has an octahedral coordination geometry in contradistinction with the sulfur-donor analogues. Carbon–oxygen bond lengths of the ligands average to 1.353 (6) Å, a value associated with localized catecholate ligands.[5a] Rhenium–oxygen bond lengths average to 1.932 (4) Å, a value shorter than other reported Re–O lengths to all but oxo ligands by more than 0.05 Å. For comparison, Herrmann has recently reported Re–O lengths of 1.99 (1) Å for the Re(V) complex $(\eta^5\text{-}C_5Me_5)Re(Cl_4Cat)_2$.[11] As a d^1, Re(VI) complex, $Re(DBCat)_3$ has a solid-state magnetic moment of 1.18 (1) μ_B, showing the pronounced effect of spin–orbit coupling, and a uniquely simple solution EPR spectrum (Figure 2). The isotropic spectrum recorded at room temperature in dichloromethane solution consists of six lines due to the $I = {}^5/_2$ ^{185}Re and ^{187}Re isotopes. Spacing between lines shows evidence of a strong second-order effect. Correction for this effect gave isotropic $\langle g \rangle$ and A values of 2.010 and 0.002 cm^{-1}. Other Re(VI) complexes show only a broad signal in solution at room temperature with no resolved hyperfine in cases where a signal can be observed.[12] Cyclic voltammetry on $Re(DBCat)_3$ shows a reversible, one-electron reduction to the Re(V) species, $Re(DBCat)_3^-$, at −0.656 V (vs. Fc^+/Fc), and a reversible oxidation at +0.594 V.[13] Oxidation may occur either at one ligand to give the species $Re(DBSQ)(DBCat)_2^+$ with mixed-charge quinone ligands or at the metal to give the Re(VII) complex $Re(DBCat)_3^+$.

Charge distribution within the metal catecholate or, more generally, the metal quinone chelate ring is determined by the relative energies of metal and quinone electronic levels. Effects which change this order result in transfer of charge between quinone and metal. One particular effect is related to the position of the metal in the group and valence d-orbital energy. Neutral bis- and tris(quinone) complexes of first-row metals contain semiquinone ligands, while related complexes prepared with metals of the second and third transition series contain catecholates with higher oxidation state metal ions. For example, complexes of chromium are of the form tris(semiquinone)chromium(III), while molybdenum analogues are tris(catecholate)molybdenum(VI) species.[1a,14,15] Differences in form and charge distribution between $[Mn(DBSQ)_2]_4$ and $Re(DBCat)_3$ further illustrate this property.

The most striking property of $Re(DBCat)_3$ is its unreactivity. The molybdenum analogue reacts with trace quantities of oxygen to give oxomolybdenum species and benzoquinone.[14] No such sensitivity to oxygen or to trace quantities of water contained in solvents has been noted for $Re(DBCat)_3$. In fact, Herrmann has prepared $(\eta^5\text{-}C_5Me_5)Re(Cl_4Cat)_2$ by displacement of oxo ligands from $(\eta^5\text{-}C_5Me_5)ReO_2$ with tetrachloro-1,2-benzoquinone.[11] This behavior is unusual for a high oxidation state metal ion and appears facilitated by the strong π-donor bonding of the catecholate ligands.

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Supplementary Material Available: Tables of atomic positional and thermal parameters for tris(3,5-di-*tert*-butylcatecholato)-rhenium(VI) (2 pages); observed and calculated structure factors for tris(3,5-di-*tert*-butylcatecholato)rhenium(VI) (34 pages). Ordering information is given on any current masthead page.

(11) Herrmann, W. A.; Kusthardt, U.; Herdtweck, E. *J. Organomet. Chem.* **1985**, *294*, C33–C36.

(12) (a) Baldas, J.; Boas, J. F.; Bonnyman, J.; Pilbrow, J. R.; Williams, G. A. *J. Am. Chem. Soc.* **1985**, *107*, 1886–1891. (b) Al-Mowali, A. H.; Porte, A. L. *J. Chem. Soc., Dalton Trans.* **1975**, 250–252. (c) Gibson, J. F.; Lack, G. M.; Mertis, K.; Wilkinson, G. *J. Chem. Soc., Dalton Trans.* **1976**, 1492–1495. (d) Holloway, J. H.; Raynor, J. B. *J. Chem. Soc., Dalton Trans.* **1975**, 737–741.

(13) Cyclic voltammetry was carried out in dichloromethane solution, using $n\text{-}Bu_4N(PF_6)$ as electrolyte, referenced to $Ag/Ag(CH_3CO_2)$. Scan rates of 100 and 200 mV/s were used. The ferrocene/ferrocenium couple, 0.257 mV under these conditions, was used as an internal reference.

