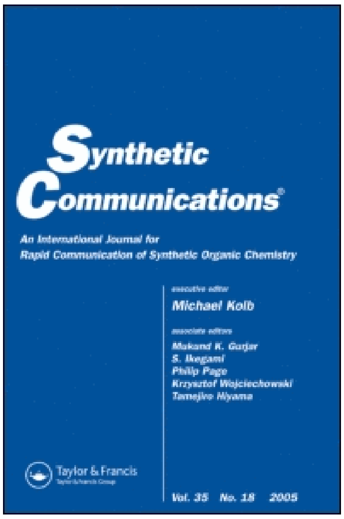

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PREPARATION AND CATALYTIC ENANTIOSELECTIVE REACTIONS OF C_3-SYMMETRIC TRIS(OXAZOLINE)S DERIVED FROM KEMP'S TRIACID

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Abstract: Kemp's triacid was elaborated to optically pure tris(β-hydroxylamide)s and tris(oxazoline)s. The resulting C_3-symmetric compounds were used in diethylzinc additions to benzaldehyde and allylic oxidations of cyclopentene, based on Kharash reaction conditions, to give the corresponding products in good chemical yields and moderate enantioselectivities.

Chiral C_2-symmetric bis(oxazoline)s have been successfully employed as ligands in numerous asymmetric catalyses,[1] such as C–H,[2] C–C,[3] C–N,[4] and C–O[5] bond formation reactions. Use of C_2-symmetric ligands can reduce the number of competing diastereomeric pathways, and thus enhances the enantioselectivity of the thereby catalyzed reactions. Highly symmetrical symmetrical C_3-ligands may also be useful in enantioselective reactions. Indeed, efforts have been exerted on the development of chiral C_3-symmetric compounds such as

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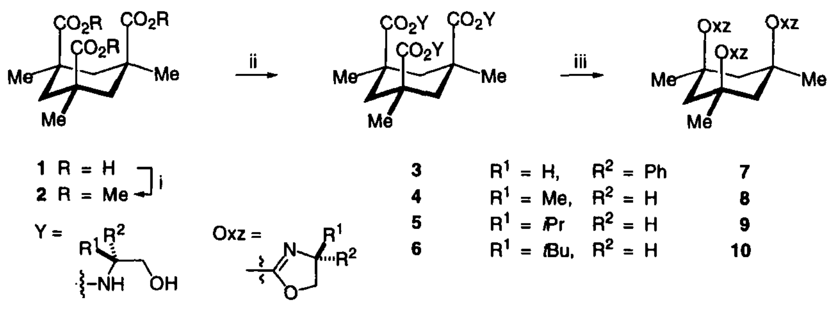
phosphines,[6] tris(pyrazole)s,[7] tris(alkanol)s[8] and tris(amidoamine)s[9] for catalytic asymmetric reactions. Two C_3-symmetric tris(oxazoline)s have been prepared from nitrilotriacetic acid and chiral β-amino alcohols; their use in allylic oxidation of alkenes[10] and in diethylzinc addition to aldehydes[11] have been reported.

Kemp's triacid (*cis,cis*-1,3,5-trimethylcyclohexane-1,3,5-tricarboxylic acid)[12] has a well-defined conformation with all three carboxylic groups on axial positions. Thus, Kemp's triacid (**1**) and its derivatives can be utilized as units for molecular recognition.[13] Use of Kemp's triacid and its derivatives as building scaffold for asymmetric synthesis and combinatorial synthesis has also been explored.[14] For example, a chiral imide oxazoline prepared from Kemp's triacid and (1*R*,2*S*)-2-amino-1,2-diphenylethanol has been successfully employed in enantioselective protonation of enolates.[14d-f] As an endeavour to develop useful chiral C_3-symmetric catalysts, we elaborated Kemp's triacid to the new tris(oxazoline)s **7−10** with rigid backbone of cyclohexane ring. We then examined the effects of **7−10** in two model reactions: the diethylzinc addition to benzaldehyde and the allylic oxidation of cyclopentene.

