Synthesis of *N*,*N*′-Disubstituted (1*R*,2*R*)-1,2-Diaminocyclohex-4-enes by a Ruthenium-Catalyzed Ring-Closing Metathesis Reaction

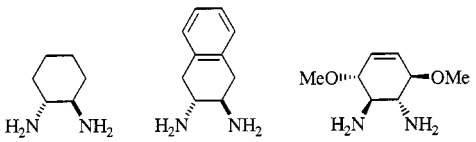
Giuseppe Alvaro,[a][+] Stefano Grilli,[a] Gianluca Martelli,[a] and Diego Savoia*[a]

Keywords: Ruthenium / Ring-closing metathesis / Metathesis / EPC synthesis / 1,2-Diaminocyclohex-4-ene

Enantiopure (1*R*,2*R*)-1,2-diaminocyclohex-4-ene derivatives have been synthesized by the ruthenium-catalyzed ring-closing metathesis reaction of (4*R*,5*R*)-*N*,*N*′-bis[(*S*)-1-phenylethyl]-4,5-diamino-1,7-octadiene dihydrochloride.

Introduction

Together with a few other C_2-symmetric 1,2-diamines, homochiral *trans*-1,2-diaminocyclohexane, e.g. (*R*,*R*)-**1** (see Figure 1), are widely used as ligands, or as an auxiliary, in asymmetric synthesis.[1] Moreover, the platinum(II) complexes of 1,2-diamines have found uses in medicinal chemistry owing to their antineoplastic activity.[2] In this connection, it is noteworthy that the [(*R*,*R*)-**1**]$PtCl_2$ complex was found to be more active than the (*S*,*S*) and *meso* complexes. Similarly, diaminocyclohexanes carrying hydroxy substituents on the ring have been prepared as racemic compounds from 1,2-diaminocyclohex-4-ene dihydrochloride or 1,3-cyclohexadiene, and their (1,2-diamine)$PtCl_2$ complexes display antitumor activity, which is dependent on the relative stereochemistry of the hydroxy and amino substituents.[3][4] *N*,*N*′-Disubstituted 1,2-diaminocyclohexanes are also potent opioid analgesics, and for certain analogous ring-substituted molecules activity and selectivity are affected by both the structure and the absolute stereochemistry.[2c,5,6] In one instance the racemic compound was resolved, and, whilst one enantiomer displayed high K-receptor affinity and selectivity, the other was neither selective nor a potent analgesic.[5a]



(*R*,*R*)-**1**[6,9] **2**[10] (*R*,*R*,*R*,*R*)-**3**[13]

Figure 1. C_2-symmetric 1,2-diaminocyclohexane and derivatives prepared until now by asymmetric synthesis

Resolution of the racemic diamine **1** can be easily performed on a large scale,[7][8] and both enantiomers are commercially available, so little effort has been devoted to the enantioselective preparation of this compound and its ring-substituted derivatives. The two asymmetric syntheses of **1** reported so far, which start from materials already containing the carbocyclic ring, suffer from poor diastereoselectivity.[6][9] The analogous ring-fused compound, *trans*-2,3-diaminotetralin **2**, has been prepared as a racemic compound,[10] but it should be obtainable in an enantiomerically pure form starting from the homochiral β-amino acid precursor. On the other hand, a number of C_2-symmetric diaminoheterocycles,[11] including 3,4-diaminopyrrolidine,[11a,11b] 4,5-diaminoazepine,[11c] and 3,4-diaminotetrahydrofuran,[11b] have been succesfully prepared from the corresponding enantiopure vicinal diols.

Thus, it appears that new methodologies for the asymmetric synthesis of such compounds are necessary, in particular to enable the preparation of new homochiral ring-substituted 1,2-diaminocyclohexanes, which are potentially useful in the fields of medicinal chemistry and asymmetric syntheses. In the latter case, for example, it would be interesting to assess the influence on the enantioselectivity of certain asymmetric reactions[12] of ring substituents (especially those occurring at C-3 and C-6) on the 1,2-cyclohexanediamine ligand.