(14) Cass, M. E.; Pierpont, C. G. *Inorg. Chem.* **1986**, *25*, 122–123.

(15) Buchanan, R. M.; Kessel, S. L.; Downs, H. H.; Pierpont, C. G.; Hendrickson, D. N. *J. Am. Chem. Soc.* **1978**, *100*, 7894–7900.

Asymmetric Electrophilic Amination: Synthesis of α-Amino and α-Hydrazino Acids with High Optical Purity

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The *E* silyl ketene acetal derived from (1*R*,2*S*)-*N*-methylephedrine propionate (**1**) (R = Me) was recently shown to be a very useful reagent for the $TiCl_4$-mediated asymmetric synthesis of anti α-methyl-β-hydroxy esters.[1,2] Asymmetric electrophilic formylation ($TiCl_4$, $HC(OMe)_3$) proved also to be quite successful.[3] Here we report that asymmetric electrophilic amination ($TiCl_4$, *t*-BuOOCN=NCOO-*t*-Bu (DTBAD)) can be achieved using this reagent and that this process fulfills the following requirements: (a) enantiomeric excesses in the range 78–91%; (b) reasonably good chemical yields; (c) both enantiomers of the chiral auxiliary are inexpensive, commercially available materials;[4] (d) the chiral auxiliary can be recycled; (e) the absolute configuration of the reaction products is easily predictable. By this route natural, rare,[5] and unnatural α-amino acids **4** can be easily prepared[6] (Scheme I). α-Hydrazino acids **3**, which are intermediates in the synthetic sequence (Scheme I), are very interesting compounds because of their biological properties and as building blocks for modified peptides,[7] cephalosporins, and penicillins.[8,9]

N-Methylephedrine (1*R*,2*S*) was treated with RCOCl in CH_2Cl_2 to give the corresponding esters (100%). LDA enolization (THF, −78 °C) and Me_3SiCl trapping (−78 °C) gave the silyl ketene acetals **1** (95%; $E/Z \geq 95:5$), which were worked up by evaporation without water quenching. Slow addition of 1 mol equiv of the silyl ketene acetals in methylene chloride to 1 mol equiv of the $TiCl_4$–di-*tert*-butyl azadicarboxylate (DTBAD) complex[10] at −80 °C in CH_2Cl_2 gave fair to good overall yields[11,12]

(1) Gennari, C.; Bernardi, A.; Colombo, L.; Scolastico, C. *J. Am. Chem. Soc.* **1985**, *107*, 5812.

(2) Palazzi, C.; Colombo, L.; Gennari, C. *Tetrahedron Lett.* **1986**, 1735.

(3) Gennari, C.; Bernardi, A.; Scolastico, C.; Potenza, D. *Tetrahedron Lett.* **1985**, 4129.

(4) Both enantiomers of *N*-methylephedrine are commercially available (Fluka).

(5) For a review, see: Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816.

(6) For leading references in this field, see: Sinclair, P. J.; Zhai, D.; Reibenspies, J.; Williams, R. M. *J. Am. Chem. Soc.* **1986**, *108*, 1103 and references therein.

(7) Morley, J. S.; Hennessey, T. D.; Payne, J. W. *Biochem. Soc. Trans.* **1983**, *11*, 798. Morley, J. S.; Payne, J. W.; Hennessey, T. D. *J. Gen. Microbiol.* **1983**, *129*, 3701. Bentley, P. H.; Morley, J. S. *J. Chem. Soc. C* **1966**, 60. Grupe, R.; Niedrich, H. *Chem. Ber.* **1967**, *100*, 3283.

(8) Pifferi, G.; Nasi, F.; Monguzzi, R.; Pinza, M.; Broccali, G. *Curr. Chemother.* **1978**, 609. Bolis, G.; Bellani, P.; Pinza, M. *Heterocycles* **1981**, *16*, 265. Bellani, P.; Ventura, P.; Pifferi, G. *Heterocycles* **1980**, *14*, 1. LiBassi, G.; Monguzzi, R.; Broggi, R.; Broccali, G.; Carpi, C.; Pifferi, G. *J. Antibiot.* **1977**, *30*, 376. Balsamo, A.; Macchia, B.; Macchia, F.; Rossello, A.; Giani, R.; Pifferi, G.; Pinza, M.; Broccali, G. *J. Med. Chem.* **1983**, *26*, 1648.

