamura, M.; Shirakawa, E.; Hayashizaki, K.; Hayashi, T. *Tetrahedron Lett.* **1988**, *29*, 235-238. (h) Ito, Y.; Sawamura, M.; Hayashi, T. *Tetrahedron Lett.* **1987**, *28*, 6215-6218. (i) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405-6406.
4. (a) Pastor, S. D.; Kesselring, R.; Togni, A. *J. Organomet. Chem.* **1992**, *429*, 415-420. (b) Pastor, S. D.; Togni, A. *Helv. Chim. Acta* **1991**, *74*, 905-933. (c) Togni, A.; Blumer, R. E.; Pregosin, P. S. *Helv. Chim. Acta* **1991**, *74*, 1533-1543. (d) Togni, A.; Pastor, S. D. *J. Org. Chem.* **1990**, *55*, 1649-1664. (e) Pastor, S. D.; Togni, A. *Tetrahedron Lett.* **1990**, *31*, 839-840. (f) Togni, A.; Pastor, S. D.

Tetrahedron Lett. **1989**, *30*, 1071-1072. (g) Togni, A.; Pastor, S. D.; Rihs, G. *Helv. Chim. Acta* **1989**, *72*, 1471-1478. (h) Pastor, S. D.; Togni, A. *J. Am. Chem. Soc.* **1989**, *111*, 2333-2334.