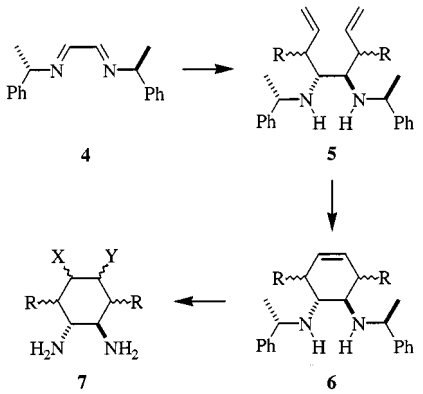
Recently, the synthesis of a new and interesting 2,3-diaminoconduritol, i.e. (1*R*,2*R*,3*R*,4*R*)-1,4-dimethoxy-2,3-diaminocyclohex-5-ene [(*R*,*R*,*R*,*R*)-**3**] from D-mannitol has been reported. Here the six-membered ring was constructed together with the C=C double bond by a Ramberg−Backlund reaction.[13] This has prompted the authors to report herein on the results obtained on the synthesis of enantiopure 1,2-diaminocyclohex-4-ene and -cyclohexane derivatives according to the strategy described in Scheme 1, which also involves the construction of a carbocyclic ring. To this purpose, the use of a transition-metal-catalyzed ring-closing metathesis (RCM) reaction[14] was envisaged in order to obtain the 1,2-diaminocyclohex-4-ene derivative **6** from the optically pure 4,5-diamino-1,7-octadiene derivative **5**,[15] which is in turn available by the addition of allylic organometallic reagents to the glyoxal diimine **4**.[16] Double-bond functionalization would then lead to the ring-substituted 1,2-diaminocyclohexanes **7**, eventually, when X = Y and depending on the successful control of the configuration of the newly formed stereocentres, with C_2 symmetry.

[a] Dipartimento di Chimica "G. Ciamician", Università di Bologna,
via Selmi 2, I-40126 Bologna, Italy
Fax: (internat.) + 39-051/259456
E-mail: savoia@ciam.unibo.it
[+] Present address: GlaxoWellcome S.p.A., Medicines Research Centre,
via A. Fleming 4, I-37100 Verona, Italy

  1434−193X/99/0707−1523 $ 17.50+.50/0

It is noteworthy that it should be possible to prepare *ent*-**7** by the same synthetic sequence using the (*R*) auxiliary.

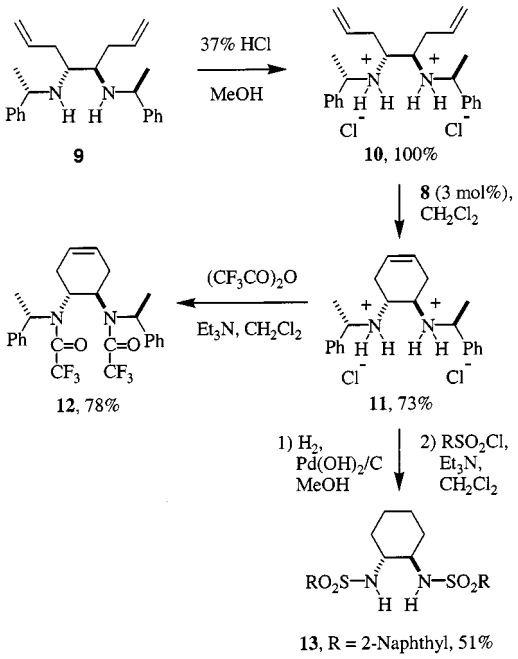
The RCM reactions of **1**, ω-dienes, -enynes and -diynes, using mainly (carbene)ruthenium or -molybdenum complexes as catalysts, have emerged in the last decade as a poweful tool for the synthesis of carbo- and heterocyclic compounds; even those containing a variety of functional groups.[14] Especially relevant to the present research was the reported preparation of amino-substituted cycloalkenes, such as 4-(acylamino)cyclohexenes,[17] through the RCM reaction of racemic 4-acylamino-1,7-octadienes, and of homochiral α-amino acids in which the α-carbon atom was incorporated in a carbocyclic ring.[18]



Scheme 1. Envisioned route to enantiopure ring-substituted 1,2-diaminocyclohex-4-enes and -cyclohexanes