The commercially available Kemp's triacid (**1**) was treated with diazomethane to give the corresponding triester **2** in a quantitative yield.[12a] Otherwise, a large quantity of triester **2** could be prepared from *cis,cis*-cyclohexane-1,3,5-tricarboxylic acid in a sequence:[12b] (i) esterification



Scheme 1

Synthesis of tris(oxazoline)s **7-10**. Reagents and conditions: i, CH_2N_2; >99%. ii, YH (amino alcohol), NaH, $PhCH_3$, rt, 12 h; **3**, 20%; **4**, 18%; **5**, 54%; **6**, 36%. iii, DAST, CH_2Cl_2, -78 °C, 1 h; or Ph_3P, CCl_4, Et_3N, CH_3CN, rt, 12 h; **7**, 80%; **8**, 50%; **9**, 81%; **10**, 67%.

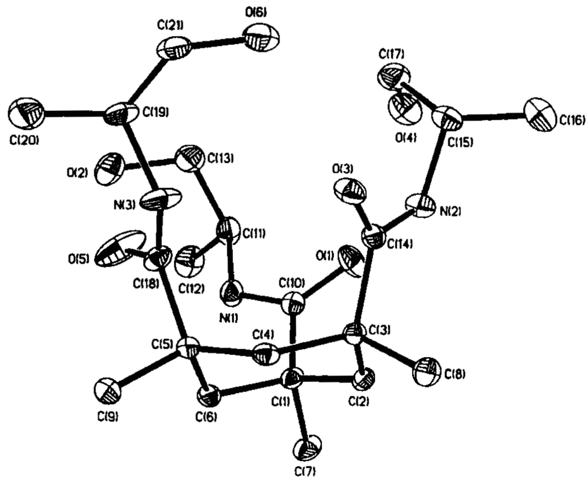


Figure 1. ORTEP plot of the crystal structure of compound **4**.[17]

with MeOH in the presence of $SOCl_2$, (ii) metalation of the resulting triester with LDA in an Et_2O solution, and (iii) subsequent alkylation with Me_2SO_4. A series of optically active β-amino alcohols were then reacted with triester **2** to afford tris(β-hydroxylamide)s **3–6**, which underwent cyclizations on treating with Et_2NSF_3 (DAST)[15] or Ph_3P/CCl_4[16] to give the desired tris(oxazoline)s **7–10**.

An X-ray diffraction of the tris(β-hydroxylamide) **4**[17] showed the pseudo-C_3 symmetric structure, of which three amide groups oriented on the axial positions of the cyclohexane ring with a dihedral angle of 116°, slightly deviated from the ideal 109° for the sp^3 hybridization.

Unlike the less stable tris(oxazoline)s prepared from nitrilotriacetic acid, the tris(oxazoline)s **7–10** prepared from Kemp's triacid are stable compounds. No apparent decomposition occurred when compounds **7–10** were kept in refrigerator for one month.

The C_3-symmetric tris(β-hydroxylamide)s and tris(oxazoline)s were used as catalysts in the addition of diethylzinc to benzaldehyde.[18] The reaction using tris(β-hydroxylamide)s **4** or **5** yielded 1-phenylpropanol with lower ee values than that using tris(oxazoline)s **8**, **9** or **10**

Table 1. Asymmetric addition of diethylzinc to benzaldehyde by the catalysis of tris(β-hydroxylamide)s or tris(oxazoline)s, giving 1-phenylpropanol.[a]

Entry	Ligand	Yield [%]	Ee [%]	Abs. Config.
1	**4**	58	13	*S*
2	**5**	61	18	*R*
3	**8**	75	36	*R*
4	**9**	46	43	*R*
5	**10**	75	33	*S*

[a] Standard conditions: In toluene solution with a molar ratio of PhCHO/ Et_2Zn/ligand = 1 : 2.64 : 0.086 at 25 °C for 16 h. The *ee* values and the configuration of major enantiomer were determined by comparison of optical rotation with the reported value,[19] and by HPLC analyses using a chiral stationary phase.