(9) The previously reported syntheses of optically active α-hydrazino acids used α-amino acids as starting materials and were quite laborious and inefficient. See: (a) Karady, S.; Ly, M. G.; Pines, S. H.; Sletzinger, M. *J. Org. Chem.* **1971**, *36*, 1949. (b) LiBassi, G.; Ventura, P.; Monguzzi, R.; Pifferi, G. *Gazz. Chim. Ital.* **1977**, *107*, 253. (c) Achiwa, K.; Yamada, S. *Tetrahedron Lett.* **1975**, 2701. (d) Niedrich, H.; Grupe, R. *J. Prakt. Chem.* **1965**, *27*, 108.

(10) Both DEAD and DTBAD can be used in the electrophilic amination reaction. By complexation with $TiCl_4$, DEAD showed a more pronounced downfield shift in the ^1H NMR spectrum (CD_2Cl_2, −50 °C) than did DTBAD and gave higher yields of the addition products. DTBAD was chosen because of the milder conditions in the hydrolysis step. No reaction occurred without $TiCl_4$.

(11) The only by-products were the unreacted ephedrine ester and di-*tert*-butyl hydrazinodicarboxylate, which was probably generated by diimide reduction of DTBAD. Diimide was generated by acidic decomposition of DTBAD (−2 (2-methylpropene), $-2CO_2$).

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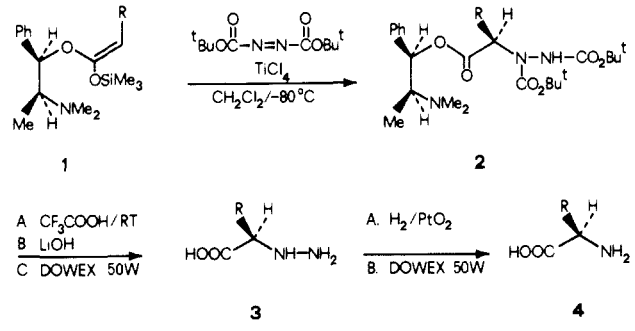
Table I. α-Hydrazino and α-Amino Acid Synthesis Using (1*R*,2*S*)-*N*-Methylephedrine

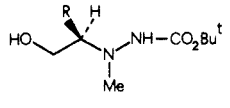
R	2, % yield	3, % yield	4, % yield	4		
				% ee (from crude 3)	% ee (from 3 after crystallization[b])	absolute config
CH_3	70[a]	78[b]	92	90.6[c]	≥98[c]	*R*
CH_2Ph	45[a]	81[b]	89[d]	91.0[d]	≥98[d]	*R*
$CH_2CH(CH_3)_2$	70[a]	81[b]	91	81.5[c]	≥98[c]	*R*
CH_2CH_3	65[a]	80[b]	93	84.0[c]	≥98[c]	*R*
$(CH_2)_3CH_3$	45[a]	78[b]	90	78.0[c]	≥98[c]	*R*

[a] The major stereoisomer can be separated and isolated by flash chromatography. [b] By use of the isolated major stereoisomer **2**, or by recrystallization of the α-hydrazino acid from EtOH–H_2O, ≥98% enantiomerically pure compound **3** was obtained. [c] The α-hydrazino acid hydrochloride was hydrogenolyzed (H_2–PtO_2) in water: by use of increasing amounts of HCl (from 0.1 to 6.0 N), increasing degrees of racemization were observed. [d] Hydrogenolysis of the α-hydrazino acid hydrochloride (H_2–PtO_2) in aqueous 0.05 N HCl gave *R*-cyclohexyl alanine with no racemization (see: Waser, E.; Brauchli, E. *Helv. Chim. Acta* **1924**, *7*, 740). Data reported in the table refer to (*R*)-cyclohexylalanine.

Scheme I



of the amination products with remarkable stereoselectivity (Table I).[13] The crude adducts **2** can be reduced (LAH, Et_2O, room temperature) to give *N*-methylephedrine and β-hydrazino alcohols **5**. Alcohol **5** (R = Me) was transformed into the stereoisomeric



5

Mosher esters ((–)-MTPA-Cl, Py, CCl_4),[14] and the diastereoisomeric excess was checked by 200-MHz ^1H NMR (≥95:5). Alternatively the crude adducts **2** were hydrolyzed (CF_3COOH, room temperature, 1.5 h) to give α-hydrazino esters which were saponified (LiOH, MeOH–H_2O, room temperature).[15] The mixture was then acidified, evaporated, and chromatographed on Dowex W50-X8 ion-exchange resin to give α-hydrazino acids **3** which were obtained ≥98% optically pure with a single recrystallization process. Reduction with H_2/PtO_2 gave the corresponding α-amino acids in high yield. The enantiomeric excess was checked by $[\alpha]_D$ comparison and by HPLC[16] or, much more efficiently, capillary VPC[17] using chiral columns.

In summary, a new practical method for the preparation of α-hydrazino acids and of natural and unnatural α-amino acids in both the *R* and *S* configuration has been developed.