Accordingly, the RCM reaction was used as the key step in the sequence described in Scheme 2 for the preparation of 1,2-diaminocyclohex-4-ene derivatives, and the Grubbs (benzylidene)ruthenium complex $Cl_2(PCy_3)_2Ru{=}CHPh$ (**8**) was chosen, since it presents several advantages with respect to the Schrock carbene complex based on molybdenum:[14] It is both commercially available and straightforwardly prepared from phenyldiazomethane,[19] it is stable in air and also easier to use. However, differing markedly from the molybdenum complex,[20] the ruthenium complex **8** is strongly coordinated by amines, which inhibit the metathesis activity. Hence, primary and secondary amines have generally been protected as acyl- or sulfonylamides, but formation of the hydrochloride proved viable for a tertiary amine when a ruthenium complex analogous to **8** was used.[21]

The diamine **9**, easily obtained by addition of allylzinc bromide to the corresponding glyoxal diimine,[16] could not be satisfactorily converted into any diamide by treatment with a variety of acyl and sulfonyl chlorides and anhydrides, as the monoamide was mainly formed instead. As a consequence the corresponding dihydrochloride **10** was prepared in a quantitative yield, and thoroughly dried in vacuo. The RCM reaction was carried out on this salt in a deaerated dichloromethane solution at room temp. in the presence of a catalytic amount of the complex **8** (3 mol-%). The reaction was complete after 6 h, as determined by GC-MS analysis of a sample obtained by the basic treatment. It is



Scheme 2. Synthesis of (1*R*,2*R*)-1,2-diaminocyclohex-4-ene and -cyclohexane derivatives through a RCM reaction catalyzed by $Cl_2Ru(PCy)_3Ru{=}CHPh$ (**8**)

noteworthy that to a large extent the product, 1,2-diaminocyclohex-4-ene dihydrochloride (**11**), separates from the dark solution as white crystals, which can be easily isolated in high yield after concentration of the heterogeneous mixture, filtration and washing with dichloromethane. Crystallization from methanol gave the pure diaminocyclohexene dihydrochloride **11** with a yield of 73%.

Contrary to the failure previously observed with the diamine **9**, it was possible to prepare diamides through the diamine formed in situ from the salt **11** and an excess of triethylamine in dichloromethane. For example, treatment with trifluoroacetic anhydride readily afforded the diamide **12** in a good yield. On the other hand, removal of the auxiliary from the salt **11** and concomitant hydrogenation of the double bond was achieved using palladium hydroxide on carbon, affording the intermediate (1*R*,2*R*)-1,2-diaminocyclohexane dihydrochloride, which was immediately converted into the disulfonamide derivative **13** by a routine procedure using 2-naphthylsulfonyl chloride. The optical purity of the amide **13** was assessed by comparison of the value for its optical rotation with that reported in the literature for the authentic compound.[22]

It should be observed that, when aiming to prepare ring-substituted compounds **7** as described in Scheme 1, functionalization of the cyclohexene double bond must be carried out before the reductive cleavage of the auxiliary in diamides such as **12**. Moreover, substituents at C-3 and C-6 can be introduced in the former step by the reaction of the diimine **4** with the proper γ-substituted allylmetal reagents, thus hopefully controlling the relative stereochemistry. These goals are actively pursued by the present authors.

Experimental Section

General: General methods and instrumentation were as previously described.[15] The ruthenium complex **8** was purchased from Fluka.

(4*R*,5*R*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-4,5-diamino-1,7-octadiene Dihydrochloride (10): 37% HCl (0.45 mL, $4.5\cdot10^{-3}$ mol) and benzene (5 mL) were added to a solution of diamine **9**[16] (1.43 g, $4.11\cdot10^{-3}$ mol) in MeOH (5 mL), and the solvents were then evaporated at reduced pressure. MeOH (5 mL) and benzene (5 mL) were then added, and the mixture again concentrated at reduced pressure. This procedure was repeated to afford 1.72 g of **10** (100%). A sample was recrystallized from MeOH for analytical purposes. − M.p. 180°C (dec.). − $[\alpha]_D^{20} = -29.8$ (*c* = 1.06, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (d, *J* = 6.8 Hz, 6 H, CHC*H*$_3$), 2.50−2.62 (m, 2 H, NCHCHN), 2.70−2.85 (m, 4 H, C*H*$_2$CH=CH$_2$), 4.26 (d, *J* = 16.8 Hz, 2 H, CH=C*H*$_2$), 4.38 (q, 2 H, C*H*CH$_3$), 4.75 (d, *J* = 10.2 Hz, 2 H, CH=C*H*$_2$), 4.87−5.02 (m, 2 H, C*H*=CH$_2$), 5.31 (s, 2 H, NH), 7.40−7.55 (m, 6 H, Ph), 7.60−7.70 (m, 4 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 20.5, 32.8, 53.5, 57.8, 121.0, 127.9, 129.8, 130.0, 130.7, 135.0.

