conformation is quadrangular [1363][11] with the six bonds joining C(3) to C(29) forming a "convex side" and a pseudo mirror plane transfixing the double bond and the C(6) atom.

The chloride ion is held within the molecule by hydrogen bonding with two NH and one OH groups. The positive charge resides on the pyrrolidinium nitrogen atom as attested by the longer than usual bond lengths (~1.522 Å) of the attached α-carbon atoms.[12]

In summary, the structure of manzamine A hydrochloride is unprecedented in nature.[13] Moreover, its provenance is problematical as there appears to be no obvious biogenetic path.

Acknowledgment. We thank Prof. K. L. Rinehart, Jr., University of Illinois, for recording the mass spectra.

Supplementary Material Available: Tables of atomic coordinates, anisotropic displacement parameters, bond lengths, bond angles, and torsional angles (8 pages); table of structure factors (45 pages). Ordering information is given on any current masthead page.

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Catalytic Asymmetric Aldol Reaction: Reaction of Aldehydes with Isocyanoacetate Catalyzed by a Chiral Ferrocenylphosphine-Gold(I) Complex

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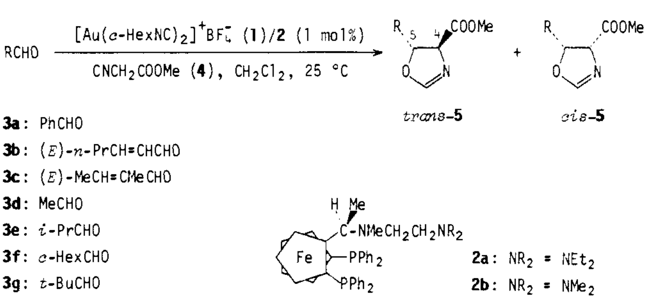
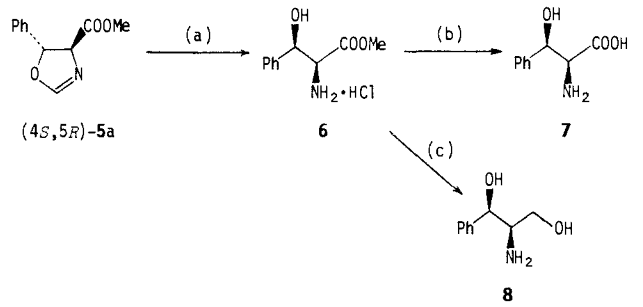
There has been great interest in the enantioselective aldol reactions of enolates with aldehydes to produce optically active β-hydroxycarbonyl compounds[1] and considerable efforts have been devoted to developing effective chiral enolates, e.g., boron enolates of chiral ketones[2] and imides[3] and tin enolates coordinated with chiral diamines.[4] Yet, there have been few reports on the use of chiral catalysts for such reactions.[5] Here we report that a chiral ferrocenylphosphine-gold(I) complex catalyzes the asymmetric aldol reaction of an isocyanoacetate with aldehydes,[6-8] producing optically active 5-alkyl-2-oxazoline-4-carboxylates with high enantio- and diastereoselectivity which are useful synthetic intermediates to optically active β-hydroxyamino acids and their derivatives.

Scheme I



Scheme II[a]



[a] (a) Concentrated HCl, MeOH, 50 °C, 3 h. (b) 6 N HCl, 80 °C, 6 h; amberlite IR-120B (H$^+$). (c) LiAlH$_4$/THF, reflux, 4 h; H$_2$O.

In numerous studies carried out in this laboratory, we have found that the gold complex generated in situ by mixing bis(cyclohexyl isocyanide)gold(I) tetrafluoroborate (I)[9] and (*R*)-*N*-methyl-*N*-[2-(dialkylamino)ethyl]-1-[(*S*)-1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine (**2**)[10,11] is an effective catalyst for the reaction of various types of aldehydes (**3**) with methyl isocyanoacetate (**4**) (Scheme I). A typical procedure is given for the reaction of benzaldehyde (**3a**). To a solution of the cationic gold complex **1** (27.5 mg, 0.055 mmol), the ferrocenylphosphine **2a** (39.7 mg, 0.056 mmol), and **4** (0.549 g, 5.54 mmol) in dry dichloromethane (5.5 mL) was added **3a** (0.642 g, 6.05 mmol), and the mixture was stirred under nitrogen at 25 °C for 20 h.[12] Evaporation of the solvent followed by bulb-to-bulb distillation (ca. 110 °C (0.3 mmHg)) gave 1.08 g (95% yield) of 4-(methoxycarbonyl)-5-phenyl-2-oxazoline (**5a**) (trans/cis = 89/11). The enantiomeric purities of *trans*-**5a** ($[\alpha]^{20}_{\mathrm{D}}$ +297° (*c* 1.2, THF)) and *cis*-**5a** ($[\alpha]^{20}_{\mathrm{D}}$ −80° (*c* 1.2, THF)), readily separated by column chromatography on silica gel (hexane/ethyl acetate = 1/2), were determined to be 96% ee and 49% ee, respectively, by ^{1}H NMR studies using Eu(dcm)$_3$.[13] The *trans*-**5a** was converted in high yields into known L-(−)-*threo*-β-phenylserine (**7**)[14] and (1*R*,2*R*)-(−)-1-phenyl-2-amino-1,3-propanediol (**8**)[15] via methyl phenylserinate (**6**) (Scheme II). Therefore, (+)-*trans*-**5a** has the

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(3) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

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(9) Bonati, F.; Minghetti, G. *Gazz. Chim. Ital.* **1973**, *103*, 373.