(Table 1). The (*R*)-enantiomer of 1-phenylpropanol predominated by using compounds **5**, **8** and **9** as catalysts, whereas the (*S*)-enantiomer predominated by using compounds **4** and **10**. The enantiotopic preference appeared to vary with respect to individual ligand, even these ligands all have (*S*) stereogenic centers. The reason for this stereochemical discrepancy is unclear.

The asymmetric allylic oxidation of cyclopentene was carried out (Table 2), based on Kharash reaction[20] process, to give the corresponding 2-cyclopentenyl benzoate. The ee values and the configuration of major enantiomer were determined by comparison of optical rotation with the reported value and by HPLC analyses on a Chiralcel OD column. The effects of reaction temperature, solvent and molecular sieves in the allylic oxidation catalyzed by using the copper complex of phenylglycinol-derived tris(oxazoline) **7** were examined. The reaction was very sluggish at –20 °C in the absence of molecular sieves (entry 1), giving a low yield (22%) of 2-cyclopentenyl benzoate after 10 days. The reaction was significantly accelerated by raising the reaction temperature to 4 °C (entry 2), giving a 92% yield of the desired product in less than 5 days. The reaction rate was further enhanced by the presence of molecular sieves (entry 4). Thus, allylic oxidation of cyclopentene (4 equiv) with *tert*-butyl perbenzoate (1 equiv) by the catalysis of $Cu(OTf)_2$ (0.05 equiv) and tris(oxazoline) **7** (0.1 equiv) proceeded smoothly at 4

Table 2. Allylic oxidation of cyclopentene with *tert*-butyl perbenzoate by the catalysis of $Cu(OTf)_2$ and tris(oxazoline) ligands, giving 2-cyclopentenyl benzoate.[a]

Entry	Ligand	Solvent	Additive	Reaction Temp. [°C]	Reaction Time [h]	Yield [%]	Ee [%]	Abs. Config.
1	**7**	Me_2CO	none	-20	240	22	45	*S*
2	**7**	Me_2CO	none	4	117	92	40	*S*
3	**7**	Me_2CO	MS	-20	92	31	48	*S*
4	**7**	Me_2CO	MS	4	40	94	45	*S*
5	**7**	Me_2CO	MS	20	40	87	44	*S*
6	**7**	MeCN	MS	-20	92	10	49	*S*
7	**7**	PhMe	MS	-20	92	29	42	*S*
8	**8**	Me_2CO	MS	-20	92	29	49	*R*
9	**9**	Me_2CO	MS	-20	252	17	43	*R*
10	**9**	Me_2CO	MS	4	40	51	31	*R*
11	**9**	Me_2CO	MS	20	40	68	21	*R*
12	**10**	Me_2CO	MS	-20	92	12	3	*R*

[a] Standard conditions: Molar ratio of cyclopentene/ $PhCO_3tBu/Cu(OTf)_2$/ligand = 4 : 1 : 0.05 : 0.1. The yield was calculated based on *tert*-butyl perbenzoate used. The *ee* values and the configuration of major enantiomer were determined by comparison of optical rotation with the reported value,[10b] and by HPLC analyses using a chiral stationary phase.

°C in the presence of molecular sieves (4 Å) to give a 94% yield of 2-cyclopentenyl benzoate with predominance of the (*S*)-enantiomer (45% ee). During the reaction course, the color of the solution changed from blue green to light purple, an indication for reduction of Cu(II) into Cu(I) species. Acetone is the solvent of choice for the allylic oxidation, otherwise, yields decreased greatly by using acetonitrile or toluene as the solvents. This solvent effect was comparable to that using tris(oxazoline) ligand[10] but in contrast to that using bis(oxazoline) ligand.[5a,b] Increase of the molar ratio of ligand/$Cu(OTf)_2$ from 2 to 5 did not show any significant effect on either yield or ee of the product.