(1*R*,2*R*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-1,2-diaminocyclohex-4-ene Dihydrochloride (11): A deaerated solution of complex **5** (0.123 g, 0.15 mmol, 3 mol-%) in CH_2Cl_2 (10 mL) was added to the solution of salt **10** (2.11 g, $5\cdot10^{-3}$ mol) in anhydrous CH_2Cl_2 (40 mL), previously deaerated by bubbling argon through for 5 min. The mixture was magnetically stirred at room temp. for 6 h, whilst the progress of the reaction was monitored by observing the disappearance of the starting material by TLC analysis. Most of the product **8** was formed as a white powder from the solution. The mixture was then allowed to stand in air for 6−12 h, then concentrated to a volume of ca. 20 mL, cooled in an ice bath for 30 min, and filtered. The solid was washed with cold CH_2Cl_2 (2 × 2 mL) to give a white powder, which was then recrystallized from MeOH and dried in vacuo: 1.43 g, 73%. − M.p. > 180°C (dec.). − $[\alpha]_D^{20} = -40.4$ (*c* = 1.0, H_2O). − ^{1}H NMR (300 MHz, D_2O): δ = 1.39 (d, *J* = 6.8 Hz, 6 H, CHC*H*$_3$), 2.17−2.40 (m, 2 H, C*H*$_2$CH=CH$_2$), 3.06 (m, 2 H, NCHCHN), 4.35 (q, 2 H, C*H*CH$_3$), 5.62 (s, 2 H, CH=CH), 7.08−7.15 (m, 4 H, Ph), 7.25−7.40 (m, 6 H, Ph). − ^{13}C NMR (300 MHz, D_2O): δ = 18.5, 20.4, 49.9, 57.3, 121.8, 126.7, 129.4, 129.6, 134.1. − A sample of the free diamine was quantitatively obtained by treating an aliquot of the dihydrochloride **11** with an excess of aqueous NaOH and extraction with Et_2O, followed by the usual workup. − M.p. 60−61°C. − $[\alpha]_D^{20} = -107.2$ (*c* = 1.0, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 6.6 Hz, 6 H, CHC*H*$_3$), 1.55−1.67 (m, 2 H, C*H*$_2$CH=CH$_2$), 1.82 (s, 2 H, NH), 2.26 (m, 2 H, C*H*$_2$CH=CH$_2$), 2.39 (d, *J* = 17.6 Hz, 2 H, NCHCHN), 3.83 (q, 2 H, C*H*CH$_3$), 5.39−5.48 (m, 2 H, CH=CH), 7.15−7.35 (m, 10 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 25.5, 31.7, 53.8, 54.5, 124.7, 126.5, 128.3, 145.6. − MS (70 eV); *m*/*z* (%): 215 (3) [M^+ − PhCHCH$_3$], 201 (8) [M^+ − Ph(CH$_3$)CHNH], 120 (10) [PhCH(CH$_3$)NH$^+$], 105 (100) [PhCHCH$_3^+$], 77 (15) [Ph^+].