(10) The preparation of the ferrocenylphosphine **2b** has been reported.[11a] The ligand **2a** was prepared in a similar manner by use of *N*-methyl-*N*-[2-(diethylamino)ethyl]amine: $[\alpha]^{25}_{\mathrm{D}}$ −368° (*c* 0.29, chloroform). ^{1}H NMR (CDCl$_3$) δ 0.88 (t, *J* = 7 Hz, 6 H), 1.15 (d, *J* = 7 Hz, 3 H), 1.66 (s, 3 H), 1.64-2.04 (m, 2 H), 2.04-2.40 (m, 2 H), 2.38 (q, *J* = 7 Hz, 4 H), 3.54 (m, 1 H), 3.67 (m, 1 H), 3.99 (m, 1 H), 4.03-4.12 (m, 3 H), 4.36 (m, 2 H), 7.0-7.7 (m, 20 H).

(11) (a) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138. (b) Hayashi, T.; Kumada, M. *Acc. Chem. Res.* **1982**, *15*, 395.

(12) The completion of the reaction is checked by silica gel TLC (hexane/ethyl acetate = 2/1).

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(14) $[\alpha]^{20}_{\mathrm{D}}$ −50.7° (*c* 2.0, 6 N HCl). The reported rotation is $[\alpha]^{20}_{\mathrm{D}}$ −50.2 ± 2° (*c* 2, 6 N HCl): Vogler, K. *Helv. Chim. Acta* **1950**, *33*, 2111.

(15) $[\alpha]^{20}_{\mathrm{D}}$ −26.7° (*c* 1.0, methanol). The reported rotation for (1*S*,2*S*)-**8** is $[\alpha]^{22}_{\mathrm{D}}$ +26.6° (*c* 10.0, methanol): Meyers, A. I.; Knaus, G.; Kamata K.; Ford, M. E. *J. Am. Chem. Soc.* **1976**, *98*, 567.

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Table I. Reaction of Aldehydes **3** with Isocyanoacetate **4** Catalyzed by the Chiral Ferrocenylphosphine–Gold Complex[a]

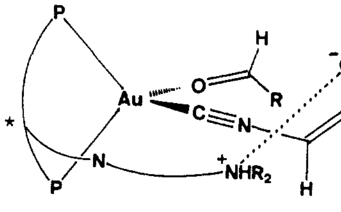
aldehyde **3**	ligand **2**	yield,[b] % of **5**	ratio[c] of trans/cis	*trans*-**5** % ee,[d] $[\alpha]^{20}_D$ (THF)[e]	*cis*-**5** % ee[d]
PhCHO (**3a**)	**2a**	98	89/11	96 (4*S*,5*R*),[f] + 297°	49[g] (4*R*,5*R*)[f]
	2b	91	90/10	94 (4*S*,5*R*),[f] +287°	4 (4*S*,5*S*)[h]
(*E*)-*n*-PrCH=CHCHO (**3b**)	**2a**	83	81/19	84 (4*S*,5*R*),[h] +230°	52 (4*R*,5*R*)[h]
	2b	97	80/20	87 (4*S*,5*R*),[h] +244°	0
(*E*)-MeCH=CMeCHO (**3c**)	**2b**	89	91/9	95 (4*S*,5*R*),[h] +311°	31 (4*R*,5*R*)[h]
MeCHO (**3d**)	**2a**	100	84/16	72 (4*S*,5*R*),[i] +173°[i]	44 (4*R*,5*R*)[h]
i-PrCHO (**3e**)	**2a**	99	98/2	92 (4*S*,5*R*),[h] +250°	
c-HexCHO (**3f**)	**2a**	95	97/3	90 (4*S*,5*R*),[h] +236°	
	2b	96	98/2	81 (4*S*,5*R*),[h] +202°	
t-BuCHO (**3g**)	**2a**	100[j]	100/0	97 (4*S*,5*R*),[h] +265°	

[a] The reaction was carried out in dichloromethane at 25 °C for 20–40 h. **3**/**4**/catalyst = 1.1/1.0/0.01. [b] Isolated yield by distillation based on **4**. [c] Determined by ^{1}H NMR analysis. [d] Determined by ^{1}H NMR spectra using chiral shift reagent Eu(dcm)$_3$. The OCH$_3$ singlet of the major enantiomer of *trans*-**5** always appeared at a higher field than that of the minor one. [e] *c* 1.0–1.5. [f] The determination of the configuration is described in the text. [g] $[\alpha]^{20}_D$ −80° (*c* 1.2, THF). [h] Configuration assigned by similarity in shifts using the chiral shift reagent. [i] Literature rotation for optically pure (4*S*,5*R*)-**5d** is $[\alpha]^{13}_D$ +231° (*c* 0.4, THF): Ito, Y.; Ito, I.; Hirao, T.; Saegusa, T. *Synth. Commun.* **1974**, *4*, 97. [j] For 60 h with 2 mol % of the catalyst.