The allylic oxidation using tris(oxazoline) ligand **9** containing isopropyl substituents showed inferior yields and ee values (entries 9 and 10), by comparison with that using the ligand **7** under similar reaction conditions (entries 3 and 4). The reaction using the ligand of alaninol-derived tris(oxazoline) **8** (entry 8) showed comparable efficiency and enantioselectivity as that using the ligand **7** (entry 3), whereas the reaction using the tris(oxazoline) **10** containing *tert*-butyl substituents gave very poor yield and ee value (entry 12). The allylic oxidation of cyclopentene using **8**, **9** and **10** derived from (*S*)-amino alcohols favored the formation of (*R*)-enantiomer, whereas the reaction using **7** derived from (*R*)-phenylglycinol favored the formation of (*S*)-enantiomer.

The mechanism of Kharash reaction has been discussed.[15, 20] Most authors suggest that the reaction proceeds with a key allyl–Cu(III)–benzoate intermediate, which rearranges subsequently via a chair-like transition state to give the observed product of allyl ester. An alternative intermediate may result from a coordination between the allyl radical and copper species.[5c] By comparison of the current study with previous reports using the tris(oxazoline)s derived from nitrilotriacetic acid,[10, 11] the ligands **7–10** appear to be less effective in asymmetric induction of allylic oxidation or diethylzinc addition. We speculate that the central nitrogen atom in the ligands derived from nitrilotriacetic acid can provide an additional coodination with copper ion for better asymmetric induction. Our future study will focus on use of these C_3-symmetric tris(oxazoline)s **7–10** for other types of reactions, especially those involving metal ions of octahedral geometry.

Experimental

General All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 120 °C and allowed to cool in a desiccator over P_2O_5 before use. Ethers were distilled from sodium benzophenone ketyl; acetone from P_2O_5; (chlorinated) hydrocarbons and amines from CaH_2. Reactions were monitored by TLC using pre-coated with a 0.2 mm layer of silica containing a fluorescent indicator (Merck Art. 5554). Column chromatography was carried out on Kieselgel 60 (40–63 μm). Optical rotations were measured on a digital polarimeter with a cuvette of 1 cm length. $[\alpha]_D$ Values are given in 10^{-1} deg cm^2 g^{-1}. ^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 and AM-300 WB spectrometers. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.26, δ_C (central line of t) 77.0]. Coupling constants (J) are given in Hz. The X-ray diffraction data were collected on a SMART/CCD system using Mo–K_α (0.7107 Å) radiation.[17] The analyses were carried out on ALPHA workstation or PC using NRC VAX and SHELEX software.

General Procedure for the Preparation of Triamides **3–6**:

Under an atmosphere of argon, a solution of (*R*)-D-phenylglycinol (1.64 g, 12 mmol) in toluene (20 ml) was added dropwise to a suspension of NaH (333 mg, 13.2 mmol, 95% dispersion in mineral oil) at 25 °C. After stirring for 2.5 h, a solution of triester **2** (600 mg, 2 mmol) in toluene (10 ml) was added. The mixture was stirred for 12 h, and quenched by addition of water (10 ml). The aqueous phase was separated and extracted with EtOAc (3 x 15 ml). The organic phases were combined, washed with brine (2 x 15 ml), dried (Na_2SO_4), and chromatographed on a silica gel column by elution with EtOAc/hexane (1:1) to give the tris(β-hydroxylamide) **3** (246 mg, 20%).

By a similar procedure, treatment of the triester **2** (600 mg, 2 mmol) with (*S*)-L-alaninol (751 mg, 10 mmol) and NaH (10 mmol) in toluene gave the tris(β-hydroxylamide) **4** (152 mg, 18%). Treatment of the triester **2** (1.2 g, 4 mmol) with (*S*)-L-valinol (2.67 g, 24 mmol) and NaH (26.4 mmol) in toluene gave the tris(β-hydroxylamide) **5** (1.1 g, 54%). Treatment of the triester **2** (600 mg, 2 mmol) with (*S*)-L-*tert*-leucinol (1.2 g, 10 mmol) and NaH (11 mmol) in toluene gave the tris(β-hydroxylamide) **6** (400 mg, 36%).

cis,cis-1,3,5-Trimethylcyclohexane-1,3,5-tris{*N*-[(1*R*)-2-hydroxy-1-phenyl-ethyl]carboxamide} (3).