(1*R*,2*R*)-*N*,*N*′-Bis[(*S*)-1-phenylethyl]-*N*,*N*′-bis(trifluoroacetyl)-1,2-diaminocyclohex-4-ene (12): Et_3N (0.45 mL, $3\cdot10^{-3}$ mol) and DMAP (12 mg, $0.1\cdot10^{-3}$ mol) were added to a stirred suspension of diamine dihydrochloride **11** (0.196 g, $0.5\cdot10^{-3}$ mol) in CH_2Cl_2 (5 mL). After 10 min, a solution of trifluoroacetic anhydride (0.28 mL, $2\cdot10^{-3}$ mol) in CH_2Cl_2 (2 mL) was added over 10 min. The mixture was further stirred for 2 h, then 2 N HCl (3 mL) was added and the organic phase extracted with Et_2O (3 × 10 mL). The collected organic layers were dried with Na_2SO_4, and concentrated to leave the diamide **12** as a yellowish solid, which was thoroughly washed with MeOH until a colourless powder was obtained: 0.200 g, 78%. − M.p. 162−163°C. − $[\alpha]_D^{20} = +30.6$ (*c* = 1.27, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.69−0.75 (m, 2 H, C*H*$_2$CH=CH$_2$), 1.60 (d, *J* = 6.8 Hz, 6 H, CHC*H*$_3$), 2.45−2.52 (m, 2 H, C*H*$_2$CH=CH$_2$), 4.43 (m, 2 H, NCHCHN), 4.99 (m, 2 H, CH=CH), 5.26 (q, 2 H, C*H*CH$_3$), 7.30−7.47 (m, 10 H, Ph). − ^{13}C NMR (300 MHz, $CDCl_3$): δ = 16.9, 27.1, 52.2, 56.5, 118.7, 123.4, 128.5, 128.9, 137.0, 157.5. − MS (70 eV); *m*/*z* (%): 217 (10) [Ph(CH$_3$)CHNHCOCF$_3^+$], 105 (100) [PhCHCH$_3^+$]. − $C_{26}H_{26}F_6N_2O_2$ (512.47): calcd. C 60.93, H 5.11, N 5.47; found C 60.95, H 5.12, N 5.45.

(1*R*,2*R*)-*N*,*N*′-Bis(2-naphthylsulfonyl)-1,2-diaminocyclohexane (13): A Parr apparatus was filled with salt **11** (0.760 g, $1.9\cdot10^{-3}$ mol), 40 mL of MeOH and 200 mg of $Pd(OH)_2$/C, then submitted to a pressure of 48 psi H_2 for 36 h. The solution was filtered through a small pad of Celite, then concentrated to leave the crude 1,2-cyclohexanediamine dihydrochloride (0.350 g, $1.88\cdot10^{-3}$ mol, 99%) as a glassy solid. Crystallization from MeOH gave 0.220 g (63%) of pure compound. − M.p. > 190°C (dec.). − $[\alpha]_D^{20} = -9.4$ (*c* = 1.01, CH_3OH). − A suspension of the salt (200 mg, $1.13\cdot10^{-3}$ mol) in CH_2Cl_2 (8 mL) was cooled to 0−5°C with an ice bath, then triethylamine (1.4 mL, $9.9\cdot10^{-3}$ mol) was added. After stirring for 15 min at 0−5°C, the mixture was cooled to −50°C, then 2-naphthylsulfonyl chloride (0.500 g, $2.21\cdot10^{-3}$ mmol) was added. After 10 min, the cooling bath was removed, and the mixture stirred for 1.5 h at room temp., then 5 mL of 2 N HCl was added, and the organic phase was extracted with Et_2O (3 × 10 mL). The collected ethereal layers were washed with brine, dried with Na_2SO_4, and concentrated to leave the diamide **13** (0.250 g, 51%) as a white solid. − M.p. 96−98°C. − $[\alpha]_D^{20} = +15.2$ (*c* = 1.0, pyridine) {ref.[23]: M.p. 96−99°C. − $[\alpha]_D^{20} = +13.7$ (*c* = 1.07, pyridine)}. − The ^{1}H-NMR spectrum was identical to that reported.[22]

Acknowledgments

This work was carried out in the framework of the National Project "Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni" supported by the Ministero dell′Università e della Ricerca Scientifica e Tecnologica, Roma, and by the University of Bologna.