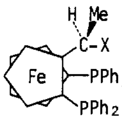
configuration of 4*S*,5*R*. Epimerization of (−)-*cis*-**5a** at C-4 with triethylamine in refluxing benzene[8b] gave (4*S*,5*R*)-*trans*-**5a**, indicating that the configuration of (−)-*cis*-**5a** is 4*R*,5*R*.

Representative results summarized in Table I were obtained under similar conditions.[16] High enantioselectivity (>90% ee) and high trans selectivity (>97%) were observed in the reaction of secondary and tertiary alkyl aldehydes **3e–g**, while acetaldehyde (**3d**) gave the lower selectivity. The gold catalyst was also effective for the reaction of α,β-unsaturated aldehydes **3b** and **3c** to give the corresponding oxazolines of 87% ee and 95% ee, respectively. It appears that the aldehydes with the larger substitutent gave the higher enantio- and diastereoselectivity.

The high efficiency of the ferrocenylphosphine ligand **2** may be visualized by the transition state A where the dialkylamino group at the end of the side chain on **2** participates in the formation of enolate of isocyanoacetate coordinated with gold.[17] It is probable that the participation may permit a favorable arrangement of the enolate and aldehyde on the gold(I) at the diastereomeric transition state to bring about high stereoselectivity. Use of the phosphine ligand **9**,[18] which is analogous to **2a** but with 3-(diethylamino)propyl side chain, resulted in the formation of **5a** with 26% ee, indicating that the distance between the amino group and the ferrocene moiety is of crucial importance for the selectivity. The ferrocenylphosphine BPPFA (**10**)[11] which lacks the side chain, as well as chiraphos,[19] DIOP,[20] and *p*-TolBINAP,[21] gave almost racemic oxazolines. It should be noted that the use of gold is essential for the high selectivity, silver or copper catalyst being much less selective. This may be ascribed to the stronger affinity of gold(I) to phosphorus atoms.[22] The ligand **2** can coordinate to gold with two phosphorus atoms leaving two nitrogen atoms free while silver or copper forms undesirable species by coordination of **2** with nitrogen atom(s) instead of phosphorus.[23]



A



9: X = NMe(CH$_2$)$_3$NEt$_2$

10: X = NMe$_2$ (BPPFA)

Supplementary Material Available: ^{1}H NMR data for the oxazolines **5** (1 page). Ordering information is given on any current masthead page.

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(16) Satisfactory spectral and analytical data were obtained on all new compounds (see supplementary material).

(17) It has been observed that the copper-catalyzed aldol reaction is accelerated by the addition of triethylamine.[7a]

(18) $[\alpha]^{25}_D$ −312° (*c* 0.69, chloroform). Prepared in a similar manner to **2b**.[11]

(19) (*S*,*S*)-1,2-Bis(diphenylphosphino)butane: Fryzuk, M. D.; Bosnich, B. *J. Am. Chem. Soc.* **1977**, *99*, 6262.

(20) (−)-2,3-*O*-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane: Kagan, H. B.; Dang, T. P. *J. Am. Chem. Soc.* **1972**, *94*, 6429.

(21) (*R*)-2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl: Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.

(22) Pearson, R. G. *J. Chem. Ed.* **1968**, *45*, 581 and 643.

(23) The ^{31}P and ^{1}H NMR spectra of the ferrocenylphosphine **2** complexed with gold(I), silver(I), or copper(I) supported the mode of the coordination, which will be fully described elsewhere.

Unusual p*K*s and Bond Paths of 1,3-Dilithiocyclobutane

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The ion triplet model introduced by Streitwieser[1] interprets the stability of dianion salts in terms of the electrostatic interactions between the dianion and two bridging cations. The stability of the ion triplet is due to its four strong attractive interactions and only two weaker repulsive interactions. Streitwieser and Swanson[2] experimentally determined the difference between the first and second p*K*s of 9,9′-bifluorenyl and 2,2′-biindenyl to be less than one p*K* unit. They concluded that the low second p*K* results from the formation of a stable ion triplet. The experimental[3] and calculational[4] work by Schleyer confirms the existence of the ion triplet. In fact, Schleyer, Kos, and Kaufman[5] have determined the disproportionation of 1,3-dilithiopropane to be 19.4 kcal mol^{-1} endothermic at the 3-21G level. This indicates that the second

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