Solid, mp 66–68 °C – $[\alpha]^{20}_D$ −124.7 (*c* 1.34, $CHCl_3$) – TLC (EtOAc/hexane (1:1)) R_f 0.2 – IR (neat): ν 3350, 2962, 1637, 1545, 1453, 1231, 755, 700 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 1.14 (3 H, d, *J* 15.5), 1.21 (9 H, s), 3.02 (3 H, d, *J* 15.5), 3.82 (6 H, d, *J* 6.0), 4.68 (3 H, br s), 4.96 (3 H, dd, *J* 6.0, 6.0), 7.20–7.33 (15 H, m), 7.94 (3 H, d, *J* 6.9). – ^{13}C (75 MHz, $CDCl_3$): δ 34.3 (3 CH_3), 41.9 (3 CH_2), 43.5 (3 C), 57.1 (3 CH), 65.9 (3 CH_2), 126.4 (6 CH), 127.5 (3 CH), 128.6 (6 CH), 139.1 (3 C), 177.0 (3 C). – MS: *m/z* 597 (M^+ – 18, 1%), 521 (8), 479 (80), 461 (20), 315 (12), 247 (42), 121 (100). – HR MS: $C_{36}H_{43}N_3O_5$ [$M^+ - H_2O$]: calcd. 597.3204; found 597.3198.

cis,cis-1,3,5-Trimethylcyclohexane-1,3,5-tris{*N*-[(1*S*)-2-hydroxy-1-methyl-ethyl]carboxamide} (4).

Solid, mp 164–165 °C – $[\alpha]^{20}_D$ +60.3 (*c* 1.3, $CHCl_3$) – TLC (EtOAc/MeOH (10:1)) R_f 0.2 – IR (CH_2Cl_2): ν 3357, 2937, 1626, 1452, 1204, 1084 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ

1.08 (9 H, d, J 6.7), 1.10 (3 H, d, J 15.7), 1.24 (9 H, s), 2.90 (3 H, d, J 15.7), 3.41–3.60 (6 H, m), 3.88–3.94 (3 H, m), 4.33 (3 H, br s), 7.35 (3 H, d, J 8.0). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.9 (3 CH_3), 34.6 (3 CH_3), 41.9 (3 CH_2), 43.4 (3 C), 48.3 (3 CH), 65.5 (3 CH_2) and 176.3 (3 C); *m/z* 430 (M^+ + 1, 2%), 399 (38), 355 (100), 337 (38), 280 (38), 185 (37), 121 (24). – $C_{21}H_{39}N_3O_6$ (429.56): calcd. C, 58.71; H, 9.15; N, 9.78; found: C, 58.42; H, 9.36; N, 9.69. The structure was confirmed by an X-ray diffraction.[17]

***cis,cis*-1,3,5-Trimethylcyclohexane-1,3,5-tris{*N*-[(1*S*)-2-hydroxy-1-(isopropyl)ethyl]carboxamide} (5).**

Solid, mp 79–81 °C – $[\alpha]^{20}_D$ +23.2 (c = 3.4, $CHCl_3$) – TLC (EtOAc/hexane (2:1)) R_f 0.2 – IR (CH_2Cl_2): ν 3383, 2961, 1636, 1548, 1467, 1071, 737 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 0.88 (9 H, d, J 7.0), 0.92 (9 H, d, J 7.0), 1.12 (3 H, d, J 15.6), 1.30 (9 H, s), 1.88 (3 H, m), 2.95 (3 H, d, J 15.6), 3.54–3.71 (12 H, m), 7.27 (3 H, d, J 9.0). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.9 (3 CH_3), 19.5 (3 CH_3), 29.9 (3 CH_3), 35.2 (3 CH), 42.1 (3 CH_2), 43.8 (3 C), 57.8 (3 CH), 62.4 (3 CH_2), 176.6 (3 C). – MS: *m/z* 513 (M^+, 0.2%), 498 (0.2), 483 (25), 411 (100), 381 (29), 213 (44), 128 (11). HR MS: $C_{26}H_{49}N_3O_5$: calcd. 483.3671; found 483.3672,