Efforts to further expand the scope and utility of this methodology are presently under active investigation in this laboratory.

Registry No. (*E*)-**1** (R = Me), 98171-04-1; (*E*)-**1** (R = CH_2Ph), 103836-61-9; (*E*)-**1** (R = CH_2Pr-*i*), 103836-62-0; (*E*)-**1** (R = Et), 103836-63-1; (*E*)-**1** (R = Bu), 103836-64-2; **2** (R = Me), 103836-65-3; **2** (R = CH_2Ph), 103836-66-4; **2** (R = CH_2Pr-*i*), 103836-67-5; **2** (R = Et), 103836-68-6; **2** (R = Bu), 103836-69-7; **3** (R = Me), 21028-13-7; **3** (R = CH_2Ph), 1202-30-8; **3** (R = CH_2Pr-*i*), 24292-07-7; **3** (R = Et), 103883-01-8; **3** (R = Bu), 103883-02-9; **4** (R = Me), 338-69-2; **4** (R = CH_2Ph), 673-06-3; **4** (R = CH_2Pr-*i*), 328-38-1; **4** (R = Et), 2623-91-8; **4** (R = Bu), 327-56-0; **5** (R = Me), 103836-70-0; DTBAD, 870-50-8; CH_3COCl, 75-36-5; $PhCH_2COCl$, 103-80-0; *i*-$PrCH_2COCl$, 108-12-3; CH_3CH_2COCl, 79-03-8; $CH_3(CH_2)_3COCl$, 638-29-9; (1*R*,2*S*)-*N*-methylephedrine, 552-79-4; (1*R*,2*S*)-*N*-methylephedrine acetate, 74111-77-6; (1*R*,2*S*)-*N*-methylphedrine 2-phenylethanoate, 103836-59-5; (1*R*,2*S*)-*N*-methylphedrine 3-methylbutanoate, 103836-60-8; (1*R*,2*S*)-*N*-methylphedrine propanoate, 53135-04-9; (1*R*,2*S*)-*N*-methylphedrine pentanoate, 74059-53-3.

Supplementary Material Available: Detailed experimental procedures for the reactions, analyses, optical rotations, and spectroscopic data (^1H NMR, IR) for the compounds (9 pages). Ordering information is given on any current masthead page.

(12) Steric hindrance has a negative effect on the condensation reaction. For example in the case of N-methylephedrine isovalerate (R = *i*-Pr) yields were poor (ca. 35%).

(13) Both DTBAD and the ephedrine NMe_2 group are expected to bind to $TiCl_4$, which usually ligates two-electron-donating molecules to form cis-octahedral, six-coordinate complexes. Therefore the conformational freedom of the system is likely to be dramatically reduced, and the C–N bond formation occurs on the six-coordinate metal in a highly stereoselective way.

(14) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(15) Optically pure *N*-methylephedrine was recovered here by CH_2Cl_2 extraction (≥95%).

(16) Supelcosil^R LC-(*R*)-urea: the amino acids were injected as PTH derivatives (see: Edman, P. *Acta Chem. Scand.* **1950**, *4*, 277).

(17) Chirasil-Val III FSOT Column (AllTech Associates, Inc.): the amino acids were injected as TFA isopropyl ester derivatives (see: Parr, W.; Howard, R. Y. *Anal. Chem.* **1975**, *47*, 951).

Stereoselective Amination of Chiral Enolates. A New Approach to the Asymmetric Synthesis of α-Hydrazino and α-Amino Acid Derivatives

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Nonproteinogenic and rare enantiomerically pure amino acids[1] are important constituents in peptide-derived chemotherapeutics. As a consequence, the development of new reaction methodology which provides an expedient, general approach to the synthesis of this family of compounds continues as an active area of investigation.[2] Recent advances in this field have featured the development of several highly effective chiral glycine enolate synthons which may be employed in diastereoselective alkylation reactions (eq 1).[2b] The purpose of this paper is to report a complementary approach to the synthesis of α-amino acids via the electrophilic amination of chiral enolates (eq 2). One positive attribute of this latter process is that its scope is not so strictly defined by the alkyl (aryl) substituent in the given amino acid target. Such constraints are quite apparent in the related alkylation reactions (eq 1).

(1) For a recent review, see: Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816.

(2) (a) Sinclair, P. J.; Zhai, D.; Reibenspies, J.; Williams, R. M. *J. Am. Chem. Soc.* **1986**, *108*, 1103–1104. (b) Schollkolpf, U. *Top. Curr. Chem.* **1983**, *109*, 66–84. (c) Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390–5402. (d) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106–112.

0002-7863/86/1508-6395$01.50/0