5. (a) Hayashi, T.; Uozumi, Y.; Yamazaki, A.; Sawamura, M.; Hamashima, H.; Ito, Y. *Tetrahedron Lett.* **1991**, *32*, 2799-2802. (b) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Org. Chem.* **1990**, *55*, 5935-5936.
6. Reaction of α-metalated isocyanide with imines has been reported: Meyer, R.; Schöllkopf, U.; Böhme, P. *Liebigs Ann. Chem.* **1977**, 1183-1193.
7. Bonati, F.; Minghetti, G. *Gazz. Chim. Ital.* **1973**, *103*, 373-386.
8. Transition metal-catalyzed aldol-type reaction of imines has been reported: (a) Shida, N.; Kubota, Y.; Fukui, H.; Asao, N.; Kadota, I.; Yamamoto, Y. *Tetrahedron Lett.* **1995**, *36*, 5023-5026. (b) Yamamoto, Y.; Kubota, Y.; Honda, Y.; Fukui, H.; Asao, N.; Nemoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 3161-3162.
9. (a) Love, B. E.; Raje, P. S.; Williams II, T. C. *Synlett* **1994**, 493-494. (b) Boger, D. L.; Corbett, W. L. *J. Org. Chem.* **1992**, *57*, 4777-4780. (c) Trost, B. M.; Marrs, C. *J. Org. Chem.* **1991**, *56*, 6468-6470.
10. Under similar reaction conditions (at 40 °C, 1 mol % AuCl(*c*-HexNC) in MeCN), benzaldehyde gave *trans*-oxazolinecarboxylate predominantly (*cis/trans* = 30/70).
11. ^{1}H NMR spectra (270 MHz, $CDCl_3$) for *cis*-imidazolines **2** are as follows: *cis*-**2a:** δ 2.38 (s, 3 H), 3.14 (s, 3 H), 5.15 (d, *J* = 11.6 Hz, 1 H), 5.22 (dd, *J* = 11.6, 2.0 Hz, 1 H), 6.99 (d, *J* = 8.3 Hz, 2 H), 7.08-7.22 (m, 5 H), 7.41 (d, *J* = 8.3 Hz, 2 H), 7.77 (d, *J* = 2.0 Hz, 1 H). *cis*-**2b:** δ 2.40 (s, 3 H), 3.20 (s, 3 H), 5.14 (d, *J* = 11.6 Hz, 1 H), 5.21 (dd, *J* = 11.6, 2.0 Hz, 1 H), 6.81 (t, *J* = 8.6 Hz, 2 H), 6.95-7.02 (m, 2 H), 7.18 (d, *J* = 8.3 Hz, 2 H), 7.42 (d. *J* = 8.3 Hz, 2 H), 7.77 (d. *J* = 2.0 Hz, 1H). *cis*-**2c:** δ 2.39 (s, 3 H), 3.21 (s, 3 H), 3.74 (s, 3 H), 5.12 (d, *J* = 11.2 Hz, 1 H), 5.19 (dd, *J* = 11.2, 2.0 Hz, 1 H), 6.62 (d, *J* = 8.6 Hz, 2 H), 6.90 (d, *J* = 8.6 Hz, 2 H), 7.14 (d, *J* = 8.3 Hz, 2 H), 7.40 (d, *J* = 8.3 Hz, 2 H), 7.76 (d, *J* = 2.0 Hz, 1 H). *cis*-**2d:** δ 2.40 (s, 3 H), 3.30 (s, 3 H), 5.09 (d, *J* = 11.2 Hz, 1 H), 5.18 (dd, *J* = 11.2, 2.3 Hz, 1 H), 5.85 (d, *J* = 1.3 Hz, 1 H), 5.89 (d, *J* = 1.3 Hz, 1 H), 6.34 (d, *J* = 1.7 Hz, 1 H), 6.55 (dd, *J* = 8.3, 1.7 Hz, 1 H), 6.59 (d, *J* = 8.3 Hz, 1 H), 7.18 (d, *J* = 8.6 Hz, 2 H), 7.44 (d, *J* = 8.6 Hz, 2 H), 7.75 (d, *J* = 2.3 Hz, 1 H). *cis*-**2e:** δ 2.33 (s, 3 H), 3.58 (s, 3 H), 4.82 (dd, *J* = 10.9, 9.2 Hz, 1 H), 5.04 (dd, *J* = 10.9, 2.3 Hz, 1 H), 5.54 (dd, *J* = 15.8 Hz, 9.2 Hz, 1 H), 6.52 (d, *J* = 15.8 Hz, 1 H), 7.07-7.12 (m, 3 H), 7.15 (d, *J* = 8.3 Hz, 2 H), 7.21-7.28 (m, 2 H), 7.64 (d, *J* = 8.3 Hz, 2 H), 7.67 (d, *J* = 2.3 Hz, 1 H).
12. ^{1}H NMR spectra (270 MHz, CD_3OD) for α,β-diamino acids **4** and esters **5** are as follows: *erythro*-**4a**: δ 2.34 (s, 3 H), 4.39 (d, *J* = 5.3 Hz, 1 H), 4.76 (d, *J* = 5.3 Hz, 1 H), 7.10-7.25 (m, 7 H), 7.60 (d, *J* = 8.3 Hz, 2 H). *erythro*-**5a**: δ 2.31 (s, 3 H), 3.75 (s, 3 H), 4.39 (d, *J* = 6.3 Hz, 1 H), 4.71 (d, *J* = 6.3 Hz, 1 H), 7.07-7.23 (m, 7 H), 7.54 (d, *J* = 8.3 Hz, 2 H). *threo*-**4a**: δ 2.30 (s, 3 H), 4.14 (d, *J* = 8.9 Hz, 1 H), 4.68 (d, *J* = 8.9 Hz, 1 H), 6.99-7.18 (m, 7 H), 7.47 (d, *J* = 8.3 Hz, 2 H). *threo*-**5a**: δ 2.28 (s, 3 H), 3.44 (s, 3 H), 4.24 (d, *J* = 8.9 Hz, 1 H), 4.68 (d, *J* = 8.9 Hz, 1 H), 6.99 (d, *J* = 8.3 Hz, 2 H), 7.06-7.19 (m, 5 H), 7.47 (d, *J* = 8.3 Hz, 2 H).
13. ^{1}H NMR spectra (270 MHz, $CDCl_3$) for *trans*-imidazolines **2** are as follows: *trans*-**2a:** δ 2.39 (s, 3 H), 3.70 (s, 3 H), 4.66 (dd, *J* = 7.6, 2.3 Hz, 1 H), 5.08 (d, *J* = 7.6 Hz, 1 H), 7.15-7.27 (m, 7 H), 7.46 (d, *J* = 8.3 Hz, 2 H), 7.65 (d, *J* = 2.3 Hz, 1 H). *trans*-**2b:** δ 2.42 (s, 3 H), 3.71 (s, 3 H), 4.63 (dd, *J* = 7.6, 2.0 Hz, 1 H), 5.06 (d, *J* = 7.6 Hz, 1 H), 6.93 (t, *J* = 8.6 Hz, 2 H), 7.02-7.18 (m, 2 H), 7.22 (d, *J* = 8.3 Hz, 2 H), 7.48 (d, *J* = 8.3 Hz, 2 H), 7.64 (d, *J* = 2.0 Hz, 1 H). *trans*-**2c:** δ 2.40 (s, 3 H), 3.70 (s, 3 H), 3.78 (s, 3 H), 4.65 (dd, *J* = 7.6, 2.0 Hz, 1 H), 5.04 (d, *J* = 7.6 Hz, 1 H), 6.75 (d, *J* = 8.9 Hz, 2 H), 7.06 (d, *J* = 8.9 Hz, 2 H), 7.19 (d, *J* = 8.3 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 7.64 (d, *J* = 2.0 Hz, 1 H). *trans*-**2d:** δ 2.41 (s, 3 H), 3.70 (s, 3 H), 4.62 (dd, *J* = 7.6, 1.7 Hz, 1 H), 5.00 (d, *J* = 7.6 Hz, 1 H), 5.89 (t, *J* = 1.0 Hz, 1 H), 5.92 (t, *J* = 1.0 Hz, 1 H), 6.49 (s, 1 H), 6.68 (s, 2 H), 7.22 (d, *J* = 8.3 Hz. 2 H). 7.49 (d, *J* = 8.3 Hz, 2 H), 7.63 (d, *J* = 1.7 Hz, 1 H). *trans*-**2e:** δ 2.39 (s, 3 H), 3.73 (s, 3 H), 4.55 (dd, *J* = 7.6, 2.3 Hz, 1 H), 4.74 (dd, *J* = 8.3, 7.6 Hz, 1 H), 5.83 (dd, *J* = 15.8 Hz, 8.3 Hz, 1 H), 6.60 (d, *J* = 15.8 Hz, 1 H), 7.21-7.33 (m, 7 H), 7.58 (d, *J* = 2.3 Hz, 1 H), 7.68 (d, *J* = 8.2 Hz, 2 H).
14. Base-catalyzed isomerization of an oxazolinecarboxylate has been reported: Matsumoto, K.; Ozaki, Y.; Suzuki, M.; Miyoshi, M. *Agric. Biol. Chem.* **1976**, *40*, 2045-2050. See also ref 3i.

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