***cis,cis*-1,3,5-Trimethylcyclohexane-1,3,5-tris{*N*-[(1*S*)-2-hydroxy-1-(*tert*-butyl)ethyl]carboxamide} (6).**

Solid, mp >190 °C (dec.) – $[\alpha]^{20}_D$ +60.1 (c 2.3, $CHCl_3$) – TLC (EtOAc/hexane (7:3)) R_f 0.2 – IR (KBr): 3386, 2965, 1651, 1540, 1473, 1367, 1058 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 0.93 (27 H, s), 1.14 (3 H, d, J 15.8), 1.33 (9 H, s), 2.99 (3 H, d, J 15.8), 3.62 (3 H, m), 3.70 (6 H, br d, J 5.0), 4.31 (3 H, br s), 7.20 (3 H, d, J 9.4). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.1 (9 CH_3), 34.9 (3 C), 35.4 (3 CH_3), 42.3 (3 CH_2), 43.8 (3 C), 59.7 (3 CH), 61.3 (3 CH_2), 176.8 (3 C). – MS: *m/z* 540 (M^+ – 15, 3%), 525 (17), 439 (100), 426 (34), 409 (31), 339 (10), 322 (21). – $C_{30}H_{57}N_3O_6$ (555.80): calcd. C, 64.83; H, 10.33; N, 7.56; found C, 64.95; H, 10.48; N, 7.26.

General Procedure for the Preparation of Trioxazolines **7–10**:

Method A: Under an atmosphere of argon, diethylaminosulfur trifluoride (DAST, 0.1 ml, 0.76

mmol) was added dropwise to a solution of tris(β-hydroxylamide) **3** (30 mg, 0.048 mmol) in CH_2Cl_2 (2 ml) at −78 °C. The mixture was stirred for 1 h, and quenched by addition of cold aqueous NH_4OH (2 *N*, 2 ml). The mixture was extracted with CH_2Cl_2 (3 x 10 ml). The combined extracts were washed with brine (5 ml), dried (Na_2SO_4), concentrated and chromatographed on a silica gel column by elution with EtOAc/hexane (1:1) to give the tris(oxazoline) **7** (21.5 mg, 80%).

Method B. Under an atmosphere of argon, a mixture of the tris(β-hydroxylamide) **3** (350 mg, 0.56 mmol), Et_3N (2.4 ml), CCl_4 (2.4 ml) and Ph_3P (881 mg, 3.3 mmol) in MeCN (5 ml) was stirred at room temperature (22 °C) for 12 h. After which, EtOAc (20 ml) was added, and the mixture was washed with saturated $NaHCO_3$ (2 x 5 ml) and brine (2 x 5 ml). The organic phase was dried (Na_2SO_4), concentrated and chromatographed on a silica gel column by elution with EtOAc/hexane (1:1) to give the tris(oxazoline) **7** (190 mg, 60%).

According to Method A, the tris(β-hydroxylamide) **5** (50 mg, 0.097 mmol) was treated with DAST to give the tris(oxazoline) **9** (36 mg, 81%). According to Method B, the tris(β-hydroxylamide) **4** (140 mg, 0.32 mmol) was treated with Ph_3P/CCl_4 to give the tris(oxazoline) **8** (60 mg, 50%). Tris(β-hydroxylamide) **5** (240 mg, 0.46 mmol) was treated with Ph_3P/CCl_4 to give the tris(oxazoline) **9** (110 mg, 52%). Tris(β-hydroxylamide) **6** (75 mg, 0.13 mmol) was treated with Ph_3P/CCl_4 to give the tris(oxazoline) **10** (45 mg, 67%).

cis,cis-1,3,5-Trimethyl-1,3,5-tris[(4*R*)-4-phenyl-1,3-oxazolin-2-yl]cyclohexane (7).