[1] Y. L. Bennani, S. Hanessian, *Chem. Rev.* **1997**, *97*, 3161−3195.
[2] [2a] A. Pasini, F. Zunino, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 615−624. − [2b] S. E. Sherman, S. J. Lippard, *Chem. Rev.* **1987**, *87*, 1153−1181. − [2c] E. T. Michalson, J. Szmuszkovicz, *Progr. Drug Res.* **1989**, *33*, 135−149. − [2d] Y. Kidani, *Drugs Fut*. **1989**, *14*, 529−532. − [2e] J. Reedijk, *Chem. Commun*. **1996**, 801−806.
[3] [3a] D. T. Witiak, D. P. Rotella, J. A. Fillpi, J. G. Gallucci, *J. Med. Chem*. **1987**, *30*, 1327−1336. − [3b] D. T. Witiak, D. P. Rotella, Y. Wei, J. A. Fillpi, J. G. Gallucci, *J. Med. Chem*. **1989**, *32*, 214−217. − [3c] D. Witiak, Y. Wei, *J. Org. Chem*. **1991**, *56*, 5408−5417.
[4] S. Hanessian, J. Wang, *Can. J. Chem*. **1993**, *71*, 2102−2108.
[5] [5a] P. R. Halfpenny, D. C. Horwell, J. Hughes, J. C. Hunter, D. C. Rees, *J. Med. Chem*. **1990**, *33*, 286−291. − [5b] J. P. Freeman, E. T. Michalson, S. V. D′Andrea, L. Baczynskyj, P. F. Von Voigtlander, R. A. Lahti, M. W. Smith, C. F. Lawson, T. A. Scahill, S. A. Mizsak, J. Szmuszkovicz, *J. Med. Chem*. **1991**, *34*, 1891−1896. − [5c] L. Radesca, W. D. Bowen, L. Di Paolo, B. R. de Costa, *J. Med. Chem*. **1991**, *34*, 3058−3065.
[6] W. H. Schlichter, A. F. Frahm, *Tetrahedron: Asymmetry* **1992**, *3*, 329−332.
[7] [7a] F. Glasbol, P. Steenbol, S. B. Sorensen, *Acta Chem. Scand*. **1980**, *26*, 3605− 3611. − [7b] S. C. Benson, P. Cai, M. Colon, M. A. Haiza, M. Tokles, J. K. Snyder, *J. Org. Chem*. **1988**, *53*, 5335−5341. − [7c] J. F. Larrow, E. N. Jacobsen, Y. Gao, Y. Hong, X. Nie, C. M. Zepp, *J. Org. Chem*. **1994**, *59*, 1939−1942. − [7d] A. Matteson, C. Orrenius, N. Oehrner, C. R. Unelius, K. Hult, T. Norin, *Acta Chem. Scand*. **1996**, *50*, 918−921.

[8] Optically active *trans*-1,2-cyclopentanediamine,[8a] *trans*-1,2-dimethyl-1,2- cyclohexanediamine,[8b] 11,12-diamino-9,10-dihydro-9,10-ethanoanthracene,[8c] and *trans*-bicyclo[2.2.1]heptane-2,3-diamine[8d] have been obtained by resolution of the racemic compounds: [8a] H. Toftlund, E. Pedersen, *Acta Chem. Scand*. **1972**, *26*, 4019−4030. − [8b] W. Zhang, E. N. Jacobsen, *Tetrahedron Lett*. **1991**, *32*, 1711−1714. − [8c] B. M. Trost, D. L. Van Vranken, C. Bingel, *J. Amer. Chem. Soc*. **1992**, *114*, 9327−9343. − [8d] K. Hatano, T. Takeda, R. Saito, *J. Chem. Soc., Perkin Trans. 2* **1994**, 579−584.

[9] D. Enders, J. Wiedemann, *Synthesis* **1996**, 1443−1450.

[10] P. Gmeiner, E. Hummel, *Synthesis* **1994**, 1026−1028.

[11] [11a] T. Tsubomura, S. Yano, K. Kobayashi, T. Sakurai, S. Yoshikawa, *J. Chem. Soc., Chem. Commun*. **1986**, 459−460. − [11b] D. R. Reddy, E. R. Thornton, *J. Chem. Soc., Chem. Commun*. **1992**, 172−173. − [11c] J. Skarzewski, A. Gupta, *Tetrahedron: Asymmetry* **1997**, *8*, 1861−1867. − [11d] M. Torneiro, W. C. Still, *Tetrahedron* **1997**, *53*, 8739−8750.

[12] The salen derivative of optically pure *trans*-1,2-diamino-1,2-dimethylcyclohexane, obtained by resolution of the racemic compound,[8b] exhibited a lower enantioselectivity with respect to the salen derivative of enantiopure *trans*-1,2- diaminocyclohexane in the epoxidation of *cis*-β-methylstyrene: E. N. Jacobsen, W. Zhang, A. R. Muci, J. R. Ecker, L. Deng, *J. Am. Chem. Soc*. **1991**, *113*, 7063−7064.