Solid, mp 43–45 °C – $[\alpha]^{20}_D$ +16.0 (*c* 1.0, $CHCl_3$) – TLC (EtOAc/hexane (3:7)) R_f 0.2 – IR (KBr): 2965, 2896, 1656, 1452, 1181, 1078, 988, 699 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 1.45 (9 H, s), 1.58 (3 H, d, *J* 14.7), 2.94 (3 H, d, *J* 14.7), 3.95 (3 H, dd, *J* 8.4, 8.4), 4.48 (3 H, dd, *J* 8.4, 8.4), 5.02 (3 H, dd, *J* 8.4, 8.4), 7.18–7.25 (15 H, m). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 30.3 (3 CH_3), 36.2 (3 C), 41.0 (3 CH_2), 69.6 (3 CH), 74.6 (3 CH_2), 126.6 (6 CH), 127.2 (3 CH), 128.5 (6 CH), 142.9 (3 C), 174.3 (3 C). – MS: *m/z* 561 (M^+, 12%), 546 (4), 531 (4), 506 (40), 443 (20), 333 (48), 265 (100), 229 (46). – HR MS: $C_{36}H_{39}N_3O_3$: calcd. 561.2992; found 561.2999.

cis,cis-1,3,5-Trimethyl-1,3,5-tris[(4_S_)-4-methyl-1,3-oxazolin-2-yl]cyclohexane (8).

Solid, mp 61–63 °C – $[\alpha]^{20}_D$ –64.0 (*c* 1.7, $CHCl_3$) – TLC (EtOAc/MeOH (4:1)) R_f 0.2 – IR ($CHCl_3$): 2967, 1656, 1451, 1375, 1188, 1065, 983 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 1.20 (9 H, d, *J* 6.7), 1.35 (9 H, s), 1.50 (3 H, d, *J* 14.8), 2.65 (3 H, d, *J* 14.8), 3.70 (3 H, dd, *J* 7.7, 7.7), 4.06 (3 H, m), 4.28 (3 H, dd, *J* 9.3, 7.7). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4 (3 CH_3), 29.6 (3 CH_3), 36.0 (3 C), 40.5 (3 CH_2), 61.4 (3 CH), 73.8 (3 CH_2), 173.1 (3 C). – MS: *m/z* 375 (M^+, 4%), 360 (27), 320 (30), 250 (20), 209 (63), 167 (12), 141 (100). – HR MS: $C_{21}H_{33}N_3O_3$: calcd. 375.2524; found 375.2521.

cis,cis-1,3,5-Trimethyl-1,3,5-tris[(4_S_)-4-isopropyl-1,3-oxazolin-2-yl]cyclohexane (9).

Oil – $[\alpha]^{20}_D$ –49.8 (*c* 2.5, $CHCl_3$) – TLC (EtOAc/hexane (1:2)) R_f 0.2 – IR (CH_2Cl_2): 3284, 2959, 1658, 1466, 1370, 1192, 1081 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 0.83 (9 H, d, *J* 6.8), 0.93 (9 H, d, *J* 6.8), 1.35 (9 H, s), 1.54 (3 H, d, *J* 14.5), 1.75 (3 H, m), 2.62 (3 H, d, *J* 14.5), 3.80 (3 H, m), 3.89 (3 H, dd, *J* 9.6, 7.4), 4.14 (3 H, dd, *J* 9.6, 8.2). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.2 (3 CH_3), 19.5 (3 CH_3), 30.0 (3 CH_3), 32.9 (3 CH), 36.6 (3 CH_2), 40.9 (3 C), 70.2 (3 CH_2), 72.3 (3 CH), 173.9 (3 C). – MS: *m/z* 459 (M^+, 1%), 416 (0.2), 375 (50), 347 (21), 265 (24), 195 (29), 154 (38). – $C_{24}H_{38}N_3O_3$: calcd. 416.2907; found 416.2913.

cis,cis-1,3,5-Trimethyl-1,3,5-tris[(4_S_)-4-(1,1-dimethylethyl)-1,3-oxazolin-2-yl]cyclohexane (10).