[13] V. Cerè, F. Peri, S. Pollicino, A. Ricci, *Synlett* **1998**, 1197−1198.

[14] [14a] K. Ivin, *Olefin Metathesis and Metathesis Polymerization*, Academic Press, New York, **1997**. − For reviews, see: [14b] R. H. Grubbs, S. H. Pine in *Comprehensive Organic Synthesis* (Ed.: B. M. Trost), Pergamon Press, New York, **1991**, vol. 5, ch. 9.3. − [14c] R. H. Grubbs, S. J. Miller, G. C. Fu, *Acc. Chem. Res.***1995**, *28*, 446−452. − [14d] H.-G. Schmalz, *Angew. Chem. Int. Ed. Engl*. **1995**, *34*, 1833−1836. − [14e] K. J. Ivin, *J. Mol. Catal*. **1997**, *133*, 1−16. − [14f] A. S. K. Hashmi, *J. Prakt. Chem*. **1997**, 195−199. − [14g] M. Schuster, S. Blechert, *Angew. Chem. Int. Ed. Engl*. **1997**, *36*, 2037−2056. − [14h] A. Furstner, K. Langemann, *Synthesis* **1997**, 792−803. − [14i] C. Pariya, K. N. Jayaprakash, A. Sarkar, *Coord. Chem. Rev*. **1998**, *168*, 1−48. − [14j] S. K. Armstrong, *J. Chem. Soc., Perkin Trans. 1* **1998**, 371−388. − [14k] T. Naota, H. Takaya, S. Murahashi, *Chem Rev*. **1998**, *98*, 2599−2660.

[15] We have also performed zirconium-catalyzed and -promoted reductive cylization reactions on the diamine **9**: F. Grepioni, S. Grilli, G. Martelli, D. Savoia, *J. Org, Chem.*, in press.

[16] G. Alvaro, F. Grepioni, D. Savoia, *J. Org. Chem*. **1997**, *62*, 4180−4182.

[17] M. E. Maier, T. Lapeva, *Synlett* **1998**, 891−893.

[18] [18a] S. J. Miller, R. H. Grubbs, *J. Am. Chem. Soc*. **1995**, *117*, 5855−5856. − [18b] S. J. Miller, H. E. Blackwell, R. H. Grubbs, *J. Am. Chem. Soc*. **1996**, *118*, 9606−9614. − [18c] J. Pernerstorfer, M. Schuster, S. Blechert, *Chem. Commun*. **1997**, 1949−1950. − [18d] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 2309− 2322. − [18e] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 5925−5936. − [18f] K. Hammer, K. Undheim, *Tetrahedron* **1997**, *53*, 10603−10614. − [18g] K. Hammer, K. Undheim, *Tetrahedron: Asymmetry* **1998**, *9*, 2359−2368. − [18h] D. J. O′Leary, S. J. Miller, R. H. Grubbs, *Tetrahedron Lett*. **1998**, *39*, 1689−1690. − [18i] A. D. Piscopio, J. F. Miller, K. Koch, *Tetrahedron Lett*. **1998**, *39*, 2667−2670. − [18j] S. Kotha, N. Sreenivasachary, E. Brahmachary, *Tetrahedron Lett*. **1998**, *39*, 2805−2808. − [18k] R. M. Williams, J. Liu, *J. Org. Chem*. **1998**, *63*, 2130−2132. − [18l] J.-M. Campagne, L. Ghosez, *Tetrahedron Lett*. **1998**, *39*, 6175−6178. − [18m] J. J. N.Veerman, J. H. van Maarseveen, G. M. Visser, C. G. Kruse, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *Eur. J. Org. Chem.* **1998**, 2583−2589.

[19] P. Schwab, R. H. Grubbs, J. W. Ziller, *J. Am. Chem. Soc*. **1996**, *118*, 100−110.

[20] Y.-S. Shon, T. R. Lee, *Tetrahedron Lett*. **1997**, *38*, 1283−1286.

[21] G. C. Fu, S. T. Nguyen, R. H. Grubbs, *J. Am. Chem. Soc*. **1993**, *115*, 9856− 9867.

[22] H. Takahashi, T. Kawakita, M. Ohno, M. Yoshioka, S. Kobayashi, *Tetrahedron* **1992**, *48*, 5691−5700.

Received January 8, 1999
[O99004]