Solid, mp 57–59 °C – $[\alpha]^{20}_D$ –59.2 (*c* 0.9, $CHCl_3$) – TLC (EtOAc/hexane (3:7)) R_f 0.2 – IR ($CHCl_3$): 2955, 1664, 1478, 1363, 1186, 1083, 982 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ 0.86 (27 H, s), 1.37 (9 H, s), 1.58 (3 H, d, *J* 14.4), 2.62 (3 H, d, *J* 14.4), 3.73 (3 H, dd, *J* 10.0, 7.4), 3.99 (3 H, dd, *J* 8.7, 7.4), 4.11 (3 H, dd, *J* 10.0, 8.7). – ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.8 (9 CH_3), 29.2 (3 CH_3), 33.8 (3 C), 36.1 (3 CH_2), 40.3 (3 C), 68.3 (3 CH_2), 75.4 (3 CH), 173.1 (3 C). – MS: *m/z* 501 (M^+, 0.5%), 486 (5), 444 (100), 334 (10), 244 (13), 168 (12), 91 (21). – HR MS: $C_{30}H_{51}N_3O_3$: calcd. 501.3932; found: 501.3930.

Typical Procedure for Diethylzinc Addition to Benzaldehyde (Table 1)

A solution of tris(oxazoline) ligand (0.043 mmol) in toluene (1 ml) was added dropwise to Et_2Zn (1.32 mmol, 1.2 ml of 1.1 *M* toluene solution) at room temperature (25 °C) under an atmosphere of argon. The mixture was stirred for 0.5 h, benzaldehyde (0.05 ml, 0.5 mmol) was added. After 16 h, the reaction was quenched by addition of 1*N* hydrochloric acid. The mixture was extracted with EtOAc (10 ml). The organic phase was washed with water (2 x 10 ml) and brine (2 x 10 ml), dried (Na_2SO_4), concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexan (1:9) to give 1-phenylpropanol. The ee values and the configuration of major enantiomer were determined by comparison of optical rotation with the reported value, $[\alpha]^{25}_D$ +46.0 (c = 5.2, $CHCl_3$, *R*-enantiomer),[19] and by HPLC analyses on a Chiralcel OD column (0.46 cm i.d. × 25 cm) with elution of *i*PrOH/hexane (2.5:97.5, 1 ml/min flow rate); t_R 10.2 min (*R*-enantiomer), t_R 11.8 min (*S*-enantiomer).

Typical Procedure for Allylic Oxidation of Cyclopentene (Table 2)

A 10 ml flask was charged with pre-dried $Cu(OTf)_2$ (4 mg, 0.011 mmol). To the flask was added a solution of the tris(oxazoline) ligand **7** (13 mg, 0.022 mmol) in acetone (0.3 ml) under an atmosphere of argon. The solution was stirred at 20 °C for 1 h. The resulting solution was transferred to another flask containing acetone (0.35 ml) and powdered 4 Å molecular sieves (100 mg) and cyclopentene (60 mg, 0.88 mmol). After being stirred for 30 min, *t*-butyl perbenzoate (42 mg, 0.22 mmol) was added dropwise at indicated temperature. After being stirred for indicated time, the mixture was filterred through a short silica-gel column by using EtOAc/hexane (1:10). The filtrate was concentrated *in vacuo* to give crude product. Purification by silica-gel chromatography using EtOAc/hexane (1:99) as eluent gave 2-cyclopentenyl benzoate. The ee values and the configuration of major enantiomer were determined by comparison of optical rotation with the reported value, $[\alpha]^{17}_D$ −179 (c = 0.37, $CHCl_3$, 93% ee in favor of *S*-enantiomer),[10b] and by HPLC analyses on a Chiralcel OD column (0.46 cm i.d. × 25 cm) with elution of heptane (0.5 ml/min flow rate); t_R 33.4 min (*R*-enantiomer), t_R 27.3 min (*S*-enantiomer).

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